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SYNCHRONOUS ACTIVITY IN THE VISUAL SYSTEM

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ABSTRACT

Synchronous activity among ensembles of neurons is a robust phenomenon observed in many regions of the brain. With the increased use of multielectrode recording techniques, synchronous firing of ensembles of neurons has been found at all levels in the mammalian visual pathway, from the retina to the extrastriate cortex. Here we distinguish three categories of synchrony in the visual system, (*a*) synchrony from anatomical divergence, (*b*) stimulus-dependent synchrony, and (*c*) emergent synchrony (oscillations). Although all three categories have been well documented, their functional significance remains uncertain. We discuss several lines of evidence both for and against a role for synchrony in visual processing: the perceptual consequences of synchronous activity, its ability to carry information, and the transmission of synchronous neural events to subsequent stages of processing.

INTRODUCTION

Synchronous neuronal activity is found in many forms in the mammalian visual system, from the sub-millisecond synchrony of several cells in the lateral geniculate nucleus (1), to the slower, coherent firing of large ensembles of neurons in the visual cortex (2, 3). In this review, we discuss a broad range of synchronous activity, which we have classified into three categories. The first category, synchrony from anatomical divergence, can include examples of the tightest synchrony, on the millisecond time scale. It is caused by strong, divergent input from a single source onto multiple targets. The second category, stimulus-dependent synchrony, includes forms that can be independent

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of specific neural connections. Most simply, an external stimulus can excite a group of neurons in a time-locked fashion so that they all fire with a stereotyped time course. Finally, there is the category we call emergent synchrony, which includes phenomena that rely on the complex dynamics of the network as a whole. This category includes the oscillatory activity of ensembles of neurons in the visual cortex (reviewed in 2, 3).

At the outset, it is important to define what we mean by synchrony. The difference in spike timing between two neurons will never be exactly zero, thus synchrony must be defined in terms of an arbitrary upper bound on this difference. The distinction between synchrony and slower forms of correlated activity can be related to the distinction between a temporal code and a rate code. Although making this distinction is notoriously difficult, the debate can be recast in terms of either the interspike intervals of the presynaptic neurons or the time constants of integration by the postsynaptic neurons. In one formulation, "the interesting question is whether sensory neurons produce large numbers of spikes or small numbers of spikes in the time windows relevant for behavior and decision making." (4, p. 29). Here we make a similar distinction. We call correlated activity synchronous only when it occurs within a time window not much greater than the interspike interval or, alternatively, the integration time of postsynaptic neurons. A special case can be termed fast synchrony, when two neurons fire synchronous spikes at a scale significantly shorter than the interspike interval.

All three forms of synchrony considered in this review—anatomical, stimulus-dependent, and emergent—are present throughout the visual system, but their presence need not imply that they serve a function. It is entirely possible that neural synchrony is an epiphenomenon and is not necessary for normal visual processing. The strongest test of the importance of synchrony must be at the perceptual level: If synchrony is either disrupted or artificially induced, are there perceptual consequences? A slightly weaker test would be to determine whether synchronous activity can be transmitted to the next level. This could mean either the transmission of synchrony from one ensemble to the next, or the preferential response of postsynaptic targets to synchronous input. The distinction is important: In the one case, synchrony is merely reproduced faithfully but not selectively; in the other, it is read off. Finally, the potential importance of synchrony has been examined by asking whether synchronous activity might carry information about the stimulus that would be unavailable if the activity of individual neurons were considered separately. In this review, we examine the three forms of synchrony and then discuss their potential use at later stages of visual processing.

SYNCHRONY FROM ANATOMICAL DIVERGENCE: COMMON INPUT

It has frequently been suggested that action potentials in a single presynaptic neuron induce synchronous firing among multiple postsynaptic targets (5–7; see 8). One of the earliest examples of synchronous firing based on common input comes not from vision, but from studies in the spinal cord, where ensembles of intercostal motoneurons display extensive synchronous firing (9–12). Similarly, in the rabbit somatosensory cortex, synchronous activity has been found among suspected inhibitory neurons that receive divergent, monosynaptic input from neurons in the ventrobasal nucleus of the thalamus (13, 14).

In the visual system, synchrony based on common input has been found at several different levels of processing. Synchronous firing based on ascending common input has been described for neurons in the retina (15, 16) and the dorsal lateral geniculate nucleus (LGN) (1, 17, 18). Synchronous firing has also been described in the primary visual cortex (19–22), although its source is likely a mix of common input and reciprocal excitation that cannot be reliably distinguished. A more complex form of synchrony (or slower correlated activity) from anatomical divergence is induced by selectively activating a common presynaptic pool, such as the feedback connections from cortex to the LGN (23).

