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Temporal coding in the visual cortex: new vistas on integration in the nervous system

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Although our knowledge of the cellular components of the cortex is accumulating rapidly, we are still largely ignorant about how distributed neuronal activity can be integrated to contribute to unified perception and behaviour. In the visual system, it is still unresolved how responses of feature-detecting neurons can be bound into representations of perceptual objects. Recent crosscorrelation studies show that visual cortical neurons synchronize their responses depending on how coherent features are in the visual field. These results support the hypothesis that temporal correlation of neuronal discharges may serve to bind distributed neuronal activity into unique representations. Furthermore, these studies indicate that neuronal responses with an oscillatory temporal structure may be particularly advantageous as carrier signals for such a temporal coding mechanism. Based on these recent findings, it is suggested here that binding of neuronal activity by a temporal code may provide a solution to the problem of integration in distributed neuronal networks.

During the past few decades, neuroscience has been pervaded by the idea that the relevant level for describing how nervous systems work is that of the single cell. Guided by this assumption, which has been addressed by Barlow as the 'single neuron doctrine'[1], considerable progress has been made in understanding the constituents of neuronal systems at the cellular and molecular level. In contrast, our knowledge about the integrative functions of the nervous system is still poorly developed. This problem is particularly evident in cortical neurobiology. Although much has been learned concerning the structural and functional properties of single neurons and their connections, crucial questions concerning integration of cortical activity are still unresolved[2,3]. Increasing evidence suggests that many cortical functions are based on distributed processes that occur in parallel at different sites. However, it is still enigmatic how relationships are established between such distributed neuronal activities, even though this seems required to represent information about the environment or the internal states of the organism and finally to achieve coherent perception or action.

Visual information processing may be taken as an example to illustrate this need for integration, which is commonly addressed as the 'binding problem'[3]. It is well known by now that the visual system exhibits a high degree of functional specialization[4–8]. Neurons in most areas of the visual cortex process information only from a limited part of the visual field and respond only to a restricted range of feature constellations. Thus, the outputs of numerous cells must be integrated to create a complete representation of a particular object. Moreover, neurons detecting different attributes of an object tend to be compartmentalized in a modular fashion, and it has been argued that different features such as form, colour or motion are analysed independently by separate processing streams[4–8]. Accordingly, object representation requires integration across these different pathways. Unfortunately, there is no evidence for convergence of these processing streams onto a single target region that could provide the basis for a unified percept[3,8]. In the visual system, the binding of features pertaining to individual objects appears to be a prerequisite for figure–ground segregation and scene segmentation, i.e. for the distinction between several objects present in the visual field. Of course, similar problems arise in other sensory modalities, and mechanisms for binding are also required where sensory events have to be linked with motor acts or when stored information must be recombined during memory recall[3].

Classical approaches to the binding problem

In the framework of the 'single neuron doctrine' it is assumed that the binding problem can be solved by convergence of input from the primary processing stages onto single cells with highly specific response properties[1]. Such 'cardinal cells' are supposed to be located in 'higher' integrative cortical areas that correspond to the presumed final stages of visual information processing. However, a number of arguments suggest that single cell representations, while perhaps effective for specialized functions, cannot provide a general solution to the binding problem[2,3]. (1) This model suffers from a 'combinatorial explosion'. Since every new feature constellation would require a new 'cardinal unit', far too many cells would be needed to cope with the complexity of the perceived world and the variability of its aspects. (2) A large number of uncommitted cells would have to be reserved for the representation of new objects. (3) The model lacks unequivocal experimental support. The discovery of

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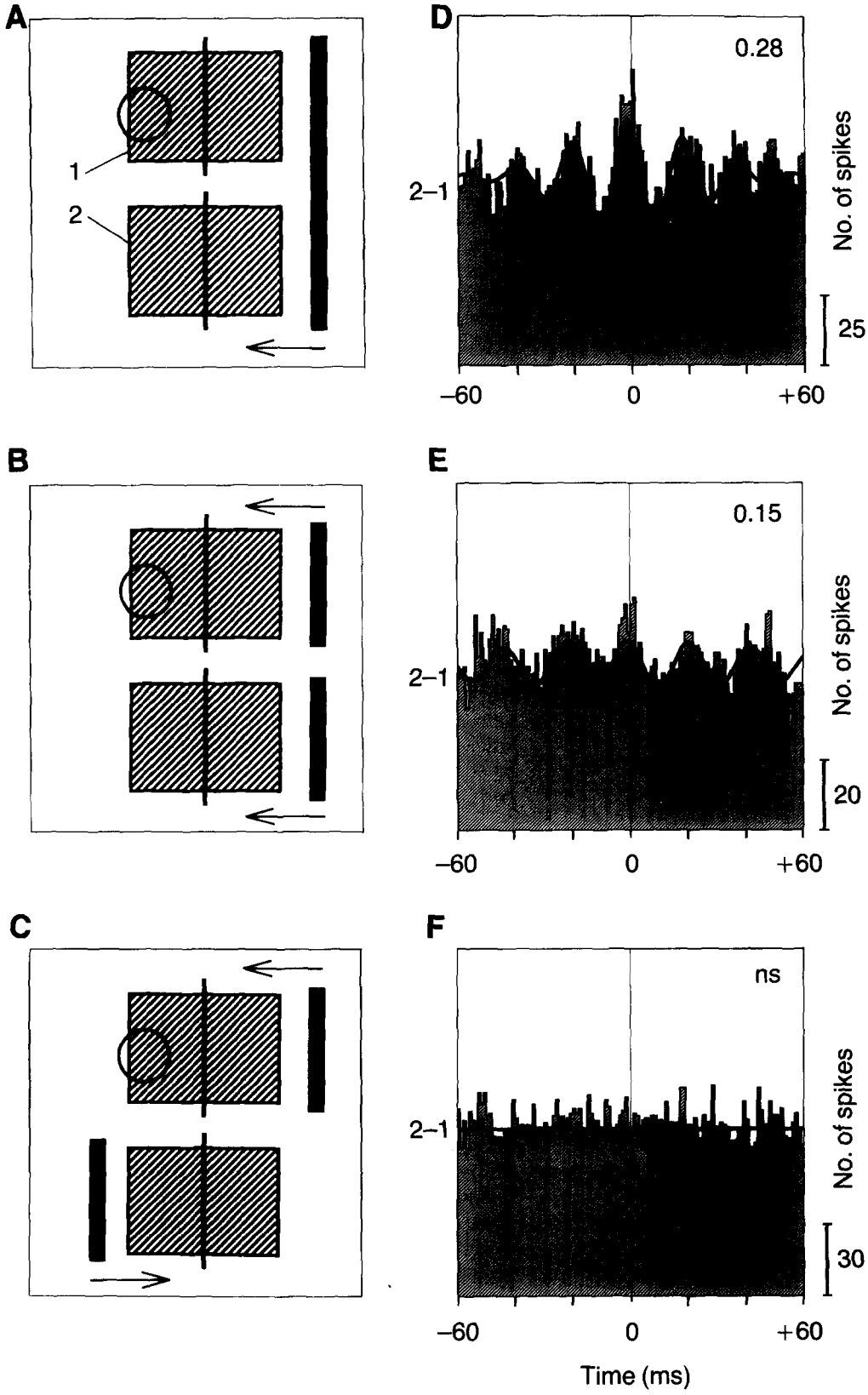

