
BRAIN THEORY

SPATIO-TEMPORAL ASPECTS
OF BRAIN FUNCTION
A. AERTSEN / EDITOR



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Integration, Synchronicity and Periodicity

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Introduction

The basic properties of nerve cells and connections between nerve cells are such that very precise timing of firing or delays does not seem to be a principal objective. In spite of this, men and animals can perform with amazing time accuracy. A person listening to a sound delivered to both ears can detect when the sound in one ear is delayed by as little as 10 μ s relative to the other [Moore, 1982]. When throwing a small rock at a 20cm target from distances of more than 7m, the launch window (accuracy of release time) is less than 1 ms [Calvin, 1983]. Some of the mechanisms for achieving such high time accuracy are well understood, while others are still enigmatic.

This contribution deals with ways by which a neuron, acting as a leaky integrator in a noisy environment can achieve a high degree of time accuracy. It reviews the general concepts of timing, synchrony, and oscillations in the mammalian brain with a special emphasis on cortical networks. Special concern is given to theoretical considerations and experimental evidence associated with synchronized activity in cell assemblies, consisting of sets of neurons connected with multiple diverging and converging links.

1. TIMING BY EXTERNAL EVENTS

Assessing of brain responses is usually done by measuring the neural response around an external event. This may be a stimulus, in which case one speaks of *evoked activity*, or it may be a motor action, in which case one speaks of *event related activity*. Typically one measures a number of realizations of the same process and then averages the resulting activity. When the brain activity is evaluated by measuring a potential (from the scalp or from within the tissue) an average response is computed, when activity of a single unit is measured the average firing rate is computed by constructing a histogram (PETH - Peri Event Time Histogram [Gerstein and Kiang, 1960]).

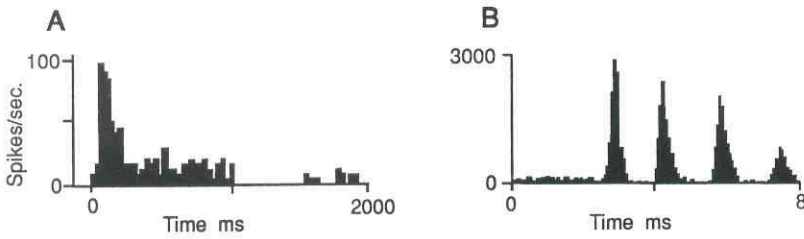


Figure 1. Comparison of response timing in the Visual and Auditory systems. A. The response of an Y-type ganglion cell in the retina of the cat. A grating at the optimal position, was flashed on, at time 0. Adapted from Hochstein and Shapley 1976, with permission. B. Response of an Auditory nerve fiber in the cat to a 0.1 ms click. Note that since the first spike time is concentrated within less than 1 ms, its peak instantaneous firing rate is higher than 1000/s. Adapted from Kiang et al. 1962 with permission. Note the drastically different time scales.

Different sensory systems may show very different types of responses. In the visual system, for example, the processes at the transduction level are quite sluggish and therefore the neural responses develop slowly and after a considerable delay. In the auditory system the peripheral delay is very brief and the spike timing is very accurate. Compare the response of a visual neuron shown in Fig. 1A to the response of an auditory nerve fiber shown in Fig. 1B.

Timing of activity plays a major role in localizing sound sources in the auditory space. Sound from a source placed directly in the front of the face at a distance of 1m arrives simultaneously at both ears. A movement of 1 deg. to the right will result in the sound to the right ear leading the sound to the left ear by 12 μ s. However, comparison between the two ears is not based directly on the activity in the acoustic nerve axons. It happens only at a later processing stage (to which the activity arrives after being relayed through at least one synapse). Accurate comparison needs accurate transmission times and these are assured by an appropriate anatomy.

Fig. 2 illustrates a drawing of the synaptic connection between an axon delivering information from the cochlear nucleus onto the cell body of a neuron in the trapezoid nucleus. The axon thickens as it reaches its target, branches and embraces the cell body. A thin section through this region shows the axon forming a "cup" around the cell body. This structure is named after its discoverer the "calyx of Held". A small piece of such a section may look like Fig. 2C. The synaptic contacts formed by the incoming axon (marked S1) have round synaptic vesicles and a-symmetric membrane thickening. Such a-symmetric synapses are generally excitatory. (In contrast to the symmetric thickening and the pleomorphic vesicle of the synapses marked S2 which are usually inhibitory.) The

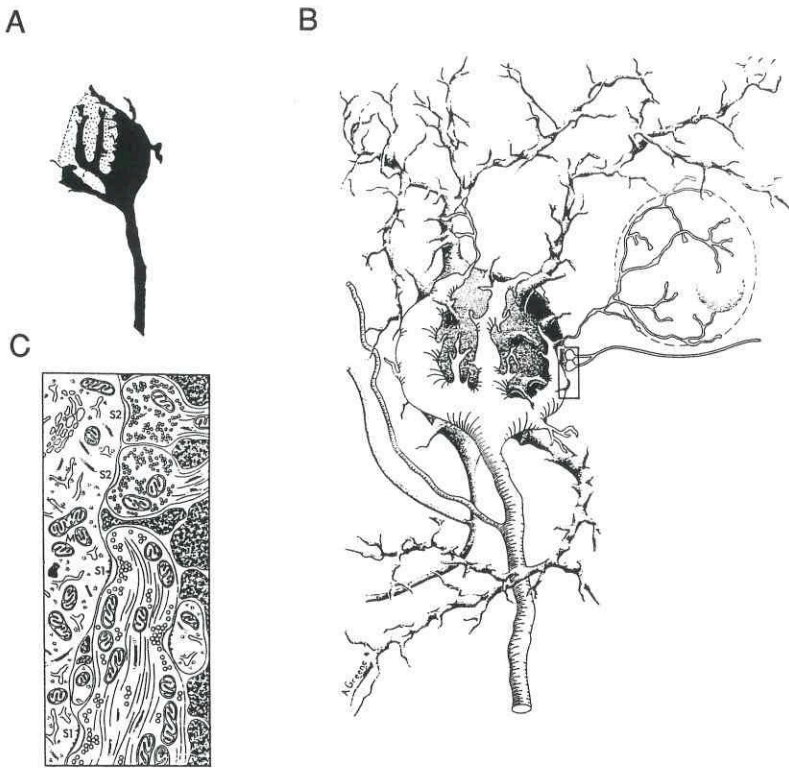


Figure 2. A synapse between an axon from the interstitial cochlear nucleus and a principal cell in the medial nucleus of the trapezoid body. A. Golgi staining of the axon and its calyx. B. An Interpretative drawing of the calyx and the principal cell. C. Drawing of an electron microscope image of a tip of the calyctic synapse and two other (S2) synapses. Adapted from Morest 1968, and Morest et al. 1973 with permission.

calyx contains hundreds of synaptic sites which ensure very reliable transmission. Note that before the information coming from the two ears has any chance to interact in the superior olivary complex it must be transferred through one or two such synapses. The arrival timing of the impulses to the superior olive is critical for producing the acute sensitivity to interaural delays. The demand for precise transmission timing in the auditory system is fixed throughout life and persisted throughout the development of the vertebrate animals. Nature provided the auditory nervous system with the a device that assures reliable and time-wise accurate transmission of impulses from the ear to the superior olive.

In the general case, if activity has to pass through N synaptic stations each producing a delay of D with a variance of σ^2 the total delay will be:

$$N \cdot D \pm \sigma \sqrt{N}$$

Typical synaptic delays (D) contain the conduction time along the axon, the synaptic delay (0.5-1. ms), and the delay from the start of the EPSP until the spike itself is generated (1.-3. ms). Among these events, conduction times along axons and synaptic release have very small jitter in the range of few tens of μ s [Lass and Abeles, 1975; Cope and Mendell, 1982]. Thus most of the variability is expected to come from the delay between the beginning of the EPSP and the generation of a spike. This delay can be understood by considering the following situation: The EPSP rides on the "resting" potential of the post-synaptic cell. It shows gradual buildup lasting a few ms. Due to the random fluctuations of the "resting" membrane potential it may hit threshold at various time delays after its initiation. If the rise time of the EPSP is very short, and the amplitude is very big, as is the case for the calices of Held, then the synaptic delay jitter will be very small. However for smaller and slower EPSP's, as prevails in the cortex, this jitter is appreciable. [See Abeles, 1991 pp241-249, for a more detailed analysis of jitter in transmission timing.]

While nature found simple ways to overcome the unreliable character of synaptic transmission when there is a fixed demand for secure transmission, it had to resort to more intricate tricks when secure transmission had to be dynamically turned on and off in the noisy environment of the cerebral cortex. The next two chapters deal with possible mechanisms of generating accurate internal timing.

2. TIMING BETWEEN SUCCESSIVE SPIKES

In this section the mechanisms which determine interspike intervals are discussed. Two mechanisms which determine the spike firing times are usually described: The *pace-maker* mechanism and the *integrate and fire* mechanism [see, for instance, MacGregor, R.J., Lewis, E.R., 1977; and many references therein]. In the pace-maker, internal ionic processes generate periodic oscillations of membrane potentials, while in the integrate and fire neuron all synaptic currents add up and are integrated by the leaky membrane capacitor. When the membrane potential which is generated by these processes hits the threshold, the neuron fires and the membrane potential is reset to some initial value.