When there is divergent input from a common source onto several targets, the degree of synchronous firing evoked in the targets is dependent on both the number and the strength of common inputs. If an ensemble of postsynaptic neurons is driven strongly by only a few common inputs (for instance, input from retinal ganglion cells to geniculate neurons), then a large percentage of the ensemble's spikes should be synchronous. If an ensemble is weakly driven by many common inputs (for instance, input from geniculate cells to cortical simple cells), then synchrony should be weaker. These two cases are illustrated in Figure 1. In each example, two postsynaptic neurons receive half of their excitatory drive from a common presynaptic source. If the first pair of postsynaptic neurons (Figure 1*a*) receives its common input from only one presynaptic neuron that has 40% efficacy (40% of the input spikes evoke an output spike), then this pair of postsynaptic neurons will fire 8% of their spikes synchronously. The value 8% comes from the product of the following values $[0.5 \cdot 1 \cdot (40\%)^2]$: (0.5 of excitatory drive) · (1 common input) · $(40\%)^2$ of input spikes. Of the spikes from the common input, 40% evoke a spike in each of the output neurons, therefore, assuming independence, $(40\%)^2$ evoke synchronous spikes in both output neurons. If the second pair (Figure 1*b*) receives its common input from 10 uncorrelated presynaptic neurons, each of which has 4% efficacy, then only 0.8% of the spikes will be synchronous $[0.5 \cdot 10 \cdot (4\%)]$. In general,

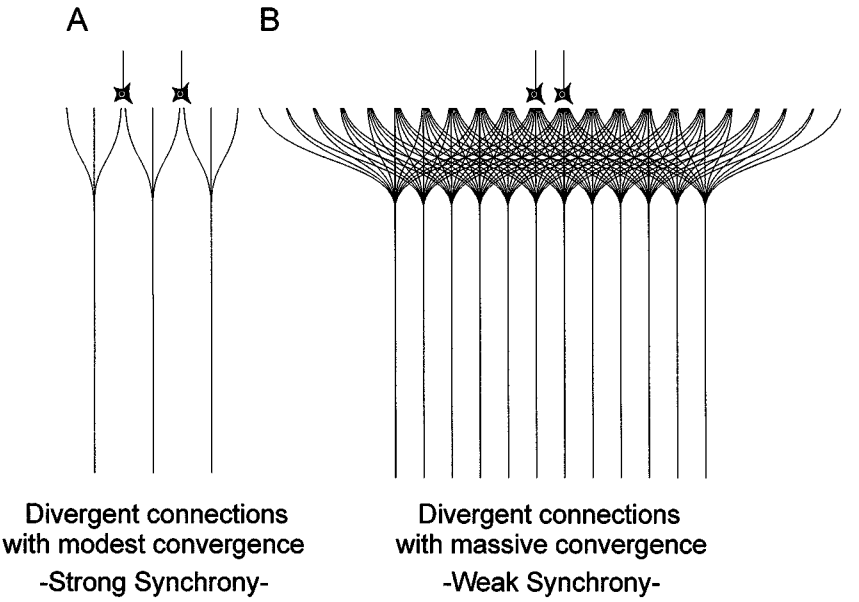


Figure 1 Divergent connections lead to synchronous activity, but convergence limits the amount of synchrony. In general, if two postsynaptic neurons are strongly driven by only a few common inputs (as in *A*), then they will fire many synchronous spikes (*Strong Synchrony*). In contrast, if a pair of neurons are weakly driven by many common inputs (as in *B*), then they will fire fewer synchronous spikes (*Weak Synchrony*).

given two neurons that have a pool of common presynaptic inputs of a given total strength, the degree of induced correlation between these two neurons will be inversely proportional to the number of neurons that provide this shared input. These arguments make two assumptions—that the presynaptic neurons are uncorrelated and that all presynaptic spikes are equally effective—neither of which is strictly true in the visual system (17, 18). Nevertheless, the general principle holds: While divergence will usually lead to synchrony, the degree of convergence strongly affects the magnitude of this synchrony.

In the following sections, we discuss synchrony resulting from common input for neurons in the retina, LGN, and visual cortex. Before describing the types of synchrony encountered in each of these structures, it is useful to quickly review how the firing patterns of multiple neurons are typically analyzed. The primary tool for examining the relationship between spike trains in two neurons is the cross-correlogram (6, 24, 25). In a cross-correlogram, all of the spikes occurring in cell *A* are considered to occur at time zero. Spikes occurring in cell *B* are then plotted relative to the firing of spikes in cell *A*. If there is a peak to

the right of zero, then cell *B* tends to fire spikes at some latency after a spike in cell *A* (perhaps the result of a monosynaptic connection between cell *A* and cell *B*; see Figure 2, Ret A → LGN B, which appears later in text). If the cross-correlogram has a peak centered at time zero, then the two cells tend to fire spikes simultaneously (perhaps the result of common input; see Figure 2, LGN B—LGN C). Cross-correlograms can exhibit an enormous range of features, each of which is consistent with several interpretations. Given anatomical knowledge of the system, however, certain types of correlograms can be interpreted with relative certainty in terms of neural connections. As a prime example, cross-correlograms have been usefully applied to understanding the circuitry within the retina, between the retina and LGN, and between the LGN and visual cortex.