Fig. 1. *Long-range synchronization is influenced by stimulus coherence. Multiunit activity was recorded from two sites in area 17 of cat visual cortex that were separated by 7 mm. The two cell groups preferred vertical orientations.* **(A), (B), (C)** *Plots of the receptive fields. The colinear arrangement of the fields allowed the comparison of three different stimulus paradigms: a long continuous light bar moving across both fields (A), two independent light bars moving in the same direction (B), and the same two bars moving in opposite directions (C). The circle represents the center of the visual field, and the thick line drawn across each receptive field indicates the preferred orientation.* **(D), (E), (F)** *The respective crosscorrelograms obtained with each stimulus paradigm. Using the long light bar, the two oscillatory responses were synchronized, as indicated by the strong modulation of the crosscorrelogram with alternating peaks and troughs (D). If the continuity of the stimulus was interrupted, the synchronization became weaker (E), and it totally disappeared if the motion of the stimuli was incoherent (F). This change of the stimulus configuration affected neither the strength nor the oscillatory nature of the two responses (not shown). The graph superimposed on each of the correlograms represents a Gabor function that was fitted to the data to assess the strength of the modulation[26]. The number in the upper right corner indicates the 'relative modulation amplitude', a measure of correlation strength that was determined by computing the ratio of the amplitude of the Gabor function to its offset. Abbreviation: ns, not significant. Scale bars indicate the number of spikes.*

so-called face-selective cells in monkeys was first considered as a verification of Barlow's proposal (reviewed in Ref. 9). However, it has now been recognized that most of these cells respond to a range of face stimuli too broad to be compatible with the notion of 'cardinal cells'[10,11]. Moreover, neurons selective for many other items of our visual world have so far not been identified.

These problems have solicited alternative proposals that go back to the work of Hebb[12,13]. Hebb suggested that visual objects should be represented by assemblies of interconnected neurons rather than by the activity of single cells. Such assemblies are assumed to consist of neurons encoding elementary features and thus, in contrast to Barlow's proposal, complex representations can in fact be formed at early processing stages. In Hebb's model, cells responding to features of a particular object are bound into an assembly by the concurrent elevation of their average firing rate. Representing objects by assemblies has

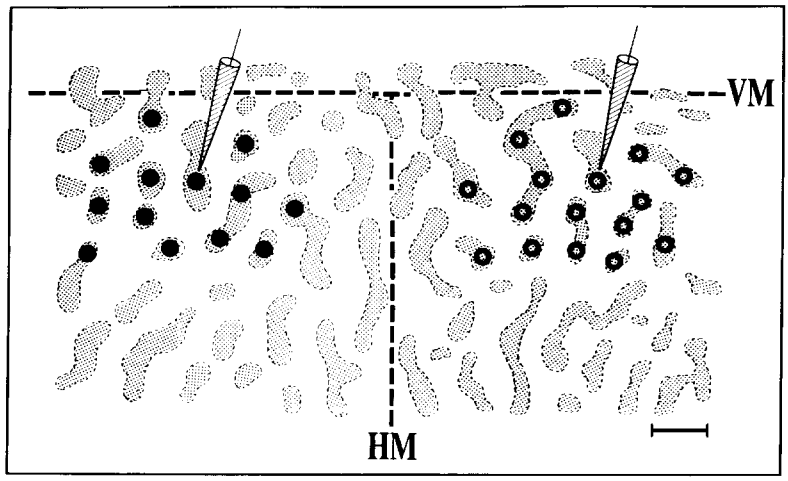

Fig. 2. *Cartoon of the experiment illustrated in Fig. 1. The recording situation was projected onto a map of orientation columns in area 17 generated by the 2-deoxyglucose technique (kindly provided by S. Löwel). Shaded areas represent bands of orientation columns responding to vertical contours. Electrode symbols indicate the two cell groups from which recordings were taken. The cartoon illustrates the measurement shown in Fig. 1C, F, where recordings were taken in response to light bars moving in opposite directions. The two cell groups are presumed to be part of two large assemblies (represented by dots and circles), which are activated by the two light bars. It can be assumed that the members of each of the assemblies oscillate in synchrony, whereas no constant temporal relationship exists between them, as shown by the physiological measurement. Note that the two assemblies are spatially separate. Using the long continuous light bar, the intervening shaded orientation bands would also be activated, thereby bridging the gap and inducing the formation of one large assembly of synchronously oscillating groups. Scale bar is 1 mm. Abbreviations: HM, representation of the horizontal meridian; VM, representation of the vertical meridian.*

several distinct advantages[13]. (1) Representations are more resistant to the loss of individual neurons. (2) Because individual feature detectors can at different times participate in different assemblies, this binding strategy economizes on the number of cells required for object representation. However, there is a major drawback of the Hebb model, which has only recently been recognized[14,15]. It relies on the assumption that only one assembly is activated at a time in a particular region of cortex, whereas other assemblies are suppressed[13]. While this might hold true for representations at very high levels of processing, it cannot be the case at more peripheral stages where processing of natural scenes, which always contain multiple objects on a complex background, requires the coactivation of several assemblies. This, in turn, poses a severe problem, because the concurrent activation of cells responding to different objects in the same cortical region makes it impossible to determine which cells belong to which particular assembly. As a result, false conjunctions of features become unavoidable[14,15]. This dilemma has been addressed as the 'superposition catastrophe' of the Hebb model[15].