2.1. Pace Makers

The usual mechanism of action-potential generation is meta-stable. It contains one or more positive feed-back mechanisms and several negative feed-back mechanisms. Its behavior depends on the various gains and time constants of these mechanisms. As most of the processes are non linear, it is very easy to switch from the stable, resting behavior, to an unstable, periodic behavior and back.

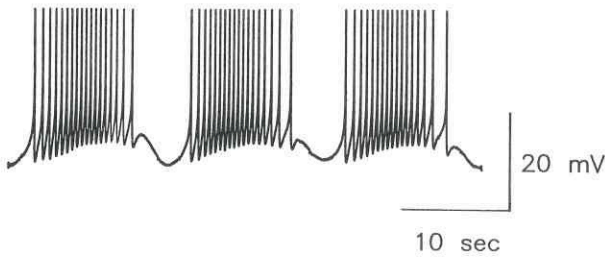


Figure 3. Pace-maker activity recorded from an unidentified neuron in the abdominal ganglion of *Aplysia californica*. The top of the action-potentials are clipped. Courtesy of Ruth Oren.

During the action potential the sodium conductivity is very high and the membrane potential rises very fast towards the sodium equilibrium potential. However, after a very short delay (much less than 1 ms in most mammalian neurons) the sodium conductivity starts to fall back and the potassium conductivity rises, which pulls the membrane potential back towards its resting value. This repolarizing stage of the action potential is also fast (approximately 1 ms). Its speed is assured by the high levels of potassium conductivity which then recovers slowly towards its resting level. The time course of this potassium conductivity causes the membrane potential to hyperpolarize (become more negative as compared to the resting level) immediately after the action potential and then slowly depolarize towards a steady state level. If the firing threshold of the neuron is below this steady state level, the neuron will fire again and, hence, would never reach a stable resting membrane potential. In addition, activation of calcium conductance by depolarization and delayed potassium conductances can cause oscillations of membrane potentials in many neurons. These are the classical *pacemaker* mechanisms. Fig. 3 shows periodic pacemaker activity in which several such mechanisms produce periodic bursts of action potentials.

2.2. The Motor Neuron of the Spinal Cord.

The motor neuron of the spinal cord is the classical example of an *integrate and fire* neuron. Its properties were described by the pioneering work of Eccles [1957] and served ever since as the model for the mammalian neuron. In the living animal this neuron is usually firing periodically, albeit with variable firing rates.

Periodic firing can be demonstrated in most neurons. Typically they behave like pace makers when depolarized by a constant current. The motor neuron, with its huge dendritic tree collects the input currents generated by about 100,000 synaptic boutons which together generate an approximately constant current. Fig. 4 shows the membrane potential of a motor neuron in the spinal cord of the cat when firing at ten spikes per second. The figure shows a superposition of 5 traces, each composed of two successive spikes with the hyperpolarizing wave that follows them. The actual spikes are clipped, being approximately 100 mV above

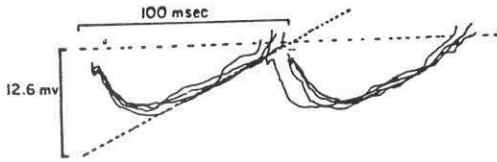


Figure 4. Repetitive firing of a motor neuron in the spinal cord of the cat. Further explanations in text. From Calvin and Stevens 1968, with permission.

threshold. We see in Fig. 4 that after each spike the motor neuron is deeply hyperpolarized, then it recovers gradually. On top of the internal processes leading to recovery, the incoming EPSP's add a (noisy) depolarization; both processes build up until the membrane potential hits threshold again. The whole procedure then starts again, whereby an almost periodic firing is generated. The remaining jitter in the inter-spike intervals is, according to Calvin and Stevens [1968], mainly due to the synaptic noise.

2.3. The Cortical Neuron.

Whereas the motor neuron shows periodic firing in its every day performance, this type of behavior is seen only seldom in cortical neurons. Most of them become periodic only at high firing rates. A major cause for this difference is probably the absence of a deep after hyper-polarization in the cortical neurons. This can be seen in the intracellular records shown in Fig. 5, taken from the work of Douglas et al. [1991] on the visual cortex of the cat.

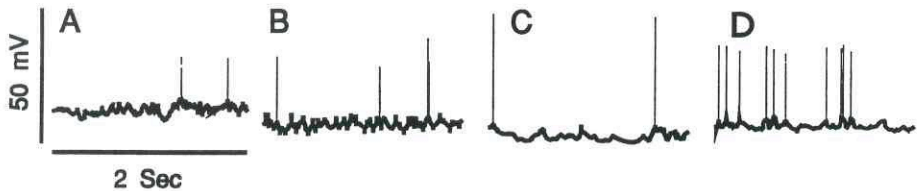


Figure 5. Membrane potentials and spikes in 4 neurons from the visual cortex of the anesthetized cat in the absence of visual stimuli. A. Unknown neuron in layers 2-3, B. Spiny stellate cell in layer 4, C. Pyramidal cell in layer 5, D. Pyramidal cell in layer 6. Adapted from Douglas et al. 1991, with permission.

Not all cortical neurons behave in that way, some do show deep and prolonged

hyperpolarization after each spike. Such neurons would reach periodic firing pattern at lower rates. The changes in excitability which follow each spike may be studied by means of the *auto-correlation* function. This function shows how the firing rate of a single neuron varies after it has just fired (this is equivalent to the *renewal density* function of renewal point processes [Cox, 1962]). Fig. 6 illustrates several examples of such auto-correlation functions in cortical neurons.

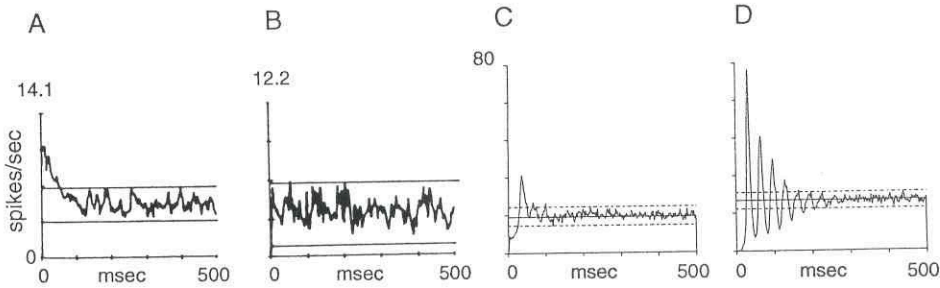


Figure 6. Auto-correlation functions of 3 neurons in the cortex of unanesthetized animals. A. and B. Two neurons from the auditory cortex of the cat, C. and D. from one neuron in somatosensory area II of the monkey. C and D by courtesy of E. Ahissar.

Fig. 6A shows the most common shape of cortical auto-correlation functions - after a very brief (1-5 ms) period of refractoriness the cell is hyper-excitable and then returns to its resting firing level. Fig. 6B shows the next common shape in which after the initial refractoriness the cell returns to its basal Poisson-like firing level. Fig. 6C shows the least frequent type of auto-correlation in which prolonged refractoriness is exhibited. This refractoriness is probably brought about by prolonged hyperpolarization following each spike, similar to what is known for the motor neurons of the spinal cord. While recording the activity of the neuron depicted in Fig. 6C it elevated its firing rate spontaneously (i.e. without any deliberate external stimulus) and started to fire periodically. A more detailed discussion of these neuronal properties can be found in Abeles [1991, pp 118-139].

While most neurons in the cortex of the awake animal do not fire periodically, they do show periodicity when placed in a dish. This is demonstrated in Fig. 7 taken from the work of [McCormick et al., 1985]. They categorized 3 main types of cortical cells: The regular spiking (Fig. 7A), the fast spiking (Fig. 7B), and the bursting (Fig. 7C). Regular spiking neurons are usually small pyramidal cells, while fast spiking neurons are probably smooth stellate cells, finally, the bursting neurons, which comprises only 5% of the population, are probably the huge pyramidal cells of layer V. Note that the three types of cells initially respond to a steady depolarizing current in a variety of ways, after which they settle down to fire periodically as if they were pace makers.

Why then does one not observe this periodic firing in cortical neurons in vivo?

The reason is not clear. There are proposals of special intracellular mechanisms which prevent periodic firing [e.g. Softky and Koch, 1993], however it is probably not necessary to invent any new mechanisms to explain this property. If the membrane potential is driven by strong noisy synaptic processes, then the cell would fire only when the random membrane fluctuations happen to hit threshold. Elevated firing rates would mean increased probability of hitting threshold either by reduction of the distance between the average membrane potential and the threshold or by increasing the variance of the membrane fluctuations. This situation holds as long as the membrane potential looks like a noisy wave around a steady mean level. That is, as long as the after hyperpolarization is short relative to the mean interspike intervals (which doesn't seem implausible in view of both the small hyperpolarization in cortical neurons and their typically low firing rates), the spike events will tend to occur stochastically, rather than in a periodic fashion.