Intraretinal Synchrony

In the adult retina, synchronous spiking of neighboring ganglion cells has been described in the cat, rabbit, salamander, and goldfish (15, 16, 26–33). In cats and salamanders, ensembles of ganglion cells display three distinct types of synchronous firing that differ in their time course—slow, medium, and fast—and in their underlying circuitry. While slow synchrony (40–50 msec for cat; 50–100 msec for salamander) requires chemical synaptic transmission, both fast (<1 msec) and medium (2–10 msec for cat; 10–50 msec for salamander) synchrony appear to involve current passed through gap junctions (31, 33). Both slow and medium synchrony between retinal ganglion cells appear to result from common input. Slow synchrony is most likely due to noise in the visual transduction reactions of photoreceptors; it is slowest in the dark, where it is thought to reflect single quantal events, and somewhat faster in the light (15, 34). Slow synchrony can be established by the divergent connections of either the photoreceptors onto bipolar cells, or the bipolar cells onto ganglion cells. Medium synchrony (2–10 msec for cat; 10–50 msec for salamander) is thought to arise from amacrine cells that provide common input to ganglion cells (31, 33). Although amacrine cells provide predominantly inhibitory input to ganglion cells via chemical synapses, they also provide excitatory input via gap junctions (35–38). Because most amacrine cells generate graded potentials rather than action potentials, the synchronous responses they elicit in ganglion cells are slower than those resulting from gap junctions between ganglion cells (described below).

The fastest synchrony (<1 msec) displayed by nearby ganglion cells is not the result of common input from upstream sources, but most likely is the result of reciprocal excitation from other ganglion cells. For this reason, the cells tend to fire not truly synchronously, but one after the other. In the cat, cross-correlograms between these pairs of cells have two peaks, ∼1 msec on either side of zero (15, 31; these correlations are faster in the salamander, 33). For two reasons, it is likely that excitation between ganglion cells is transmitted

via gap junctions. First, antidromic activation of ganglion cells often triggers the firing of nearby ganglion cells (31). Second, fast synchrony persists in the presence of agents that block synaptic transmission (33).

The functional importance of retinal synchrony is not known. It has been shown that the receptive field of the synchronous activity of two ganglion cells is different from the receptive field of either neuron alone (16), and thus could potentially transmit distinct information to higher levels. Given the faithful transmission of activity from retina to LGN, it is likely that much of the synchrony (and therefore the information carried within it) is transmitted to the next level. Whether this synchrony is selectively transmitted, that is, whether it is read off, remains speculative.

What is certain, however, is that new forms of synchrony emerge at the level of the LGN. In the cat retina, fast synchrony is seen between only some pairs of Y cells (a class of large ganglion cells, less than 5% of the total). More importantly, in fast retinal synchrony there are always two correlogram peaks. In the principal layers of the LGN, there emerges a new form of fast synchrony between all cells, both X (the majority of cells, with smaller receptive fields) and Y. This synchrony is characterized by cross-correlograms with a single peak, centered at time zero, which is narrower (<1 msec) than the double peak seen in fast retinal synchrony (1).