Binding in the temporal domain

The outcome of these considerations is that a solution for the binding problem is needed that preserves the advantages of the Hebb model but provides additional degrees of freedom to label the cells that are part of one assembly. To this end, von der Malsburg[14,15] and Abeles[16] have suggested that assemblies might be defined by synchronous firing of cortical neurons, rather than by mere elevation of average firing rates. In such a 'correlational model', perceptual coherence of features in a visual scene is reflected by synchronous firing of the corresponding feature-detecting neurons. Thus, neurons responding to features of the same object discharge in synchrony, whereas cells responding to different objects are assumed to fire in an uncorrelated manner. This proposal is attractive for several reasons. (1) It preserves the general advantages of assembly representations, such as robustness and parsimony. (2) Binding by synchrony makes the grouping process resistant to amplitude fluctuations. (3) Assemblies are defined in a highly dynamical manner and cells can rapidly switch between assemblies by subtly changing the temporal relationships of their firing patterns. (4) Using such a temporal code would permit the coexistence of several assemblies in the same region of cortex, since the members of each assembly are tagged by their synchronous firing. Taking all of this into account, it seems that binding neurons into assemblies by a temporal code may provide an attractive solution to the binding problem.

Stimulus-induced oscillations in cat visual cortex

Recent experimental studies support the proposal that synchrony may be the 'glue' that binds distributed neuronal activity into unique representations. These studies were triggered by the discovery of stimulus-induced gamma oscillations in the primary visual cortex of the anesthetized cat[17]. Initially, these oscillations were observed in local field potentials, suggesting that numerous cells close to the recording electrode had synchronized their discharges and participated in rhythmic activity. Subsequent multiunit recordings confirmed that adjacent neurons indeed have a strong tendency to fire in synchrony and to engage in recurrent bursts at frequencies between 30 and 70 Hz[18,19]. This suggested that local groups[20] of coherently firing cells could be the building blocks for cortical representations and, based on these observations, it has been proposed that spatially separate groups might be bound into assemblies by synchronization of their oscilatory burst responses[18,19,21].

Local groups of simultaneously firing neurons seem to be particularly suited to establishing temporal relationships between spatially separate sites because these can influence distant targets much more effectively than individually discharging single cells. It should be emphasized that in this conceptual framework, which extends von der Malsburg's hypothesis, synchrony among distributed groups is the relevant code for binding, whereas the intrinsic temporal structure of the responses is, as such, not assumed to represent particular aspects of the visual input. This view is supported by the evidence that these oscillations exhibit a high degree of variability, being best described as fluctuations with a broad frequency spectrum[18,21], and do not depend on, for instance, orientation or velocity of the visual stimuli[19]. Oscillatory responses with these characteristics have also been observed in areas 18 and 19 of cat visual cortex[21,22], as well as in a visual association area located in the posteromedial lateral suprasylvian sulcus (PMLS)[23]. In addition, they have been demonstrated in the visual cortex of awake cats[24].