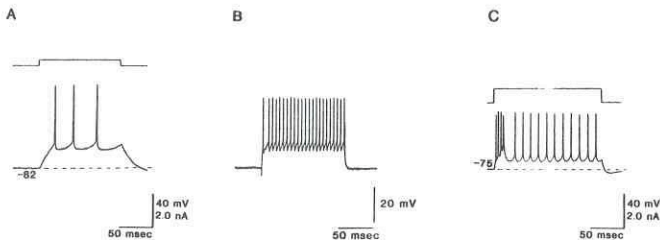


Figure 7. Three major cell types found in cortical slices. All figures show intracellular responses (lower trace) to constant current stimulation (upper trace). Adapted from McCormick et al. 1985, with permission.

For any rule that one makes about cortical properties there are many notable exceptions. In somatosensory area II of the behaving monkey, for instance, approximately 30% of the cells behave like the motor neurons [Ahissar et al., 1990]. However the same group of researchers, using the same recording techniques, in the same animals (behaving monkeys) did not find this kind of oscillations in auditory cortex, pre-motor cortex, pre-frontal cortex, or posterior-parietal cortex. There are several more reports on periodic oscillations of cortical neurons that are probably due to network behavior (and not internal properties of single neurons) which will be discussed below.

In summary, almost any neuron would show periodic (pace maker like) firing when appropriately hyper/de-polarized. This is true also for most cortical neurons. However in their natural cortical setting this property is usually not expressed, so that by themselves they would reach periodicity only at high firing rates.

2.4. Oscillations in Networks

Periodic oscillations of cortical activity are known since Berger [1929] recorded

the *alpha* EEG waves (8-12 Hz) from the scalp. Attention was brought to the relevance of *gamma* (30-70 Hz) waves to processing of information in the brain several times in the past [e.g. Sheer, 1989]. These higher frequency oscillations were brought to focus recently when two groups [Eckhorn et al., 1988; Gray and Singer, 1989] independently found that the local field potential (LFP) recorded by a metal micro-electrode in the visual cortex of anesthetized cats shows strong oscillations in the γ range when the appropriate stimulus is shown. Further support of the physiological relevance of these oscillations was provided by the observation that such oscillations in two regions may become phase locked when stimuli pass through the receptive fields of both regions in a coherent manner, much like the movement of a real object in visual space would bring about [see also Engel et al., 1992 for a review of these experiments]. Similar oscillations were recently observed in the motor cortex of behaving monkeys [Murthy and Fetz, 1992].

These oscillations are certainly not a result of the intrinsic properties of individual neurons but, instead, depend on the neural network of the brain. Indeed, it has been demonstrated that neural network may easily achieve stable oscillations. For instance, Sompolinsky et al. [1988] have shown that even in a random network of very simple neurons one can observe persistent oscillations. In their network the synaptic effects last only one ms, at each step the neuron adds all its inputs and then fires (or not) according to a sigmoid threshold curve $\tanh(gv)$ where v is the difference between the membrane potential and the threshold, and g is an arbitrary constant. They were able to show analytically that the network's behavior depends on the variability of the synaptic strengths. When the variance of the synaptic strength (σ^2) was small such that $g\sigma < 1$, the network exposed bistable behavior - either all the neurons are almost quiet, or all of them fire at a high rate. When there is a great dispersion of the synaptic values, that is $g\sigma \gg 1$, the network exhibits chaotic behavior. For intermediate values, that is $1 < g\sigma < 2$, the network oscillates starting with simple harmonic oscillations when $g\sigma$ is slightly above 1, and with more and more complex oscillations as $g\sigma$ grows. Moreover, in another study along similar lines [Erb and Aertsen, (1992)], it was observed that, again depending on the connectivity statistics, the initially coherent network activity may break up into separate subgroups of neurons ("assemblies"), with the firing of the various neurons exhibiting different and more or less independent correlation dynamics, characterized by the different time constants involved.

Thus, even a random network of very simple neurons with no intrinsic oscillatory tendency whatsoever can exhibit stable periodic oscillations. When the behavior of a network made of neurons that do exhibit a tendency to fire periodically (as was described in section 2.2) is analyzed, even richer behavior can be shown. Hanzel and Sompolinsky [1992] studied the behavior of a network of coupled oscillatory neurons, they were able to show analytically four regimes. When the coupling among the neurons is weak each of them oscillates at its internal frequency. As the coupling strength increases, the whole network starts to oscillate at the same frequency in a phase locked manner. With further increase of coupling strength the behavior becomes chaotic, however the different

neurons are not uncorrelated, as exhibited by the fact that the average activity of the net shows chaotic oscillations which do not vanish as the number of neurons becomes very large. When the coupling strength becomes even bigger, each neuron still shows chaotic behavior, but the neurons become uncorrelated.

Hence, the local cortical network has all the ingredients required for exhibiting such complex cooperative behaviors, however usually it doesn't. When a piece of cortical tissue (of approximately 1 by 1 cm) is isolated from all other brain structures, the activity within the piece stops altogether [Burns, 1958; Burns and Webb, 1979]. The same holds true for a cortical slice in a physiological salts solution. Thus the cortical activity depends on incoming excitation derived from other (cortical as well as subcortical) brain regions. The source of 8-12 Hz α activity is generally attributed to the thalamus, although the amplitude of the thalamic α activity is greatly reduced after cutting the cortico-thalamic connections [Morison and Dempsey, 1943]. The source (thalamic or cortical) of the 30-70 Hz γ activity is still the subject of debate.

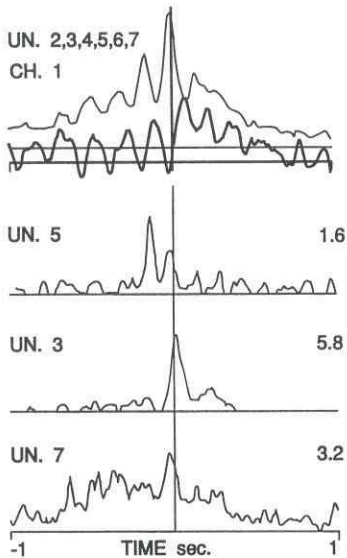


Figure 8. Cross-correlations and Local Field Potentials (LFP) in the cat. Lower trace, the cross-correlation between unit 7 and unit 1. Next trace the cross-correlation between unit 3 and unit 1. Next trace, the cross-correlation between unit 5 and unit 1. Top trace, cross-correlation between the superposed activity of units 2,3,4,5,6,7 and unit 1, and the spike triggered average of the LFP around the firing times of unit 1 (heavy trace). Adapted from Arieli 1992, with permission.

Whatever the source of the oscillatory EEG waves, they certainly affect the

firing times of the cortical neurons. During periods of drowsiness or shallow sleep when the EEG exhibits spindles (wave-packets) of α activity, the cortical neurons tend to synchronize their activity with the negative peak of the α wave. This can be seen in Fig. 8, taken from the work of Arieli [1992], in which both LFP and single unit activity were measured through several microelectrodes inserted into the supra-sylvian cortex of an unanesthetized cat. The three lower traces show crosscorrelations between unit 1 and 3 other units. The thick trace at the top shows the averaged LFP which was recorded from electrode no. 1 and averaged around the firing times of unit no. 1, recorded through the same electrode. The amplitude of the averaged LFP was of the same order of magnitude as the ongoing (non averaged) α waves in the LFP, suggesting that a considerable fraction of the spikes of unit no. 1 occur around the negative peak of that wave. The top trace in Fig. 8 shows the cross-correlation between the spike trains of unit no. 1 and a composite spike train generated by the superposition of the spike trains of six other single units recorded within 0.6 mm from unit no. 1. Clearly, unit no. 1 is firing in a coherent way with the LFP, and so do the other units.

A rough estimate of the time window in which cortical cells fire during α activity and, hence, a measure of the quality of phase locking of individual spikes to the ongoing field potential, is a quarter of a cycle, i.e. approximately 25 ms during 10 Hz oscillation. If a similar coherence exists also for the γ oscillations, then a timing accuracy of 5 ms can be expected. However, in some cases one observes much more tightly coupled firing times. These instances will be the subject of section 3.

3. TIMING of ISOLATED SPIKES

The picture drawn in the last section is of a cortical neuron with fluctuating membrane potential around a steady level which is well below the threshold. From time to time the fluctuations reach threshold and the neuron fires. This situation is idealized in Fig. 9, [Abeles, 1982a] which shows a waveform generated by post synaptic potentials arriving at random (Poissonian) times at a rate of

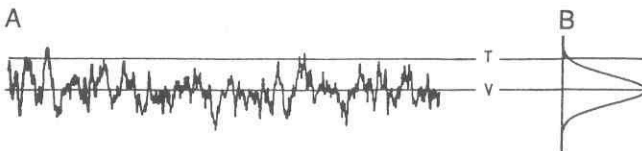


Figure 9. The concept of the noisy membrane potential and a fixed threshold. A. Noisy potential, which was generated by adding positive and negative "post synaptic potentials" arriving at random (Poissonian) times at a rate of 100,000/s. B. The probability of the potential to be above threshold (T) is equal to the area under the curve above T.