Retinal Divergence and Geniculate Synchrony

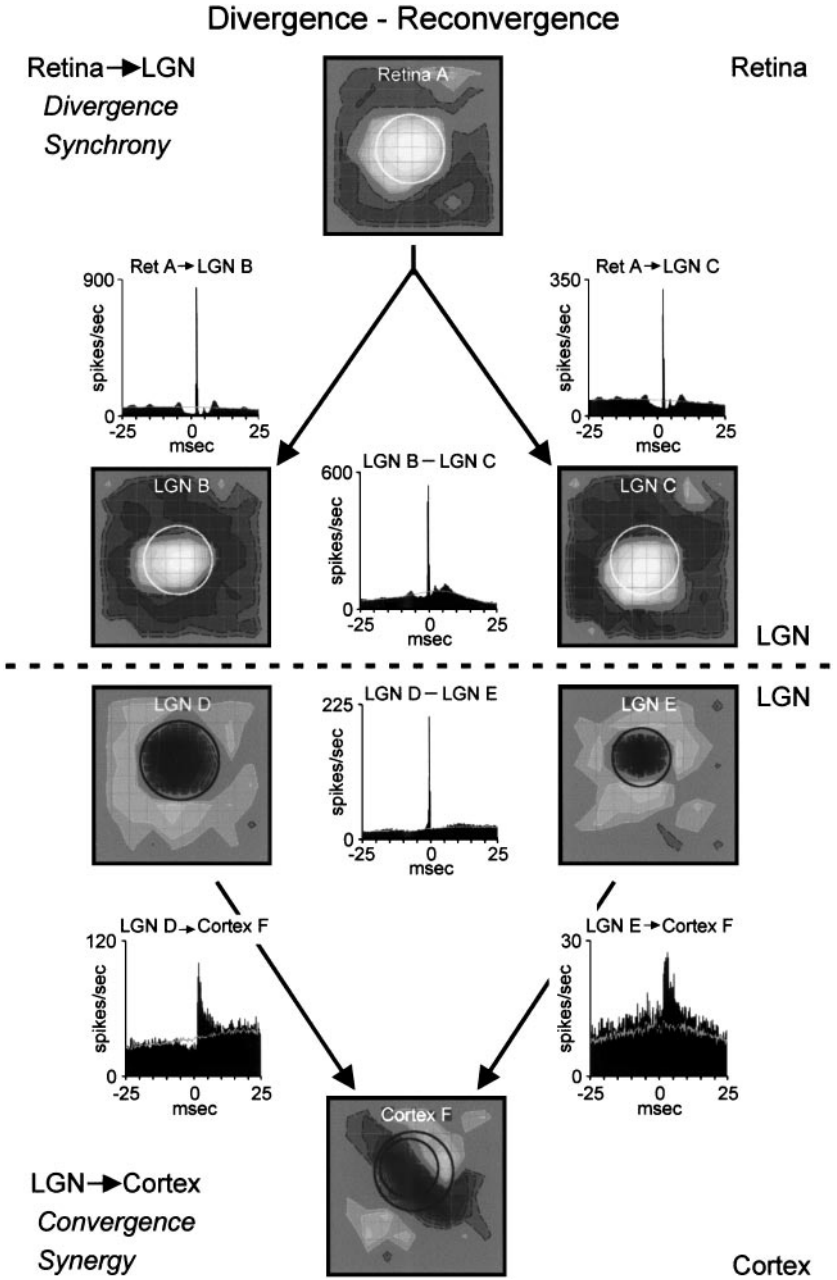
Within the retina, feedforward connections are from non-spiking neurons (with the possible exception of some spiking amacrine cells); therefore, correlations based on divergence are slow. Action potentials in divergent retinal ganglion cell axons could, however, generate much faster synchrony among thalamic targets. In the cat, there is significant numerical divergence in the retinogeniculate pathway. The retina contains on the order of 100,000 X cells and 5000 Y cells (39, 40). The number of relay neurons in the principal laminae (A and A1) of the LGN is far greater: 240,000 X cells and 120,000 Y cells (reviewed in 41). Even if each relay neuron received input from only a single ganglion cell, there should be considerable divergence. Ultrastructural examination of a single ganglion-cell axon has directly demonstrated this divergence, as well as convergence. A single ganglion cell can contribute 100% of the retinal synapses onto some relay neurons, 30–50% of the retinal synapses onto others, and a very small number (∼2%) of synapses onto yet other geniculate cells (42). Finally, dual recording studies from neurons in the retina and the LGN have identified divergent, monosynaptic connections from individual retinal ganglion cells onto multiple geniculate neurons (17, 18).

Divergent input leads to synchrony, but the degree of this synchrony depends on the strength of the connections (Figure 1). The feedforward connections

from retina to LGN are very strong (17, 18, 43–46): on average, stronger than any others in the visual pathway (1, 22, 47–50). Individual geniculate neurons typically receive very strong input from a single retinal ganglion cell and often weaker input from only 1–3 other ganglion cells (42–44). Input from the dominant ganglion cell is so strong that the evoked excitatory post-synaptic potential (S-potential) can be measured with extracellular electrodes (51–53). This feature has allowed researchers to record simultaneously the action potentials and S-potentials of individual geniculate neurons (43, 51–56). Another method for examining the strength of connections between the retina and LGN involves simultaneous recordings from neurons in both structures. This method can be used to reveal the spike trains of strong retinal inputs to geniculate neurons (those that generate S-potentials), as well as the spike trains of weaker retinal inputs. Dual recording studies have found some retinal cells that contribute 100% of the spikes that drive an individual geniculate neuron, as well as weaker connections with as low as 1% contribution (17, 18, 43–46).

As a result of divergent, highly effective connections from the retina to LGN, Cleland (57) predicted that there should be small ensembles of geniculate neurons that fire many of their spikes synchronously. He further suggested that within these ensembles, there should be a range of correlation strengths between neurons, depending on the proximity of their receptive fields. This model has recently received experimental support (1, see 23, 58–60). When spike trains from neighboring geniculate neurons were recorded with separate electrodes, cross-correlation analysis revealed strong and narrow peaks (<1 msec) centered at time zero (1; Figure 2, LGN D—LGN E). Pairs of cells with extremely similar receptive fields were the most likely to display synchronous firing, which accounted for up to 40% of either neuron's spike train. Pairs with less well overlapped receptive fields were less likely to display synchronous firing; when they did, a lower percentage of their spikes were synchronous. Subsequently, geniculate synchrony has been directly shown to result from input from single ganglion cells. For the example shown in Figure 2, a single ganglion cell (Ret A) drove 84% of the synchronous spikes that occurred between two geniculate neurons (LGN B—LGN C; 17, 18).

Fast synchrony between pairs of geniculate neurons has also been examined for a possible role in the encoding of visual information (61). For a pair of synchronized geniculate neurons, the receptive field of synchronous spikes (bicellular receptive field; 62, see 16) is slightly but significantly different from the receptive fields of either individual neuron. This raises the question: Is there useful information in the receptive field of synchronous spikes? It turns out that if the synchronous spikes could be decoded as a distinct third channel, up to 40% more information about the stimulus could be conveyed than if synchrony were ignored. Further, the amount of increased information carried in synchronous



spikes appears to be dependent on the degree of synchrony itself: The greater the synchrony, the greater the gain in information (61).