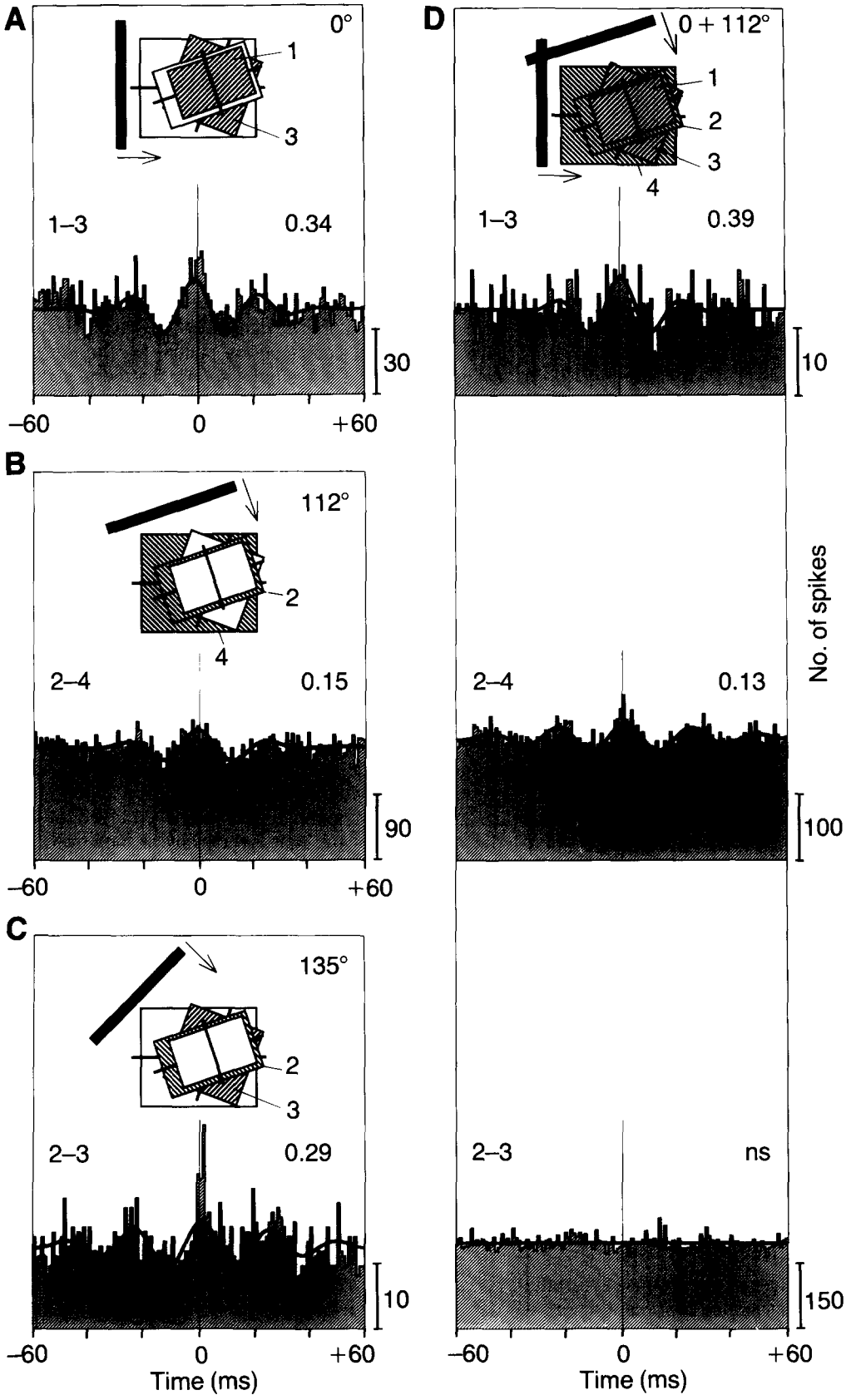

Fig. 3. *Stimulus dependence of short-range interactions. Multiunit activity was recorded from four different orientation columns of area 17 of cat visual cortex separated by 0.4 mm. The four cell groups had overlapping receptive fields and orientation preferences of 22° (group 1), 112° (group 2), 157° (group 3) and 90° (group 4), as indicated by the thick line drawn across each receptive field in (A)–(D). The figure shows a comparison of responses to stimulation with single moving light bars of varying orientation (left) with responses to the combined presentation of two superimposed light bars (right). For each stimulus condition, the shading of the receptive fields indicates the responding cell groups. Stimulation with a single light bar yielded a synchronization between all cells activated by the respective orientation. Thus, groups 1 and 3 responded synchronously to a vertically orientated (0°) light bar* **(A)**, *groups 2 and 4 to a light bar at an orientation of 112°* **(B)**, *and cell groups 2 and 3 to a light bar of intermediate orientation* **(C)**. *Simultaneous presentation of two stimuli with orientations of 0° and 112°, respectively, activated all four groups* **(D)**. *However, in this case the groups segregated into two distinct assemblies, depending on which stimulus was closer to the preferred orientation of each group. Thus, responses were synchronized between groups 1 and 3, which preferred the vertical stimulus, and between 2 and 4, which preferred the stimulus oriented at 112°. The two assemblies were desynchronized with respect to each other, and so there was no significant synchronization between groups 2 and 3. The crosscorrelograms between groups 1 and 2, 1 and 4, and 3 and 4 were also flat (not shown). Note that the segregation cannot be explained by preferential anatomical wiring of cells with similar orientation preference*[35] *because cell groups can readily be synchronized in all possible pair combinations in response to a single light bar. The correlograms are shown superimposed with their Gabor function (see Fig. 1). The number to the upper right of each correlogram indicates the relative modulation amplitude. Abbreviation: ns, not significant. Scale bars indicate the number of spikes.* (Taken from Ref. 37.)

Altogether, the phenomenon that has been denoted 'oscillation' can be defined as recurrent synchronous bursting of neuronal groups, with a fluctuation of the burst frequency over a broad range in the gamma band. As will be discussed below, the intrinsic temporal structure of such firing patterns may offer additional advantages for the establishment of synchrony between spatially distributed neurons and, hence, oscillatory signals may be well suited as carrier signals for a temporal code.

Binding within and between visual areas

Following the discovery of stimulus-induced oscillations, several predictions made by the correlational model of assembly formation have been tested in the cat. A key prediction is that spatially distributed cell groups should synchronize their responses when activated by a single coherent object. Indeed, recordings made using multiple electrodes have revealed a cross-columnar synchronization of oscillatory responses in area 17, both in anesthetized and awake

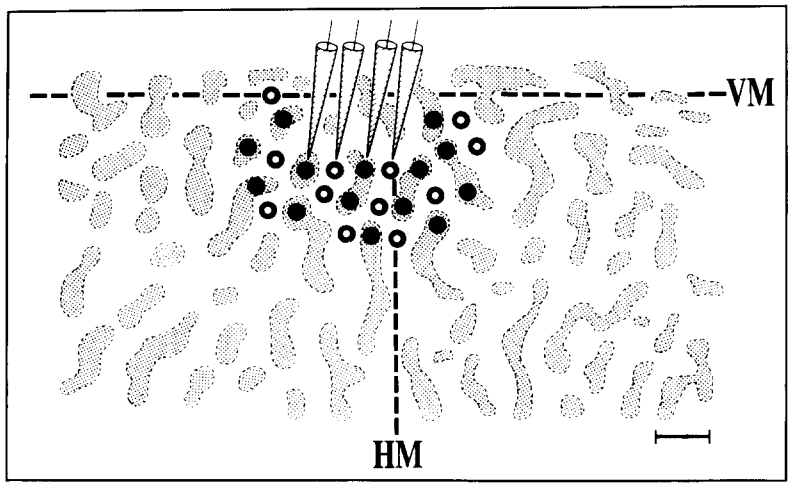

Fig. 4. *Assembly formation by cell groups with overlapping receptive fields. Shaded areas represent bands of orientation columns responding to vertical contours. If cell groups with overlapping receptive fields are stimulated by two independent objects (Fig. 3D), two spatially overlapping assemblies emerge that are desynchronized relative to each other (indicated by dots and circles). Each of these assemblies comprises synchronously firing cells, which is demonstrated directly by recording from four different sites in the cortex (Fig. 3D). In fact, the two bars activate most of the cells in this region, because the neurons have a limited orientation selectivity. By simply considering mean activity levels, it would only be known that a number of different feature detectors are active, but not whether they actually respond to two different objects or just a single one. However, with evaluation of the temporal relationships the whole set of active cells can be partitioned into two distinct assemblies. Scale bar is 1 mm. Abbreviations: HM, representation of the horizontal meridian; VM, representation of the vertical meridian.*

cats[21,24–26]. On average, the recorded cell groups synchronize with zero phase lag, even over spatial separations of more than 7 mm when activated by coherent stimuli[25,26].