100,000 per s. The probability density function (PDF) of the membrane potential amplitude is drawn at a right angle on the right of Fig. 9. If the threshold is represented by the line marked T , then the area of the PDF curve above T is the probability to observe a membrane potential above threshold. For low values, the firing rate is approximately proportional to this probability. According to this approach, the exact time of appearance of an action potential is random, and the spike train generated by a neuron may be roughly treated as a non-homogenous Poisson process, i.e. with a variable firing rate which can be estimated from peri-event-time-histograms, as illustrated in Fig. 1.

3.1. Delayed Synchronization.

There are many reports in the literature describing neurons that fire with very precise timing. Among the first to report such accurate timing were Toyama et al. [1981], who recorded the activity of two neurons within a vertical column in the visual cortex of the anesthetized cat. They reported many cases in which both cells fired with exact (less than 1 ms) synchrony, both spontaneously and while a visual stimulus was presented to the cat. Allum et al. [1982] reported such tight synchronization in the motor cortex of behaving monkeys. Very recently, Nelson et al. [1992] reported tight synchronization between neurons in area 17 and area 18 of the cat. DeRibaupierre and Abeles observed occasionally tight synchronization between two neurons in the primary auditory cortex of the cat [unpublished observations]. Tight synchronization does not seem to be consistent with the random firing model presented above. In some cases (like two neurons within a column of V1) it may be explained by assuming an extremely strong common drive from the thalamus. But even there it is not likely to be a satisfactory explanation since, in order to explain cases where up to 50% of the spikes of the two neurons are synchronized [as in Toyama et al. 1981, Fig. 1D], one would need to assume that the effects of a single thalamic axon on the cortical neuron are strong enough to evoke a post-synaptic firing with a probability of 0.7.

While such tight synchronization between neurons could, at least in principle, be explained along these lines, another type of tight synchronization is much harder to explain: tight timing after a long delay as in Fig. 10.

Fig. 10 shows several cross-correlograms among pairs of cortical neurons in the frontal cortex of behaving monkeys. In all the illustrated cases the firing rates of the neurons are low, so that when a narrow bin (1-2 ms) is used for constructing the correlogram, only few counts per bin are expected. However, in all these cases there is a single bin in which a much higher count is found. Fig. 10A illustrates a case in which the expected count per bin was <0.5 while near 372 ms there was a bin with 7 counts (the probability of obtaining such an event by chance is one in a million). Fig 10B shows the same data in an expanded scale. It reveals that all 7 counts happened within 2 ms. Frostig et al. [1985] reported such events in the forebrain of unanesthetized cats, while Landolt et al. [1985] reported such events in the visual cortex of the cat.

How does one account for such phenomena? In the cortical milieu it is extremely difficult to do so. Long delays must involve transmission through many synapses in tandem. In the cortex there are no synapses of the Calyx of Held type (Fig. 2),

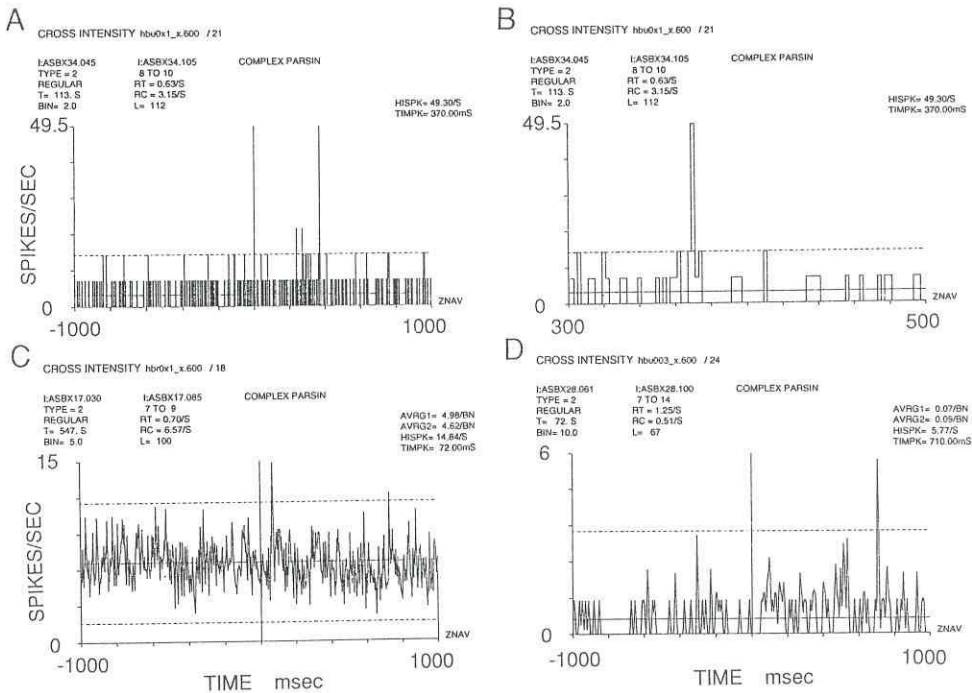


Figure 10. Delayed peaks in cross-correlations between units in frontal cortex of the behaving monkey. A. C. and D. for 3 pairs of units in a compressed time scale, B. same as A. in an expanded time scale.

in fact all the synapses on the somata of the cortical pyramidal cells are inhibitory [Peters and Kara, 1985]. Excitatory synapses are limited to the dendrites and they are all weak [Abeles 1991 chp. 3]. The model of variable Poissonian firing rates cannot support such tight synchronization, since in this model the time constants of the cross-correlogram cannot be shorter than those of the auto-correlograms of the single neurons [Sompolinsky private communication], and one does not observe 1-3 ms wide peaks in the auto-correlograms.

A phenomenon which seems to contradict the known physiology of the cerebral cortex neurons should have attracted a lot of attention. Yet, reports on this type of tight synchronization after a long delay are quite rare. Why is that so? There are probably two main reasons for that dearth. First, when we observe a phenomenon for which we have no explanation, we often discard it as "strange", particularly if it is a rare phenomenon. Second, cross-correlograms of this type are indeed rare. The 7 occurrences of unit no. 10 following unit no. 8 after exactly 372 ms described in Fig. 10B happened during 113 seconds of recording. Had units 8 and 10 had higher firing rates the excess of 7 coincidences might have passed

unnoticed. Alternatively, had we used larger bins for the cross-correlograms, the tight synchronization would be smeared out.

So much for pairwise cross-correlations. When research was aimed at events which are more complex than pairwise coupling, many such instances were invariably found [Klemm and Sherry 1981; Abeles 1982b, chp. 6; Abeles et al. 1983; Dayhoff and Gerstein 1983; Legendy and Salcman 1985; Abeles and Gerstein 1988; Villa and Abeles 1990; Bartanyan and Pyrogov 1991; Villa and Fuster 1992; Abeles et al. 1993].

Given the variety of laboratories, preparations and methods of analysis used, all of which yielded excess of compound time locking among several spikes, one cannot doubt the existence of this phenomenon. Fig. 11 is an illustration of tight time locking amongst 3 single units in the frontal cortex of a behaving rhesus monkey. In this figure the method for measuring the Joint Peri Stimulus Time Histogram (JPSTH) [Aertsen et al., 1989] was used to investigate the three-fold correlations amongst units number 12,13 and 2.

In Fig. 11 the firing times of unit number 12 were used as a *stimulus*. The delayed firings of unit number 13 after this pseudo-stimulus were plotted along the *x-axis*, the delayed firings of unit number 2 were plotted on the *y-axis*, while the joint occurrences of a spike from unit 13 and a spike of unit 2 were plotted in the *x-y plane*. Thus, the marginal histogram plotted under the *x-axis* is the pairwise correlation between units 12 and 13, the marginal histogram on the left of the *y-axis* is the pairwise correlation between units 12 and 2, while the *x-y plane* describes the 3-fold correlation among units 12, 13, and 2. Fig. 11A shows the number of compound coincidences that were actually found. Notice that we "zoomed" in on a region in the *x-y plane* which is relatively remote from the time origin. Counts in the neighborhood of the time origin reflects instances where all three events are near simultaneous. Hence, the picture there is dominated by various sources of common input (not shown here). The region shown in Fig. 11A, however, is quite far from that busy center, and hence, the counts are generally down to the baseline level. Indeed most of the bins in Fig. 11A contain few counts (5 ± 4) and appear in dark grey shading, but one bin contains over 20 counts and is plotted white. The fine grain renders the visual inspection of the histogram difficult. A small section of the histogram is blown up and plotted in 3 dimensions in Fig. 11B. There the difference between the number of actual counts and the number that would be expected by chance (if there were no compound dependencies beyond what could be expected by the pairwise dependencies described by the marginal histograms) is plotted. Finally, Fig. 11C shows the probability of observing the data in Fig.11B by chance.

Note the following features: The event $(12,2,13);(0,151 \pm 1, 289 \pm 1)$, (that is, a spike from unit 12 followed after 151 ± 1 ms by a spike from unit 2, and after 289 ± 1 ms by a spike from unit 13) stands out in isolation. This means that we observe here time locking better than 3 ms even after a delay of 289 ms. The probability of seeing such an event by chance is $\exp(-16)$, i.e. 1 in 10 millions! We encountered hundreds of such events in our recordings.