Given the finding that fast geniculate synchrony carries information, two questions arise: What is the source of this information, and can it be used at subsequent levels of processing? The information present in synchronous geniculate spikes must result from information somehow embedded in the firing patterns of single retinal ganglion cells. Recent work has shown that more information is encoded in a retinal spike train, above a simple rate code, during periods of very high spike rate (63). This information may be used by the LGN via the following mechanism. When a single ganglion cell fires two closely spaced spikes, the second spike is much more likely than the first to elicit a geniculate spike—an effect referred to as paired-spike enhancement (18; so named because, unlike paired-pulse facilitation, the mechanism is entirely unknown). The enhanced efficacy of second retinal spikes is at a maximum at very short interspike intervals (∼3–4 msec) and then declines gradually out to ∼30 msec. Thus in the transition from low to high firing rates, spikes are differentially transmitted through the LGN. Further, paired-spike enhancement not only increases the likelihood of evoking spikes in individual target geniculate neurons, but also increases the number of synchronous spikes in multiple target neurons (18). Taken together, divergent retinal axons and paired-spike enhancement act not only to increase the number of synchronous spikes in the LGN, but also to ensure that certain retinal spikes (those with more information

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Figure 2 Divergence and reconvergence in the retino-geniculo-cortical pathway of the cat. (*Upper half*) Divergence from a single retinal ganglion synchronizes two geniculate neurons. The three panels show receptive field maps of simultaneously recorded neurons (Retina A, LGN B, LGN C; each is an on-center Y cell; grid size: 0.6°). The *circles* shown over the receptive field centers correspond to the best fitting Gaussian of the retinal receptive-field center (radius: 2.5 σ_{ret}). The cross-correlograms between the retinal and geniculatpike trains (Ret A → LGN B; Ret A → LGN C) have strong and narrow monosynaptic peaks, displaced ∼ 2.5 msec to the right of zero. The two geniculate neurons fired many of their spikes synchronously (correlogram: LGN B—LGN C). Of the synchronous spikes in the two geniculate cells, 84% were driven by retinal cell *A* (adapted from 17, 18). (*Lower half*) Geniculate neurons with synchronous activity provide convergent input to cortical simple cells. The two geniculate neurons (LGN D, LGN E) are both off-center, X cells (grid size: 0. 4°. Their receptive field centers are overlapped with each other as well as with the off-subregion of a simultaneously recorded simple cell (Cortex F). The geniculate neurons fired many of their spikes synchronously (correlogram: LGN D—LGN E), most likely the result of common retinal input. The cross-correlograms between the geniculate neurons and the simple cell (LGN D → Cortex F; LGN E → Cortex F) have monosynaptic peaks (typically slower and weaker than those for retinogeniculate connections). Analysis of the geniculate spikes trains showed that synchronous geniculate spikes were 70% more effective than non-synchronous spikes in driving cortical responses (adapted from 1).

during periods of high retinal firing) are more likely to be transformed into synchronous geniculate spikes.

The second question remains: Can the information in synchronous spikes be used at later stages? Recordings from two geniculate neurons and a postsynaptic layer-4 simple cell (see Figure 2: LGN D, LGN E, Cortex F) have shown that simultaneously arriving spikes are more effective than nonsimultaneous spikes at eliciting cortical action potentials (1). The efficacy of a geniculate spike (probability that a geniculate spike will lead to a cortical spike, above chance) is greatest when it occurs within a few msec of a spike from another geniculate cell (65). Efficacy then decreases rapidly with interspike intervals between 5–10 msec. More importantly, the influence of simultaneously (<1 msec, the time-scale of intrageniculate synchrony) arriving spikes is supralinear (1). That is, the efficacy of simultaneous spikes is greater than the sum of the efficacies of nonsimultaneous spikes. While the mechanisms that underlie synergistic interactions are unknown, they almost certainly include the postsynaptic membrane threshold—a nonlinearity that would favor the generation of spikes from simultaneous inputs.

The functional consequences of divergence from retina to LGN and reconvergence from LGN to visual cortex (Figure 2) can be summarized as follows: (*a*) Divergent and strong input from single ganglion cells to multiple geniculate neurons can induce strong and fast synchronous responses (1, 18). (*b*) Paired-spike enhancement increases the amount of geniculate synchrony during periods when retinal ganglion cells are firing rapidly or rapidly increasing their rate of firing (18, see 64). (*c*) Synchronous geniculate spikes contain more information than non-synchronous spikes (61). (*d*) Geniculate spikes that arrive simultaneously to cortical neurons are synergistic in eliciting cortical spikes (1). One potential reason for this complex scenario is that while the spike trains of retinal ganglion cells carry rich temporal information, cortical neurons—which receive many convergent inputs (41)—are not particularly suited to responding to the fine temporal structure of individual inputs (66). If, however, there is an intermediate stage in the thalamus—where high individual rates are translated into distributed, synchronized ensembles of neurons—then the same information may be relayed in a form more easily detected by cortical neurons.