Another important prediction is that response synchronization should occur between the two cerebral hemispheres. Since the visual cortex of each hemisphere receives direct retinal input from only half of the visual field, interhemispheric synchronization is required to bind features of objects that extend into both hemifields. The occurrence of interhemispheric response synchronization was discovered recently by simultaneous recordings from area 17 of the left and right cerebral hemispheres and was found to be similar to synchronization within area 17 with respect to strength and average phase relationship[27].

Finally, cell groups located in different visual areas should also be capable of synchronizing their responses. This follows if binding of the different features of an object is achieved by response synchronization and if different areas indeed represent different feature domains[4–8]. Interareal synchronization has so far been observed between areas 17, 18 and 19 (Refs 21, 22) and between areas 17 and PMLS[23]. Since area PMLS seems to be involved in the analysis of motion whereas area 17 processes fine details of an object, this may be considered as evidence for binding across feature domains. Altogether, these findings suggest that features of visual objects can indeed be linked by synchronization of feature-detecting neurons on a millisecond timescale. By using such a temporal code, distributed activity could be bound across columns, areas and even different hemispheres without the need for 'cardinal cells' or anatomical convergence of processing streams onto a single integrating cortical area.

Substrate of response synchronization

These findings raise the question of how response synchronization is achieved across columns and areas. The data on interhemispheric synchronization suggest that temporal correlation is established at the cortical level[27] and is not triggered by common input from the thalamus[28,29]. Since the visual afferents to the two hemispheres remain entirely segregated beyond the optic chiasm, there is no common input available and response synchronization between areas in the left and right hemisphere can only be achieved by interhemispheric connections, such as the corpus callosum. Indeed, it has been shown that if the corpus callosum is sectioned prior to recording from the two hemispheres, the response synchronization between hemispheres disappears while synchronization within either hemisphere is preserved[27].

Further evidence for response synchronization by cortico–cortical connections comes from recent experiments with strabismic cats[30,31]. In area 17 of the visual cortex of the cat, squint is known to induce a breakdown of binocularity[32]. The two sets of monocular cells tend to be clustered in columns driven by the left or right eye[31,32]. Physiological and anatomical studies of area 17 in strabismic cats show (1) that response synchronization occurs preferentially between columns of like ocular dominance[30], and (2) that only columns with the same ocular dominance are linked by tangential connections[31]. Thus, a tight correlation between synchronization and topography of intracortical connections is observed. Altogether, these data indicate that synchrony is achieved by reciprocal coupling at the cortical level. These results have two important implications. (1) They prove that reciprocal connections can establish synchrony with zero phase lag despite finite conduction delays[33]. In case of the callosal connections, these delays may amount to several milliseconds[34]. Previously, it has always been assumed that synchronous firing without phase lag could only be achieved by common input[35]. (2) These results assign a new putative function to reciprocal connections within and between cortical areas. Rather than contributing exclusively to receptive field properties, these connections may actually mediate the binding of distributed activity.

Stimulus dependence of synchronization

If a temporal code is indeed used in the cortex for assembly formation and feature binding, it must be shown that correlated firing occurs in a stimulus-dependent manner and, moreover, that this mechanism permits the coexistence of different assemblies. Uniform and stereotyped synchrony of neuronal responses could hardly convey any useful information about the coherence of features in visual scenes. Thus, cells in the cortex should oscillate in synchrony only if they respond to the same object, but otherwise fire in an uncorrelated manner. As shown already by the Gestalt psychologists, criteria such as continuity, proximity, similarity and common fate are used perceptually to group parts into wholes[36]. If temporal correlation between cortical neurons provides a basis for object representations it should reflect these coherence criteria.

Evidence for dependence of synchronization on such Gestalt criteria has been obtained in a recent study[25]. It was demonstrated that cell groups in area 17 with nonoverlapping receptive fields oscillate synchronously if they are activated by a single continuous stimulus, whereas their firing is uncorrelated if two independent stimuli are presented that move in different directions (Fig. 1). Thus, when activated by a single stimulus, the cells join one assembly, whereas when they are activated by two stimuli, they couple to two different assemblies that are spatially disjunct and desynchronized relative to each other (Fig. 2). This experiment shows that Gestalt criteria such as continuity of contours and coherent motion are indeed important for the establishment of synchrony. Furthermore, it provides evidence for a stimulus-dependent assembly formation by response synchronization.

Similar effects can be observed if the recorded cell groups have overlapping receptive fields[37] (Fig. 3). If stimulated with a single light bar, such cells fire synchronously, even if they differ in their preferred orientation[25,26]. However, if two superimposed stimuli with different orientation and direction of motion are presented the same cells segregate into two assemblies. Although these assemblies are spatially superimposed (Fig. 4), they can be recognized as distinct because their firing is uncorrelated. These data show that response synchronization allows, in principle, the distinction of several co-existing representations in the same region of cortex. Hence, they suggest that the superposition problem may be solved by temporal coding[14,15]. Moreover, these findings underline the flexibility and parsimony of temporal coding as a potential binding mechanism. If the input configuration is altered, the very same cells can recombine into quite different assemblies by changing their temporal relationships. Figure 5 illustrates how this effect can be explained in terms of a simple model[38].

Why should cortical responses be oscillatory?