In summary, compound firing patterns, in which tight time locking is observed after long delays are abundant. These events have extremely low probability of

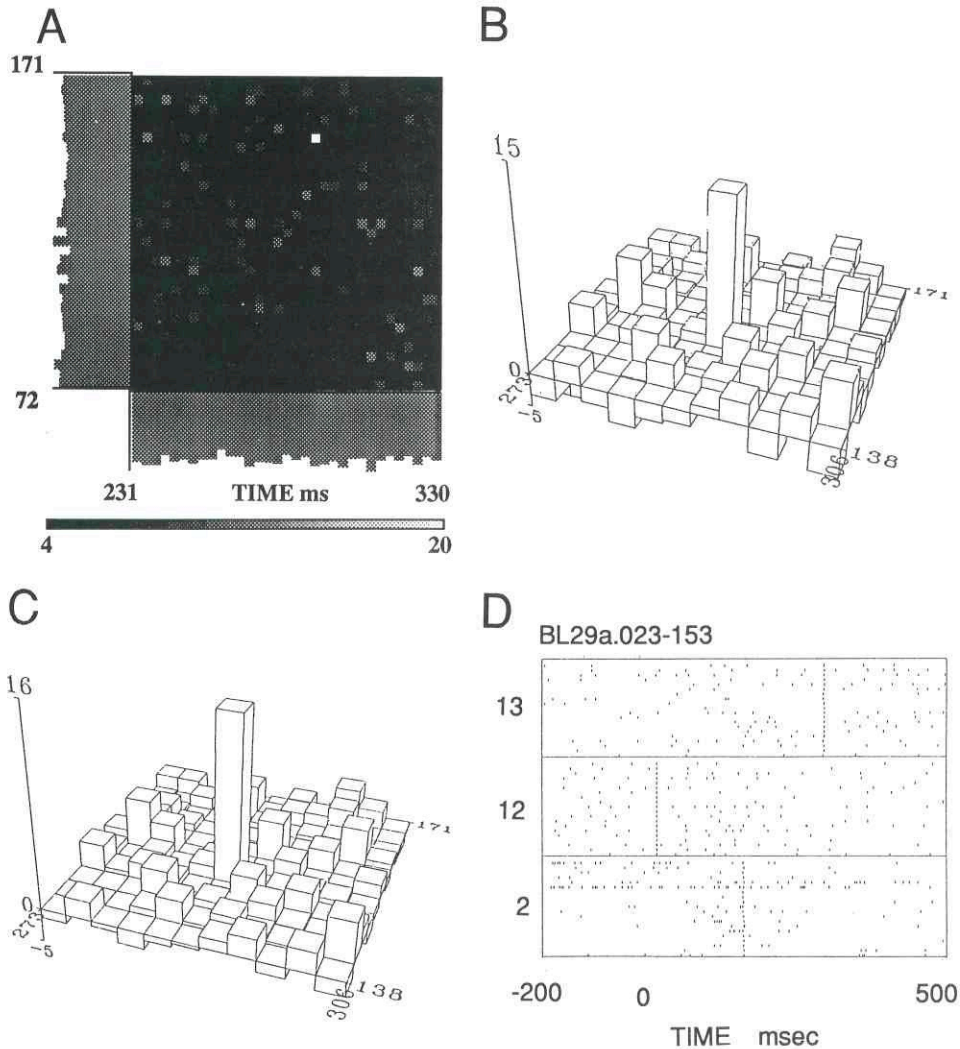


Figure 11. Triple correlation among units 12, 13, and 2 in frontal cortex of a behaving monkey. A. Grey-level plot of the raw correlogram showing one bin in which 20 delayed coincidences occurred. B. a 3-D plot of a small region around that peak, showing the difference between the counts found and the counts expected by chance. C. Surprise values of data in B. (i.e. $-\ln(\text{probability of getting by chance})$). D. Raster display of all the spikes around the 20 compound coincidences which contribute to the high bin in A, B, and C. The activity of each neuron is plotted in a different panel.

occurrence when considered as realizations of independent, time varying rate processes.

3.2. The Syn-Fire Chain.

The accurate spike timing which occurred even after delays of 500 ms must be generated by special mechanisms. Since the strength of the intra-cortical excitatory synapses is very small [Abeles, 1991, chp. 3] one must assume that any secure transmission takes the form of a convergence of several presynaptic cells on one post-synaptic cell. Similarly, since a single post-synaptic cell cannot have much of an effect on its own, there should be a group of post-synaptic cells receiving the same type of connections. This situation is illustrated in Fig.12, where two groups of cells are shown to be connected by multiple diverging-converging connections. Two qualifying points should be made when speaking of diverging-converging links: First, the drawing of Fig. 12 is not an anatomical plot, but rather a functional connectivity plot. In reality the neurons that comprise each set may be (and probably are) scattered and intermingled with each other and with many other neurons. They also make and receive thousands of additional synapses beyond those plotted in the figure. Second, it is not necessary to have every cell in the presynaptic set excite every cell in the post-synaptic set. In fact, it is sufficient to have a situation where every presynaptic cell excites only a fraction of the post synaptic cells. The rich intra-cortical connectivity supports such diverging-converging connections without the need for any special growth processes. For example, if we examine a column of 20,000 neurons in which every neuron is connected to 5000 of the neurons at random, then for almost any set of 30 neurons picked at random there exists another set of 30 neurons each of which receives synaptic contacts from 16-17 neurons in the first set. [See chp. 6 of Abeles 1991, for details about how to compute plausible cortical connectivities.]

The average cortico-cortical excitatory synapse is very weak. In the motor cortex of behaving monkeys its peak depolarization at the soma is approximately 0.1 mV [Fetz et al. 1991]. Consequently, at this level 16-17 EPSP's would have only a small effect on the firing rates. Therefore the multitude of random diverging-converging links have only small effects. However, if by learning processes these synapses become 5-10 times stronger, as was observed by Ahissar et al. [1992], these diverging-converging links may become very effective.

There is, however, a more important effect that should be taken into account when considering the combined effect of EPSP's arriving at a post-synaptic neuron. When the neurons are firing at low rate, the individual EPSP's have only a small effect on the firing of the receiving neuron. However, when these same EPSP's arrive in a synchronous mode, they can provide a very strong drive [Abeles, 1982a; Abeles, 1991 chp. 7]. In fact diverging-converging connections of the type shown in Fig. 12 act as a spatio-temporal filter which preferably transmits synchronized volleys. Thus even if the first links of a chain of diverging-converging connections is excited by prolonged excitatory processes, if the connections are of sufficient strength they would convert such diffuse

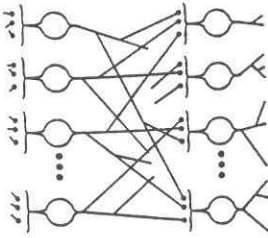


Figure 12. Multiple diverging converging connections between two sets of neurons.

excitation into a synchronous volley which is transmitted securely from link to link [Abeles, 1988; Abeles, 1991 chp. 7]. When activity is propagating in such a way within a chain of diverging-converging links, we refer to it as *syn-fire activity*. A chain that can transmit *syn-fire activity* is called a *syn-fire chain*.

We used neural network simulations to illustrate various properties of syn-fire chains. In the simulation there were 10% weak random connections among the cells but, in addition some of the neurons were connected by stronger diverging-converging connections to form a syn-fire chain. In addition, a large noisy current was delivered to each cell, to mimic the effects of many synaptic inputs from cells which are not in the simulated net. A net of this sort tends to explode by virtue of the positive feed-back provided by the excitatory connections [Abeles, 1991 chp. 5]. To prevent such "epileptic" explosion a global inhibitory mechanism was provided. The inhibitory cell population received excitatory synapses from all the neurons in the net, it responded by a firing rate that depended on the membrane potential of the inhibitory cells in a quadratic fashion [Amit and Treves, 1989]. The firing rate of the inhibitory cells affected all the excitatory cells in the net.

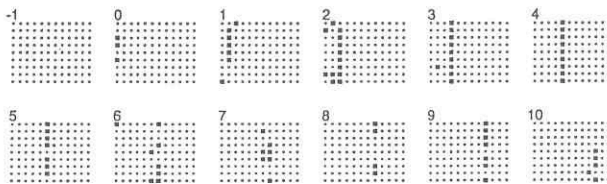


Figure 13. The initiation of syn-fire activity in a chain by constant current stimulation to the first (leftmost) three links. The stimulus was applied from time 0 to 9.

This process is illustrated in Fig. 13, where the activity of the first 10 links of a syn-fire chain with 26 links is shown. Each link was composed of 9 cells and each cell gave strong excitatory connections to 7 of the cells in the next link. The

entire syn-fire chain was embedded in a neural-net of 1000 neurons. The neurons in the first 3 links were depolarized by a weak current (0.3 nA) for 10 ms. We see how this diffuse depolarization evokes some activity in time 0 which then builds up and within 3 ms produces a synchronized volley. From then on, this propagates in a secure manner along the chain. Note that despite the continued depolarizing current during time steps 0 to 9, the input neurons do not start another cycle of syn-fire activation. The reason is that, once activity is evoked, the inhibitory PSP's which are fed-back to the entire network prevent the input neurons from regenerating a second wave.