Common Input and Intracortical Synchrony

Cross-correlation analysis has also been widely used in the study of cat primary visual cortex, primarily as a tool to assess connections between cortical neurons (19–22). Other than oscillatory firing seen under certain conditions (see below), any synchrony found in the cortex is an order of magnitude weaker than is found in either the retina or the LGN. This is most likely because neural connections in the cortex, both afferent and intrinsic, are more diffuse than those at earlier stages (41)—i.e. there is more convergence (see Figure 1*b*). For this reason,

it is difficult to determine whether neural synchrony in the cortex is caused by common input or by reciprocal excitation.

It is likely that the situation in the primate is different. At any location in layer 4 of cat visual cortex, there is overlap of 360–540 X-axons and 300–540 Y-axons (41). In the macaque visual cortex, however, the magnocellular and parvocellular thalamic afferents stratify in different cortical sublaminae (4Cα 4Cβ). In both sublaminae, there is overlap of only 24 thalamic axons (67). It is thus likely that thalamo-recipient neurons receive far fewer convergent afferent inputs in the macaque than in the cat.

Although synchrony in layer 4 of primate visual cortex has not been studied directly, preliminary analysis of thalamocortical connections suggests that synchrony in layer 4 may be both fast and strong (65). A cross-correlogram between a magnocellular afferent and a layer-4 neuron, recorded simultaneously, is shown in Figure 3. Both the strength of the correlation (efficacy 8.6%, contribution 17.6%) and its time course (0.7 msec full width at half maximum) are reminiscent of those found in retinogeniculate correlations in the cat. Because there is considerable numerical divergence between the primate LGN and layer 4C (approximately 1:20 for the parvocellular projection, 1:100 for the magnocellular; 67–69), it is likely that many cortical cells are driven by

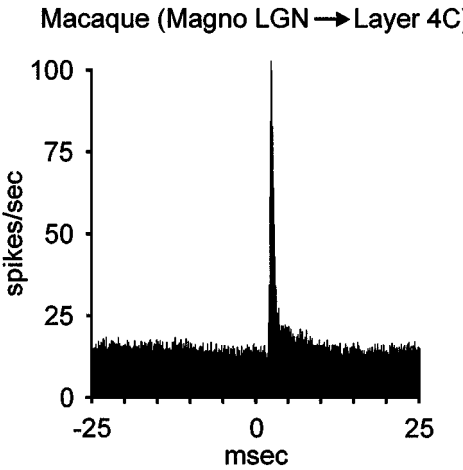

Figure 3 Cross-correlogram between a magnocellular neuron in the LGN and a neuron in layer 4C of macaque primary visual cortex (65). The narrow peak (0.7 msec full width at half maximum) displaced 2.4 msec to the right of zero indicates that the geniculate neuron provided monosynaptic input to the cortical cell. The monosynaptic input was strong; 17.6% of the cortical cell's spikes were triggered from a spike in the LGN cell. The strength of thalamocortical connections in the macaque, taken together with the anatomy of their projections—divergence with modest convergence—suggests that many neurons in layer 4C will receive strong common input and should therefore fire synchronous spikes (see text).

each thalamic afferent. Thus there should be ensembles of tightly correlated cells in layer 4C.

In the same manner that thalamic synchrony synergistically drives layer-4 neurons in the cat visual cortex, it is likely that synchrony in cortical layer 4 of the primate will be particularly effective in driving postsynaptic neurons in the cortex. Because of massive convergence of cortico-cortical connections, however, this form of synchronous firing is unlikely to be propagated to higher levels (66a).

Finally, it is an open question whether synchrony in the visual cortex can carry information about the stimulus. Ghose and colleagues have shown that the receptive field of the synchronous activity of two neurons is different from the receptive field of either neuron alone, but did not examine whether this difference could carry more information about the stimulus (62; but see 70, 71).

STIMULUS-DEPENDENT SYNCHRONY

The activity of neural populations can be synchronized by a visual stimulus in several ways. The truest form of stimulus-dependent synchrony is entirely independent of underlying neural connections, as in, for instance, the synchrony induced between the two retinas by a flash of light. There can also be a strongly stimulus-dependent component of certain types of synchrony from anatomical convergence (23) or of emergent synchrony (reviewed in 2, 3). Here, however, we consider only true stimulus-dependent synchrony of the first kind, in which a stimulus excites a neuron with a stereotyped time course. This type of synchrony—seen when an ensemble is time-locked to a stimulus—would require the faithful transmission of temporal information all the way from photoreceptors up to the neurons under study.