The data obtained in the cat indicate that stimulus-induced synchronization of distributed responses is usually associated with the generation of oscillatory activity. This raises the question of whether the intrinsic temporal structure of such oscillatory signals is relevant for synchronization. As discussed above, the oscillatory multiunit responses observed in the cat visual cortex can be characterized as burst sequences with a broad frequency spectrum. Thus, the distribution of spikes in such responses is certainly not random nor, on the other hand, is it strictly periodic. The limitation of the frequency band, i.e. the fact that the interburst intervals do not vary randomly but preferentially adopt values between 15 and 35 ms, has several potential advantages. First, cells engaged in such a rhythmic response pattern can be synchronized more easily by slowly conducting reciprocal connections than cells exhibiting entirely unstructured activity. Response synchronization between the two hemispheres provides a paradigmatic example[27]. In this case, synchronization without phase lag is possible because the oscillatory signals foster cooperative effects between coupled neurons that improve the synchronization from one burst to the next[33]. It seems hard to imagine how transcallosal synchroniz-

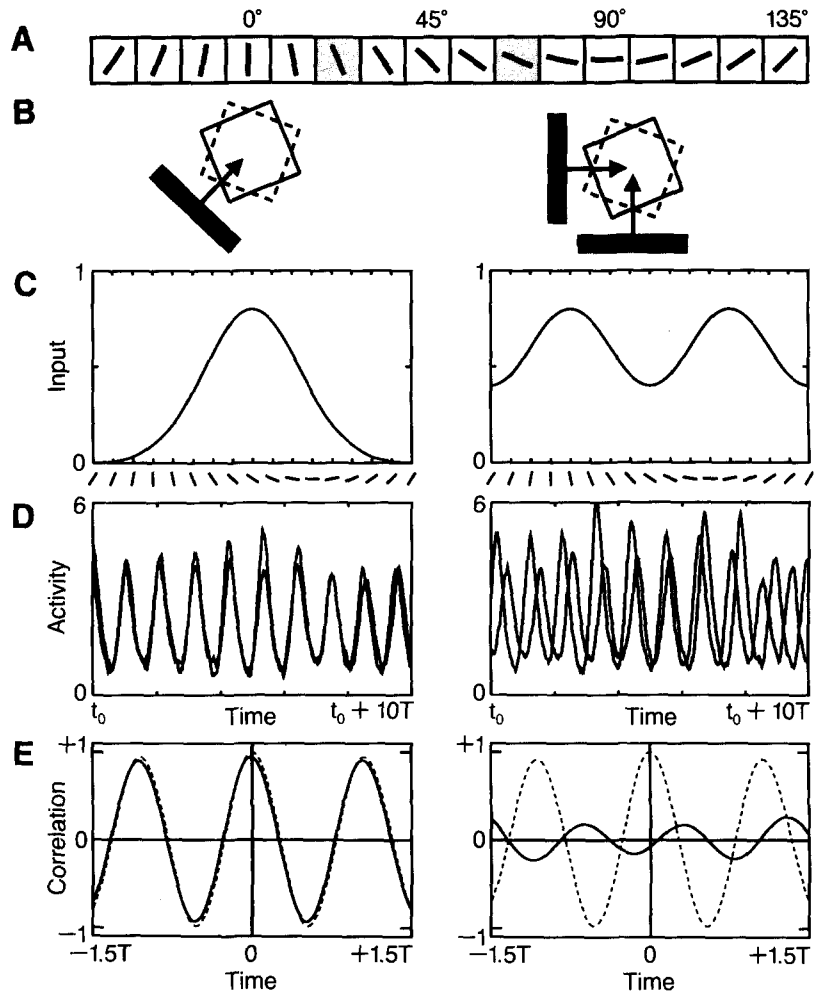

Fig. 5. *Stimulus dependence of synchronization in a neural network model.* **(A)** *The network consists of a chain of 16 oscillators that are assumed to represent orientation-selective neuronal populations with overlapping receptive fields. This arrangement is similar to that of a cortical 'hypercolumn'. Each oscillator (symbolized by a square) consists of an excitatory and an inhibitory subpopulation that are mutually coupled by delay connections. The excitatory subpopulation receives external input, which has no intrinsic temporal structure. Tangential connections between different oscillators have a dual function. Oscillators with similar orientation preference are linked by synchronizing connections. In addition, desynchronizing connections are implemented between oscillators that differ by 22° to 56° in their orientation preference. Both sets of connections are excitatory, and their differential effect results from the fact that synchronizing connections terminate at inhibitory subpopulations, whereas desynchronizing connections provide input to the excitatory subpopulation of the target oscillators[38]. The network has cyclic boundary conditions. (For further details, see Refs 33, 38.)* **(B)** *In analogy to the physiological experiment illustrated in Fig. 3, the network is tested with two stimulus configurations: either a single bar (left) or two superimposed bars (right).* **(C)** *Distribution of the input activity along the chain of oscillators (ordinate), representing the two stimulus conditions shown in (B).* **(D)** *Activity traces from the two oscillators tinted in (A). Neuronal activity is modeled as a continuous time series that is analogous to a field potential. In the case of a single stimulus (left), the two monitored oscillators are strongly synchronized and are therefore assumed to belong to the same assembly. In contrast, if the network is stimulated by two bars (right) the two oscillators do not have a fixed phase relationship and are coupled to two different assemblies. Under these input conditions the desynchronizing connections drive the two assemblies out of phase. Note that within each stimulus configuration, input to the two monitored oscillators is identical (C).* **(E)** *Mean normalized autocorrelograms (dashed line) and crosscorrelograms (solid line) of activity traces from the two oscillators shown in (D). The correlograms are averaged over 20 trials, each lasting for 20 cycles. The averaged correlograms confirm that two stimuli induce a segregation of the 'recorded' oscillators into two assemblies. This change of the temporal relationship occurs without any modification of synaptic efficacy. Abbreviation: T, period time of the isolated oscillator.*