Once a chain of diverging-converging links starts to operate in the syn-fire mode, activity propagates in a secure and time-wise accurate manner from link to link. Provided the chain is long enough, the spikes from two neurons, one taking part in an early stage, the other in a late stage, are expected to exhibit a tight, delayed time locking (such as was shown in Figs. 10 and 11).

Thus, in our view syn-fire chains are a simple and both anatomically and physiologically plausible mechanism for generating such accurate timing as was found in cortical activity.

3.3 Experimental Evidence.

The present experimental techniques do not allow us to observe directly the syn-fire activity. If each link contains, say, 30 neurons and the chain is embedded in a column containing 20,000 neurons, the probability of recording simultaneously from 3 or even 2 neurons in the same link is vanishingly small. The best that one can hope for, is to obtain a simultaneous recording from 3 neurons, each of which takes part in a different link of the same syn-fire chain. If such a recording is obtained, then whenever the syn-fire chain is activated and the synchronized volley passes through the respective links, one expects to see the associated fixed firing pattern amongst the three cells, such as was described in Fig. 11D.

In order to obtain such data an experimental setup was developed by M. Abeles, H. Bergman and E. Vaadia, which allowed us to record concomitantly the activity of up to 16 single units from the cortex of a behaving monkey [Vaadia et al. 1993]. Several different behavioral paradigms were used, with several different micro-electrode arrangements. The data shown here is taken from experiments in which 6 micro-electrodes were introduced into frontal areas. The electrodes were arranged in a circle having a radius of 0.3 mm. The monkeys were trained to perform light and sound localization tasks.

To obtain data about excessively repeating spatio-temporal firing patterns, a pattern searching algorithm, which detects any repeating pattern regardless its single unit composition or duration [Abeles and Gerstein 1988], was applied. While applying this algorithm to multi spike data as recorded in these experiments, many instances in which excessively repeating patterns appear were indeed found. The details of this finding and a detailed description of their properties can be found in Abeles et al. [1993]. Here we summarize the main results which are relevant for our deliberations.

The patterns are very often associated with some external, i.e. stimulus or behavioral, event. Often, but not always, the patterns appeared in periods which

one would characterize as having *event related activity* i.e. in which the firing rate of the units were elevated in relation to the time of some stimulus or movement.

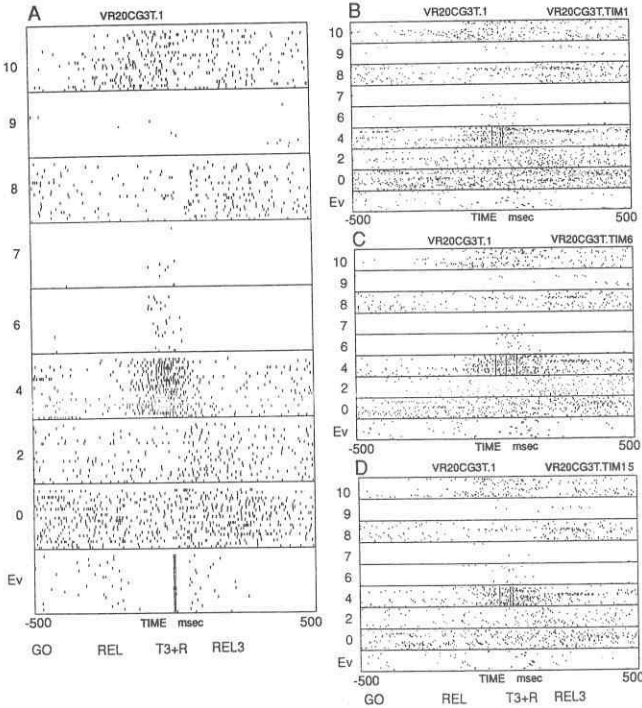


Figure 14. Event related activity and spatio-temporal firing patterns in the frontal cortex of a behaving monkey.

Raster displays of the activity of 8 neurons and the external events. A. The display is aligned around the time that the monkey touched target no. 3 (T_3) and obtained a drop of juice as reinforcement (R). The other events are the moment at which the monkey was instructed to move (GO), at which the movement started (REL), and at which the monkey released the target (REL_3). B., C., and D. Displays aligned around the first spike of $(4,4,4);(0,30\pm 1,39\pm 1)$, $(4,4,4);(0,39\pm 1,78\pm 1)$, and $(4,4,4);(0,39\pm 1,48\pm 1)$ respectively.

Fig. 14 illustrates this point. In this case the activity of 8 neurons was recorded simultaneously. All the sections from 0.5 seconds before the monkey was instructed to move, towards target no. 3, up to 0.5 seconds after he completed the movements, were collated together. The responses of these units is displayed in Fig. 14A, where all the traces are aligned around the time that the monkey touched the target and obtained a drop of juice. We see that unit 4 elevated its firing rate markedly around this time, units 6,7, and 10 showed smaller activation, while the activity of units 2 and 8 was slightly suppressed. On this data

a search for excessively repeating patterns was made. In this search all patterns that lasted up to 100 ms with a timing accuracy of 3 ms were examined. The most prominent excess was found for unit no. 4, which generated 19 different patterns, each repeating 14 or more times (Note that one would expect to see 0.443 such patterns of unit 4 by chance, which means that the actual count presents an event that had a probability of less than 1 in 10^{24} to happen by chance).

Fig. 14B shows the pattern $(4,4,4);(0,30\pm 1,39\pm 1)$ which repeated 21 times. All the traces are aligned around the time of the first spike in this pattern. Below the firing times of unit 0 the behavioral events are marked. We see that the pattern tends to appear shortly before the monkey touched the target. This pattern came intermixed with various other patterns of the type $(4,4,4)$. The 16 repetitions of one of them, $(4,4,4);(0,39\pm 1,78\pm 1)$, are plotted in Fig. 14C, the 14 repetitions of another pattern, $(4,4,4);(0,39\pm 1,48\pm 1)$, are shown in Fig. 14D, and finally there were 16 other patterns of the type $(4,4,4)$; (some other delays). In order to study the relations between the classical event related activity (Fig. 14A) and the patterns, we marked all the spikes of unit 4 that took part in one of the excessively repeating patterns and studied their relation to the external events.

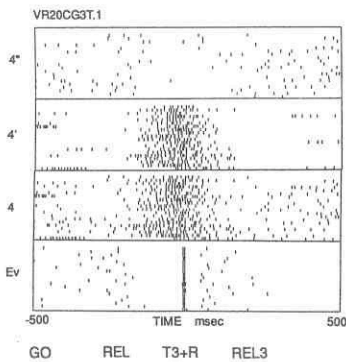


Figure 15. Event-related activity and spatio-temporal firing patterns. The same data as in Fig. 14. The panel marked by 4, displays all the spikes of unit 4, 4' displays only those spike of unit 4 which participated in excessively repeating spatio-temporal patterns, and 4'' displays the remaining spikes of unit 4.

Fig. 15 illustrates our results. The activity is aligned around the time that the monkey touched target 3 and obtained a drop of juice. The behavioral events are shown in the bottom panel. The firing times of unit 4 are shown on the next panel (these two panels are a repeated plot of Fig. 14A.) The next panel shows all the spikes that were associated with one of the excessively repeating patterns, while the top panel shows the spike of unit 4 which were not associated with such patterns. Clearly *all* the event related spike were associated with excessively repeating patterns!

We studied in detail 20 cases for which a single unit showed a marked elevation of firing rate in association of an external event and had also an excess of repeating spatio-temporal patterns. In 13 of those, all (or almost all) the spikes within the event-related activity were forming excessively repeating patterns.

In summary, a large excess of repeating spatio-temporal patterns is often found. These patterns are frequently associated with event-related elevations of firing rates. Often the patterns embrace most, if not all, of the spikes within the event related activity. Hence, one must conclude that the neuronal mechanism which causes event-related elevations of firing rates has the capacity to generate a surplus of very accurate spatio-temporal firing patterns.

3.4. Syn-Fire Reverberations

While studying the abundance of repeated spatio-temporal patterns, it became clear that the findings do not fit completely the predictions derived from the simple syn-fire chain model. For a simple syn-fire chain the patterns are expected to be composed of spikes from 3 different cells (like 12,2,13 as in Fig. 11), whereas in the experimental data most of the patterns were composed of 3 spikes from the same single neuron (like 4,4,4 as in Fig. 14). The simple syn-fire hypothesis suggests that whenever the same process repeats (say, the monkey reaches for target 3), the same spatio-temporal firing patterns should appear. While we found that typically there are several patterns associated with each process, each individual pattern repeats only part of the times (as illustrated by Fig. 14). By combing all the different patterns, however, the entire activity related to the process could be accounted for (as illustrated in Fig. 15). See Abeles et al. [1993] for a more detailed description of this situation.

One may account for repetitive appearances of spikes from the same neuron in a single pattern by assuming that this neuron participates in several links of the

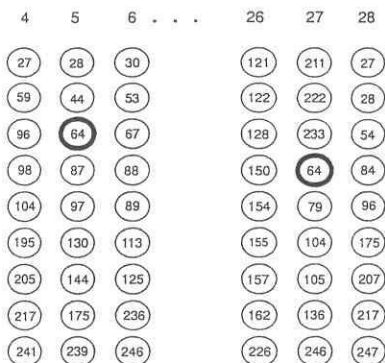


Figure 16. Syn-fire chain with repetitions.