Most studies that use cross-correlation analysis have been concerned with characterizing neural connections; thus stimulus-dependent correlations have usually been treated as contamination to be avoided (6). Because of this historical bias in the literature of visual physiology in particular, fast stimulus-dependent synchrony has been largely ignored. This is in marked contrast to the literature of auditory physiology, in which both the precise time-locked neural responses to a stimulus and the subsequent detection of synchronous activity have been extensively studied (see E Covey & J Casseday, D Oertel, and L Trussell, this volume). In vision, however, there is a growing literature on the reproducibility of spike trains to a stereotyped input, which provides strong indirect evidence that visual stimuli can synchronize neurons on the time scale of several milliseconds. If neurons can respond to many repetitions of a stimulus with high temporal precision, then, assuming a homogeneous population, these neurons could also be synchronized at the same level of precision. As noted in the introduction to this review, temporal precision is usually defined

with respect to the interspike interval. Temporal precision faster than the interspike interval has been demonstrated in the invertebrate visual system (72), the vertebrate retina (73–75), LGN (75, 76), and middle temporal (MT) cortical area in the primate (77, 78; but see 66a, 79). A similar form of synchrony, but with lower temporal precision, can be inferred from the work of Richmond, Optican, and colleagues, who studied the responses of visual neurons to instantaneously presented spatial stimuli. In these studies, a variable degree of temporal reproducibility was seen in neurons of the primate LGN (80; see 81), striate cortex (82), and extrastriate cortex (83).

Stimulus-evoked synchrony requires not only that individual responses have high temporal precision, but that the stimulus excites the population simultaneously, such as with an instantaneous onset, rather than asynchronously, such as with smooth motion. Although the argument can be made that stimulus-dependent synchrony of this sort depends on a stimulus with an unnatural time course, it has been suggested that when the eyes alight on a new scene at the end of a saccade, the retinal stimulus is very similar to an instantaneous presentation of a new pattern (82). Recently, it has been found that in freely-viewing animals, neurons in the visual cortex in fact respond with brief bursts of activity following each small saccade (84; see 85). These bursts of activity in single neurons, which certainly must correspond to highly synchronous activity in the ensemble, are very likely important in visual processing. The bursts might help prevent the fading of a static image, but they might also provide a "time-zero" signal for temporal coding mechanisms (86).

Although stimulus-dependent synchrony has received the least attention of the three forms discussed in this review, it is the one form of synchrony that we can be certain is reproduced from one level to the next (but see 87). The 2–10 msec precision seen in the reliability of spike trains of neurons in cortical area MT under some conditions (median precision ~6 msec; 78) (77, 78) suggests that synchronous activity can be transmitted reliably from one level to the next—from the retina to the LGN, the LGN to the primary visual cortex, and so on. Again, we have inferred the existence of synchrony and its transmission from studies of reproducible spike trains. These studies have been concerned primarily with issues of coding and information processing, but similar experimental protocols could prove very useful in explicitly studying the transmission of synchronous activity to successive levels of processing.

EMERGENT SYNCHRONY: COHERENT OSCILLATIONS

Coherent oscillations can be taken as a special case of synchrony, in which two (or more) neurons are oscillating at the same frequency with a small phase difference between them. This will result in an oscillatory correlogram whose

peak is centered near time zero. Coherent oscillations of neuronal ensembles have been described in many studies of visual cortex (88, 89; reviewed in 2, 3). We call this synchrony emergent because, unlike synchrony caused directly by the activity of divergent inputs or by the responses to a flashed visual stimulus, coherent oscillations are thought to depend on complex interactions between membrane properties (90; see 91) and large ensembles of neurons. While neocortical oscillations were extensively studied first in the cat visual cortex (88, 89), synchrony based on coherent oscillations has been seen in cat sensorimotor cortex (92), rat somatosensory system (but at lower frequencies, 93), primate visual cortex (94–96), and primate motor cortex (97–100).

Within the visual pathway, coherent oscillations have been reported in the retina and LGN (58, 60, 101–104) but have been studied most intensively in the visual cortex. A recent study in the cat suggests that fast ($>\sim$50 Hz) subcortical oscillations can, in some cases, be transmitted to the visual cortex, but that slower oscillations ($<\sim$50 Hz) are cortical in origin (87). The amplitude of these slower intracortical correlations is variable, but it can in some cases be quite strong. The single-peaked correlograms seen in other forms of synchrony can be quantified in a simple manner—as the percentage of a neuron's spikes that are accounted for by the peak. Oscillatory correlograms can be quantified similarly—as the ratio between the oscillation amplitude and the baseline. In the cortex, a ratio of 0.50 is not uncommon; loosely speaking, this means that one half of the activity is coherent (although it does not follow that one half of the spikes are nearly synchronous).

Although many (but not all) groups find oscillatory activity in some visual cortical neurons, the importance of coherent oscillations in sensory processing is still a matter of debate. The most comprehensive view of the importance of oscillations has been proposed by Singer and colleagues (2, 3). Because these topics have been extensively reviewed, we discuss them only briefly. In outline, coherent oscillations have been proposed to bind a group of neurons into a coherent ensemble; that is, these oscillations make distant neurons stimulated by the same object fire together. Although this conjecture is far from proven, particularly in alert animals, it has been shown that when an extended stimulus excites many neurons simultaneously, the firing of these neurons can oscillate coherently. If this concerted activity defines an ensemble, then the ensemble itself may correspond to a distributed representation of a single percept. An attractive feature of this information-coding strategy is that ensembles can be dynamic; different extended stimuli will create different coherent groupings. Thus, in primary visual cortex, even entirely novel stimuli can be represented by the coherent activity of a particular ensemble.