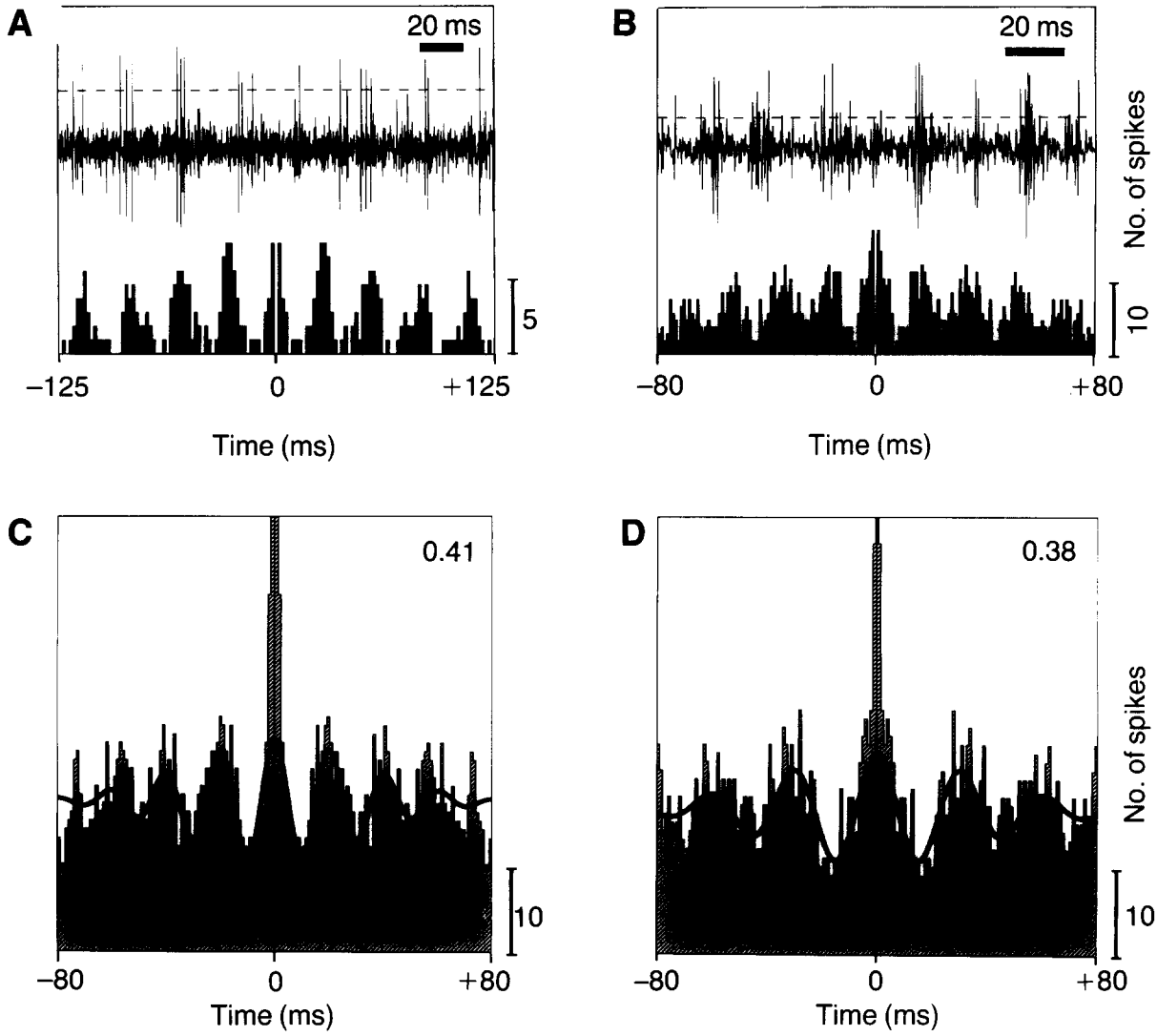

Fig. 6. *Oscillatory responses in extrastriate cortex of the awake macaque monkey. Multiunit responses to moving light stimuli were recorded from motion-sensitive areas in the superior temporal sulcus while the monkey was performing a fixation task. The figure illustrates data from four different recording sites.* **(A), (B)** *Two examples of response epochs with an oscillatory discharge pattern. Below the spike trains the corresponding autocorrelograms are shown. The presence of multiple peaks and troughs in the autocorrelograms indicates that the burst-and-pause sequences, which we term oscillations, had a comparatively narrow frequency band. Note that spikes of different cells are grouped into bursts.* **(C), (D)** *Autocorrelograms of oscillatory response episodes that were averaged over ten (C) and five (D) trials to the same stimulus, respectively. The correlograms were computed in a 500 ms window. The average oscillation frequencies were 49 Hz (C) and 33 Hz (D). Each correlogram is shown superimposed with the Gabor function (thick continuous line) that was fitted to the correlogram to assess the significance of the modulation[26] (see Figs 1, 3). Scale bars indicate the number of spikes.* (Modified from Ref. 41.)

ation could be achieved with randomly arriving spikes.

As shown by simulation studies, a second advantage of oscillatory activity is that network elements that are not linked directly can be synchronized via intermediate oscillators[33,39,40]. This may be important, for instance, to establish relationships between different sensory modalities. Finally, coupled oscillators can be reliably synchronized with zero phase lag even if the conduction delays show a broad distribution[33] and are not homogeneous in the network – a constraint that a physiological binding mechanism certainly has to cope with. In conclusion, the recurrent temporal structure of oscillatory responses seems to have crucial advantages for the synchronization of spatially separate cells in the cortex. Therefore, we suggest that oscillations, while not conveying stimulus-specific information *per se*, may be instrumental as carrier signals for the formation of assemblies by a temporal code.

On the other hand, it seems advantageous that the observed oscillations are not strictly periodic but exhibit some jitter of their frequency[41]. (1) Cell groups can be desynchronized more easily if their oscillations are broad banded so that the network can be prevented from entering global states of synchrony that would be inappropriate for information processing. (2) The number of possible representations that can coexist in the same cortical region is increased by variable oscillation frequencies, because spurious correlations due to aliasing effects will be rare and only of very short duration. Thus, a broad-banded oscillatory signal appears a reasonable compromise between several opposing constraints.

Evidence for temporal coding in other species and modalities

A question of particular interest is whether synchronization of oscillatory responses can also be

observed in the monkey visual system – in particular, when the animal is alert and performs a behavioural task. Recently, Kreiter and Singer[41] have discovered oscillatory responses, which can synchronize between spatially separate sites, in the extrastriate cortex of the awake behaving macaque (Fig. 6). As in the cat, coherent bursting of cell groups is a prominent feature of the responses. However, the oscillations seem to be more irregular in the monkey and, as a result, are even more difficult to detect with averaged autocorrelograms. Synchronized oscillatory responses have also been recorded from the striate cortex of anesthetized monkeys[42]. Furthermore, gamma activity can be observed in EEG recordings from the visual cortex of monkeys[43], providing additional evidence for synchronous activity of large neuronal populations in this frequency range. These findings demonstrate unequivocally that gamma oscillations with the overall characteristics discussed above are present in the primate visual system, and they suggest that temporal codes may be employed in species other than the cat.