The neurons in each column compose one link in a chain of diverging-converging connections. Unit 64 takes part in both link 5 and link 27.

syn-fire chain. Fig. 16 illustrates how that may happen. It shows two regions from a simulated syn-fire chain: a section around link 5 and a section around link 27. The syn-fire chain is similar in its structure to the one in Fig. 13. Unit 64 is part of the 5-th link, since it receives multiple connections from neurons 27,59, ...241, and excites neurons 30,53, ...246. Moreover, it is also part of the 27-th link, since it also receives multiple connections from neurons 121,122, ...226, and excites neurons 27,28, ...247. Whenever activity sweeps through the chain, neuron 64 is likely to fire twice with an interval of 22 ($=27-5$) synaptic delays in between.

If repetitions such as described in Fig. 16 occur often, the syn-fire chain ceases to be a straight feed-forward (multi-layered) structure, but starts to contain multiple feed-back loops. Such a structure may exhibit attractors in which a group of neurons excite themselves and maintain elevated firing rates for a long period [Hopfield 1982, 1984; see also Rubin and Sompolinsky, 1989; Amit and

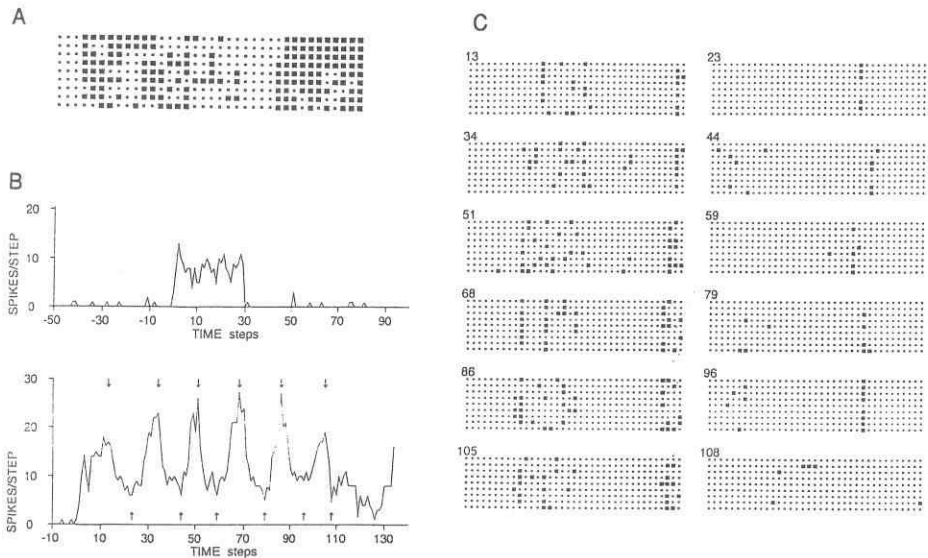


Figure 17. Reverberations in a syn-fire chain with repetitions.

A. The structure of the chain. 82 out of 256 units (plotted as fat dots) participate in two links, the others (thin dots) appear only once. B. The response to a steady stimulation of the first three links for 10 ms (steps 0 through 9). The abscissa describes the simulation time, the ordinate the total number of cells firing at that time. Top panel, the response of the syn-fire chain of Fig. 13, where every unit appeared only once. Bottom panel, the response of the syn-fire chain described in A. The arrows mark the peaks and troughs of activity levels. C. The firing constellations at the peaks (left column) and troughs (right column) of the response in B (bottom trace). A firing cell is marked by a fat dot.

Treves, 1989; Amit et al., 1990; Erb and Aertsen, 1992, for feed-back networks whose neurons do not fire at their maximal rates when the network reaches an attractor].

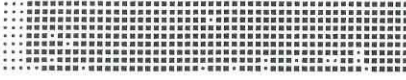
In order to examine the behavior of syn-fire chains in which the same neuron participates more than once, we extended the simulation described in section 3.2 in the following way: 12 more links were added to the syn-fire chain of Fig. 13. The neurons in the new links were selected at random from 256 neurons, 234 of which were already taking part in the chain. A neuron was not allowed to participate in two links which are closer than 9 steps apart. Fig. 17A gives an overview of this new chain. Small dots represent neurons that appear only once in the chain, large dots represent neurons that appear more often. Approximately 33% of the neurons appeared twice in the chain.

The chain was again activated by depolarizing its input neurons (first three links) continuously for 10 ms. Activity started in the same way as in the simple syn-fire chain, but then exhibited more complex propagation patterns. These settled down to reverberations, in which activity continued to cycle within the chain for a very long time. This process is illustrated in Fig. 17. Fig. 17B shows the total number of firing neurons in each step (1 ms) of the simulation. The top trace shows the level of activity for the simple syn-fire chain described in section 3.2 (Fig. 13), while the bottom trace shows the level of activity in the chain with repetitions. The firing constellations at the arrows are shown in Fig. 17C. Clearly, even when as little as 33% of the cells participate twice in the chain, complex activation patterns appear, which in this case took the form of periodic oscillations.

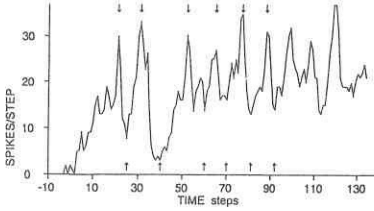
Activation patterns become even more complex as the extent of repetitions in the links increases. When the syn-fire chain of Fig. 17 was further elongated by adding 15 more links, the activity pattern as seen in Fig. 18 was obtained. The level of activity and examples of the activation constellations are shown in Fig. 18B and C. In this syn-fire chain one obtains reverberations which can maintain elevated activity for very long time. The activity levels show large undulations, however these are not periodic anymore but exhibit very complex shapes. Successive peaks and troughs of the activity levels are associated with different firing constellations. The large undulations of the activity level may tell the observer that something is being processed by this network, however what actually goes on can be specified only in terms of the spatio-temporal firing patterns.

Although activity does not propagate just between successive links, the number of different propagation trajectories is limited. Thus, if the syn-fire chain is activated many times, there would be a tendency for the same spatio-temporal firing patterns to repeat at levels higher than chance. Suppose we could insert micro-electrodes into this network of the 1000 simulated cells and pick 3 of them at random. Our chances of getting 3 different cells from the same syn-fire chain are small. As only a quarter of the 1000 neurons take part in the syn-fire chain, the chances of getting 3 members is 0.016 ($1/4$ to the third power). The chances of seeing exactly one neuron which participates in the syn-fire chain is 0.42 ($3 \cdot 1/4 \cdot 3/4 \cdot 3/4$). Thus we expect to see many more cases in which one neuron

A



B



C

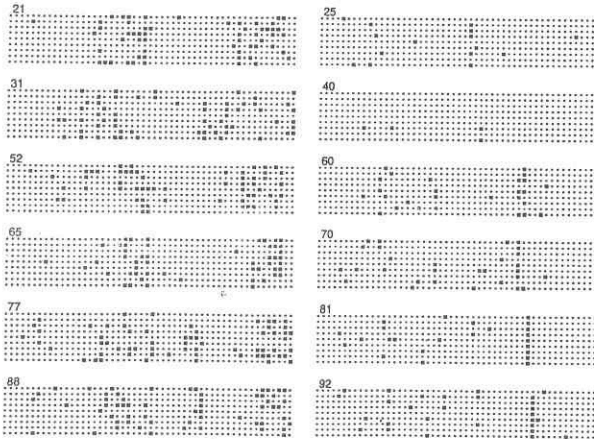


Figure 18. Reverberations in a syn-fire chain with many repetitions. A, B, and C. as in Fig. 17.

shows internal time locking amongst its spike, then cases in which three neurons show across-neuron patterns. Moreover, a single participating neuron in a syn-fire chain such as in Fig. 18, would show several repeating patterns, each associated with a different trajectory of reverberations.

3.5. Significance of Spatio-Temporal Patterns

In our data of cortical activity as recorded through micro-electrodes we found abundance of delayed synchronization. The delays can be as long as 500 ms, but a high time accuracy of ± 1 ms is maintained throughout this interval. There is close association between the appearance of such accurately repeating spatio-temporal patterns and event related activity. We argued that these findings are a sign of the neural mechanism which generates the event related activity in the cortex. Up to this point we treated the spatio-temporal patterns merely as indications for the underlying neural mechanisms, but not as containing information from the brain's point of view.

This attitude was radically changed when one of us (Y.P.) discovered that units which responded in a similar fashion to external stimuli showed different profiles of spatio-temporal firing patterns, according to the meaning that the stimuli had. This phenomenon is illustrated in the following example.