In the absence of oscillatory activity, correlations between visual cortical neurons appear to be quite weak (usually on the order of 0.1% of total spikes;

19, 20). Presumably, the higher degree of synchrony seen in stimulus-evoked coherent oscillations stems from the tendency of weakly coupled oscillators to become entrained. Thus, if synchronization represents one strategy for combining the signals from a group of neurons so that they drive postsynaptic responses more strongly, then oscillatory activity might be an effective way of implementing this strategy. Below, we discuss whether this form of synchrony has perceptual consequences or whether it can be transmitted from one neural level to the next.

CONCLUSION: THE SIGNIFICANCE OF SYNCHRONOUS ACTIVITY

All three forms of synchrony described in this review—anatomical, stimulus-dependent and emergent—are prevalent throughout the visual system, but their significance is unclear. The most important question is whether synchrony is used at the perceptual level. This question has been posed in a number of recent psychophysical studies, with varied results. In all of these studies the general strategy was to use two or more sets of precisely timed stimuli to induce synchronous or asynchronous firing in populations of neurons, and then to assess whether these manipulations affected perceptual grouping of these populations. In some cases, there appeared to be a strong relation between stimulus-induced synchrony and high-order perceptual operations, such as figure/ground segregation; in other cases, synchrony appeared to be unimportant for perception (105–109). Television provides one example of a visual stimulus that can synchronize neurons at 60 Hz, as has been demonstrated in the cat LGN (110) and primate primary visual cortex (111). Despite likely behavioral consequences of watching television, there are no overt perceptual consequences of this synchrony.

Analysis of the neuronal, as opposed to perceptual, consequences of synchrony have centered around the transmission of synchronous activity to higher levels, in particular, on coincidence detection. The general issue of the precision of neurons in responding to temporal features has been a subject of considerable attention (4, 8, 112). The specific issue of coincidence detection has been analyzed in theoretical studies (113–116) as well as in several experimental systems. In the auditory system, it is clear that coincidence detection can be performed by neurons, such as in the nucleus laminaris of birds and the medial superior olive of mammals (see D Oertel, this volume). In vision, however, the ability of neurons (cortical neurons in particular) to act as coincidence detectors, or even to respond to precise temporal features, is disputed (reviewed in 66, 66a, 117–122). Evidence against coincidence detection by cortical neurons includes the large number of weak (and therefore weakly interacting) inputs (66, 66a) and the long membrane time constants (117). Arguments for the possibility of

coincidence detection include the existence of active conductances in dendrites (114, 120; see 123) and the emerging view that the integration time of neurons (loosely defined as the mean delay between input and output) during normal activity is much faster than the classical membrane time constant (124).

A neuron's integration time is determined not by its passive membrane properties in the absence of synaptic input, but by its overall behavior in more natural settings. This behavior is determined by many factors such as the timing of presynaptic mechanisms (see B Sabatini & W Regehr, this volume), the overall level of synaptic conductances (that act to lower the membrane time constant; see, for example, 125, 125a–c), active dendritic conductances, and the somatic spiking mechanism. In the simplest example, transduction from synaptic inputs into spiking activity does not usually follow the entire time course of an excitatory postsynaptic potential, but instead only its rising phase (126; see 8). Further, neuronal integration times are far from constant but can be sped up in several ways. In particular, it has been shown that (*a*) the integration time of visual cortical neurons can be decreased dramatically by strong visual input that includes both low and high frequencies (127), (*b*) the transduction from injected current to spiking at high frequencies is enhanced by superimposing a slowly modulated current (see 128–130).

This discussion of integration times does not address directly the interaction between two or more inputs or coincidence detection. Only a few experiments have addressed this sort of interaction directly. One study analyzed the interaction between sinusoidal current and synaptic input on the spiking activity of cortical neurons (131). At certain frequencies, synaptic input will evoke spikes within only a very narrow window in the sinusoidal cycle, as short as 2–3 msec. A second study, which analyzed the interactions between two thalamic inputs to a single visual cortical neuron, demonstrated that synchronous input from two thalamic neurons is stronger than the sum of the two inputs arriving separately (1). It is unclear whether such a result would generalize to cortico-cortical connections, particularly since they are considerably less effective (19–22) than thalamocortical inputs (47–49). Although it is perhaps unlikely that pairwise, weak interactions of synchronous cortical inputs are synergistic, larger synchronous ensembles may be.

In summary, synchronous activity among ensembles of neurons is found at all levels in the mammalian visual pathway, from the retina to the extrastriate cortex. Because of the strong feedforward connections in the visual system—from retina to LGN and from LGN to visual cortex—coincidence detection is likely an important mechanism in the processing of synchronous inputs. Thus, the correlated activity of even a pair of neurons may serve an important functional role. Within the cortex, however, connections are weak and coincidence detection of pairs of inputs is unlikely. Read-off of larger synchronous ensembles, however,

remains a possibility. For technical reasons, studies in vivo have lagged behind studies in vitro of the integration of synaptic input into postsynaptic responses. With the increasing use of multielectrode arrays to record simultaneously the activity of neuronal populations in vivo it is likely not only that we will unlock the rules that underlie the transmission of synchronous activity, but that we will develop a better understanding of the functional significance of synchrony.

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