Synchronized gamma oscillations have also been observed outside the visual system. Synchronization in this frequency band is well known to occur in the olfactory bulb and entorhinal cortex of various species[44]. Remarkably, a synchronization of oscillatory activity between somatosensory and motor areas has recently been described in the awake behaving monkey[45]. This suggests the intriguing possibility of crossmodal integration by a temporal code. Moreover, recent magnetic field recordings from human subjects have also provided evidence for synchronization phenomena in the gamma frequency band[46,47]. In addition to this growing evidence for response synchronization across spatially separate sites, oscillatory activity has now been reported in a wide variety of structures. These include somatosensory[45,48], motor[45] and association[28] cortices as well as thalamic nuclei[29,49], and also the avian optic tectum[50]. In cases where this oscillatory activity has been observed in field potential or EEG recordings it can be assumed that this resulted from the synchronous activation of a large number of neurons. It needs to be emphasized, however, that the mere presence of oscillatory discharge patterns or the mere occurrence of synchronous firing are not yet sufficient evidence to prove the hypothesis of temporal coding. Rather, this requires the demonstration of feature- or action-specific synchronization, which needs to be assessed by simultaneous recording from spatially separate neurons.

Concluding remarks

This article has briefly reviewed recent experimental findings compatible with the hypothesis that integration in distributed neuronal networks occurs on the basis of a temporal code. Central to the problem of cortical integration is the need to bind distributed neuronal activity into organized patterns. A possible solution to this problem that emerges from the results discussed above can be summarized as follows: (1) Binding of cells into functionally coherent assemblies may be achieved by a temporal code using synchronization on a millisecond timescale. A crucial advantage of this mechanism would be that it permits the coexistence of several assemblies in the same region of cortex. (2) In the particular case of sensory systems, this mechanism may provide a solution to the fundamental problems of scene segmentation and figure–ground segregation. Studies of the visual cortex indicate that segmentation may be achieved by synchronization of the firing of neurons responding to the same object, while desynchronization occurs when cells code for different objects in the visual field. A similar mechanism might integrate distributed information in the motor system and in association cortices. (3) The available evidence suggests that oscillatory activity, maintained by local groups of coherently active cells, might be particularly well suited as a carrier signal for a temporal binding mechanism. Oscillations *per se* do not seem to have a representational function, but they may offer distinct advantages for the establishment of synchrony, especially between widely separated groups.

While the data available so far are compatible with the hypothesis that expressing relationships by a temporal code may contribute to the integration of parallel and distributed processes, a number of serious problems remain unresolved. One is related to the 'readout' of temporal codes. Since neurons function essentially as coincidence detectors, they are ideally suited to discriminate between synchronous and asynchronous inputs. Readout of temporally coded assemblies could thus be achieved by networks at other processing stages that are capable of treating coherent and incoherent input differentially. However, it remains an intricate problem how cell assemblies in sensory areas can be linked to assemblies in other centres, especially in those involved in controlling action. Such links must be highly dynamic and flexible since a particular sensory input can trigger quite different behavioural patterns. Hence, depending on the context, sensory assemblies must be able to couple to quite different sets of cells in effector areas. However, it should be stressed that this problem of a flexible readout is not specific to the concept of temporal coding but is of similar significance in the framework of other binding models. The temporal coding strategy advocated here might actually have certain advantages for such a dynamic readout since, as indicated by the data discussed above, binding that is flexible and dependent on context is one of the characteristic features of this mechanism.

Even if it were possible to demonstrate that evaluation of temporal relationships could, in principle, be employed to solve the binding problem and to establish flexible links between cell populations in sensory and motor areas, it remains to be shown that the nervous system actually uses temporal coding. Clearly, further experiments on alert and behaving animals are required to establish more direct correlations between the temporal relationship of simultaneously recorded neurons and perceptual or behavioural performance. Ultimately, in order to prove their causal relevance it will be necessary to manipulate these temporal relationships and to demonstrate predicted changes in behaviour.

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Local circuits for the control of leg movements in an insect

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To produce behaviour that is adaptive, local circuits in the CNS must transform mechanosensory signals from receptors on the body into changes in movement. Substantial insights into the mechanisms underlying these transformations can be obtained by analysing the local circuits of animals from which intracellular recordings can be made from identified neurones during behaviour, thus allowing the complete pathways between inputs and outputs to be followed. In the locust (Schistocerca gregaria) *these circuits contain both non-spiking and spiking local neurones so that it is possible to elucidate two basic issues of neuronal integration: (1) the operation of the reflex circuitry that must adjust locomotion, and (2) the integrative role of local circuits that use graded interactions in complex neuropil, perhaps even involving compartmentalized neurones.*

The neuronal circuits controlling locomotion and posture must generate complex yet coordinated patterns of impulses in the motoneurones that innervate the muscles of the limbs so that the appropriate joints are moved in the correct sequences. Detailed analyses of these circuits at the cellular, synaptic and network levels have already shown the necessary conditions required for motor patterns to be produced. As expected, the generalities concerning mechanisms are greater at the lower levels than at the higher ones. Nevertheless, the analyses of networks have led to a detailed understanding of the connections between neurones that lead to motor patterns in animals as diverse as worms[1], molluscs[2], insects[3], crustaceans[4], lampreys[5] and amphibians[6].

In all of these animals, the circuits must also respond to the sensory signals generated by proprioceptors as a consequence of the movements, to the signals from exteroceptors on the surface of the body that indicate contact with other objects, and to signals from other parts of the CNS. In general we know much about the behavioural effects of a sensory input, but little about the underlying integrative mechanisms. An analysis of the processing of exteroceptive signals provides a convenient point of entry for understanding these mechanisms, particularly when limited to an animal with jointed legs: the signals are not necessarily linked to a particular phase of the cycle of movements and can therefore initially be analysed in an animal that is stationary. The movements caused by stimulation of such receptors are often local responses of one leg, but the local circuits controlling

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