A rhesus monkey was trained to perform a delayed-response task in the following manner: The monkey sat in a restraining chair, with an arena of touch buttons and light sources in front of it. Below, in the center of the arena, an additional touch button (the *start-trial* button) was provided. The monkey was trained to behave according to two alternating paradigms (*go* and *no-go*). In the *go* paradigm the monkey started a trial by touching the *start-trial* button. After a variable delay a red LED, referred to as the *ready LED*, was turned on in the

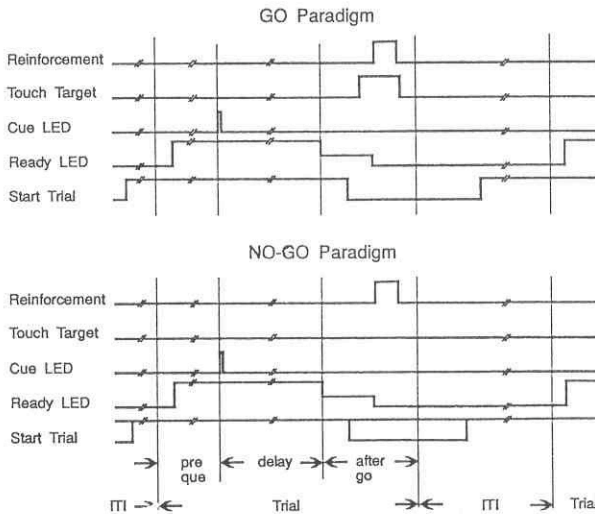


Figure 19. Timing diagram for the delayed response paradigm. The trial started half a second before the *ready LED* was turned on and ended half a second after the *reinforcement* (a drop of juice) was delivered. Breaks in the traces represent random delays introduced by the computer which controlled and monitored the behavioral experiment.

center of the arena. After another variable delay (3-6 s), a 100 ms long yellow light blink was flashed either from the left or from the right. We refer to this light blink as the *cue*. After an additional delay of 1,2,4,8,16 or 32 seconds the *ready LED* changed its color from red to orange, this served as a *GO* signal, after which the monkey had to touch the target from which the *cue* was delivered within 1.2 s. Correct responses were reinforced by a drop of juice. After 4 correct responses in the *go* paradigm, all the lights in the arena were switched on for 4 seconds; this instructed the monkey to switch its behavior to the *no-go paradigm*. In the *no-go* paradigm the same sequence of events proceeded, but the monkey had to keep its hand on the *start-trial* button after the *GO* signal. After 4 correct trials in the *no-go* paradigm, the LEDs of the arena were turned on again for 4 seconds and the monkey switched its behavior back to the *go* paradigm.

These event sequences are displayed graphically in Fig. 19. The figure also shows the division of the time into 4 periods. The *ITI* period covers the time between successive trials, the *pre-cue* period spans the time from turning on the *ready LED* until the *cue* was blinked, the *delay* period covers the time from the *cue* up to the *GO* signal, while the time from then on until the end of the trial was called the *after go* period.

On 5-May-1991 unit 6 had 80 excessively repeating patterns, however they did not occur with the same likelihood at the different time sections. The patterns (6,6,6); (0,52±1,338±1) and (6,6,6); (0,32±1,152±1) appeared most frequently during the *delay* period which followed the *cue* on the left. Fig. 20A shows the responses of unit 6 to the *cue* on the left. The responses are sorted such that the responses while the monkey was behaving according to the *no-go* paradigm are shown in the upper panel, while those made during the *go* paradigm are plotted in the lower panel. Moreover, responses within each paradigm were sorted so that the trials in which the *delay* was 1 s are displayed at the bottom, those with 2 s *delay* above them, and so on, up to *delays* of 32 seconds. Observe that unit 6 responds to the blink from the left by elevating its firing rate strongly for approximately 2 s in both paradigms. In addition, it also elevated its firing rate after the *GO* signal in the *go* paradigm.

The frequency of occurrence of the two patterns mentioned above is plotted in Fig. 20B. The occurrences of (6,6,6); (0,56±1,338±1) are marked by a dot, those of (6,6,6); (0,52±1,152±1) by a triangle. Notice that the first pattern tends to appear selectively when the monkey behaves according to the *go* paradigm, while the second pattern is the preferred one while the monkey is behaving in the *no-go* paradigm. Thus, the elevated activity of unit 6 tells us which stimulus (*cue* from the left) was given; in addition, the pattern of firing tells us what the "mental set" (*go* vs. *no-go*) of the monkey was. Such differential preference of patterns was found for all the 80 excessively repeating patterns of unit 6. However, usually the profiles were more complex than those depicted in Fig. 20B.

The differential preference of different patterns with the same single-cell composition (say 6,6,6) to appear in different states raises two questions: (1) What is the neural mechanism responsible for this phenomenon, and (2) Is this phenomenon significant for the brain, or only for the neurophysiologist studying it.

The appearance of different patterns within similar responses of the same neuron suggests that a group of neurons may reverberate in different modes. This situation is easily realized with the syn-fire concept. Just like the same neuron may participate in several different links of a single syn-fire chain, it may also

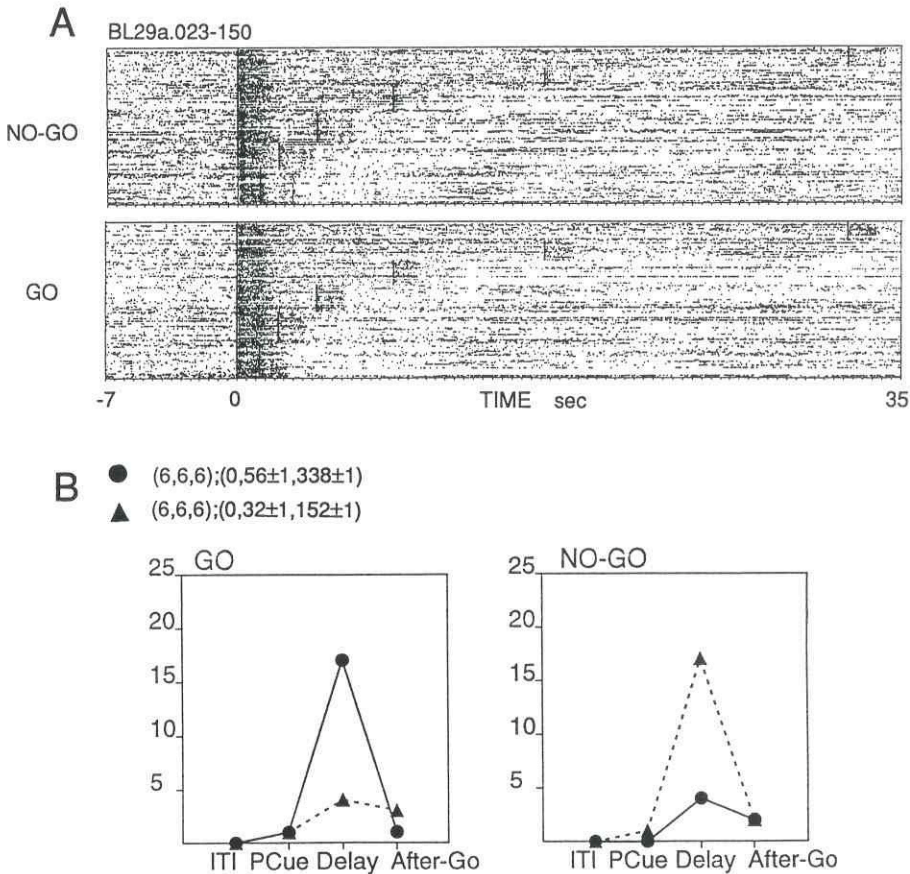


Figure 20. Profiles of spatio-temporal firing patterns of unit 6 (see text).

A. The activity of unit 6, from 7 seconds before the *left cue* up to 35 seconds after it. The heavy vertical bars at times 1,2,4,... seconds mark the times of the *go* signal. Top panel: activity while the monkey was performing according to the *NO-GO* paradigm. Bottom panel: activity while the monkey was performing according to the *GO* paradigm. B. The profiles of recurrence of two patterns in the different stages of the trial. • and the solid line, for the pattern (6,6,6); (0,56±1,338±1), ▲ and the broken line, for the pattern (6,6,6); (0,32±1,152±1).

participate in two different syn-fire chains. To test this idea we extended the simulation described in section 3.4 to a situation where 600 neurons were connected so as to form two chains of diverging-converging connections. The 3 input stages of the first chain had 25% overlap with the three input stages of the second one. Except for the input neurons, all other neurons participated in both chains, and most of them appeared twice in each chain. When the input links of chain 1 were stimulated by a constant depolarizing current for 10 ms, syn-fire activity started in this chain and continued to propagate securely through the chain until it reached the last (75-th) link. When the input links of chain 2 were stimulated, activity propagated in syn-fire mode according to the sequence of connections of the second chain. Thus, it is plausible that syn-fire chains may indeed reverberate in several different modes. The reverberation mode can contain some additional information about the event which aroused the activity.

Can the brain use this information? It was suggested by E. Bienenstock [1991; Doursat, 1991] that two syn-fire chains may be cross connected by a few connections. If the activity in these connections arrives at the appropriate times, the two syn-fire chains may in fact enhance each other and generate a more stable network. We have tested this idea by way of simulation and found this to be the case. Moreover, with the appropriate strength of cross connections, we observed that, when the activity in the two syn-fire chains becomes engaged, the overall activity levels (like those shown in Fig. 18B) of the two chains undulate in a coherent way.

In summary, syn-fire reverberations are not just a way to generate and "shape" the spatio-temporal structure of the cortical activity; they also can be used to bind the activity of multiple syn-fire chains in different cortical locations into a single coherent mental experience.

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