Cortical coordination dynamics and cognition

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New imaging techniques in cognitive neuroscience have produced a deluge of information correlating cognitive and neural phenomena. Yet our understanding of the inter-relationship between brain and mind remains hampered by the lack of a theoretical language for expressing cognitive functions in neural terms. We propose an approach to understanding operational laws in cognition based on principles of coordination dynamics that are derived from a simple and experimentally verified theoretical model. When applied to the dynamical properties of cortical areas and their coordination, these principles support a mechanism of adaptive inter-area pattern constraint that we postulate underlies cognitive operations generally.

The brain is such a complex organ that, more than other organs of the body, a fundamental issue is how to approach a comprehensive understanding of its large-scale functions. For cognitive function, in particular, although a variety of alternative proposals have purported to describe relevant underlying brain operations, it has been unclear whether a single unifying perspective exists. Despite their merits, most theoretical accounts in cognitive neuroscience have a limited focus on only one system or function. A major stumbling block concerns the coordination problem: how, for any given cognitive function, the (non-linear) coupling among component parts gives rise to a wide variety of complex, coordinated behaviors. In this review, we propose coordination dynamics as an integrating framework for cognitive function in general[1,2]. The study of coordination dynamics seeks to identify the key variables of coordination (defined as a functional ordering among interacting components) and their dynamics (rules that govern the stability and change of coordination patterns and the non-linear coupling among components that give rise to them). Our approach is first to identify neural components that are appropriate to cognitive function, and then investigate the ways in which those components change their relationships in time. We focus on the cerebral cortex, which is particularly relevant to cognition, and consider the appropriate cortical component to be the local area, because it is at this level that cortical pathways, both within the cortex and with subcortical structures, are organized. The cortical area is conceived as an organized set of locally interacting neuronal populations that receives synaptic inputs and sends axonal projections as a functional unit.

Our goal is to address the critical question of how interactions among the large number of anatomically distinct cortical areas give rise to the emergence of cognitive function in real time. We express this question more concisely by asking what are the large-scale coordination dynamics of the cortex corresponding to cognitive dynamics. The coordination dynamics of a complex system refers to the manner in which states of interdependency among the parts change with time. Framing the question in this way opens an avenue for understanding cortical interactions in terms of general principles that have been found to apply to a wide variety of coordinative phenomena. These principles derive from concepts of self-organization and pattern formation that use the language of coupled non-linear dynamics to describe how patterns of coordination arise and evolve in time[2,3]. A central concept of self-organization is that of the 'collective variable', a variable that specifies the relationships among interacting components in a dynamical system in a state-specific manner. In this review, the relative phase between two neuronal populations located in different cortical areas is considered as the primary collective variable, and is used to describe the coordination dynamics of cortical areas. Of course, depending on the level of description, other collective variables are possible. For example, the frequency of a synchronized neuronal population can be a collective variable with respect to the cellular components that are coupled together at lower levels. The phase relationship is a good choice for a candidate collective variable because it clearly captures the spatiotemporal ordering between cortical components. Moreover, relative phase changes more slowly than other variables that might describe the individual local area. Importantly, relative phase has been demonstrated, in both brain and behavioral studies, to change abruptly at state transitions[4–6].

It has long been appreciated that complex cognitive functions are organized at a global level in the brain and that they arise from more primitive functions organized in localized brain regions[7,8]. Today it is widely recognized that these dual aspects are reflected in cortical function: large-scale processing by sets of distributed, interconnected, areas and local processing within areas[9,10]. What is not as well appreciated is that this duality is a fundamental property of complex systems that are operating in a 'metastable' dynamic regime[2,11,12]. Metastable dynamics is distinguished by a balanced interplay of integrating and segregating influences[11], and metastable systems rank high when their degree of complexity is measured[13]. Through an explicit example, we demonstrate how this balance between interdependence and independence gives rise to the relative coordination that is characteristic of

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normal cortical function. We scrutinize the coordination of cortical areas by examining distributions of their relative phase. Relative coordination among cortical areas provides cortical function with a flexibility that is due, we propose, to metastable dynamics. We show that the cortex makes use of this flexibility to adapt rapidly at both large-scale and local levels to the changing contingencies of cognitive function.

Evidence for relative coordination of cortical areas

We apply here the principles of coordination dynamics (see Box 1) to the question of how cortical areas function as interacting components within the overall cortical system. Recent evidence suggests that the metastable regime of the coordination dynamics corresponding to relative coordination is crucial to understanding the interaction of cortical areas[14–16] (see Ref.2 for evidence in the fields of perception and motor control).We review this evidence in light of the theoretical considerations in Box 1 as a step toward establishing relative coordination as the basis for large-scale cortical network operations. Note that, although the focus is on cortico–cortical interactions, we realize that these must ultimately be understood within a larger, whole-brain framework that also includes cortical–subcortical interactions.

We begin with the event-related local field potential (LFP) as the signal of interest[17–21]. The LFP results from currents flowing in the extracellular field due to the synchronous dendritic activity of a group of neurons in a localized volume of cortical tissue. Although the LFP obscures the specific contributions of the individual neurons in the group, it has the advantage of revealing the part of their activity that they have in common. It is this common activity that is important for understanding the interaction of cortical areas, because the transmission of pulse activity from one area to another is effective at the level of the neuronal group, not that of the single neuron. Of course, the LFP itself is not transmitted between areas; that is accomplished by axonal pulses. However, the LFP, reflecting the joint postsynaptic dendritic activity in the local neuronal group, is directly related to the integral of pulse inputs impinging on the dendritic trees of the group, and to the integral of pulses generated on its axons. Therefore, the LFP reflects the actions exerted by cortical areas on one another over cortico–cortical fiber pathways, or through subcortical relay nuclei. Furthermore, there is growing evidence that LFP oscillations play an important role in a range of cognitive processes[22,23].

In considering the application of the coupled two-component system (Box 1) to the dynamic behavior of interacting areas in the cerebral cortex, we are led to treat the relative phase of LFPs from different cortical locations as a collective variable of the cortical system. In so doing, we are immediately in the broken symmetry condition described in Box 1, because there is evidence that areas have different characteristic spatial and temporal properties (e.g. characteristic frequencies)[24,25]. In addition, delays in transmission between areas might contribute to broken symmetry, as might other factors such as inter-area influences related to intention, learning and memory[2].

Evidence that relative coordination is a basic feature of the interrelations between cortical areas derives from a well-studied experimental paradigm in which rhesus macaque monkeys performed a visuomotor pattern discrimination task. During task performance, LFP recordings were made from chronically implanted electrodes at sites in several distributed cortical areas in one cerebral hemisphere[26]. Parametric models were constructed from the recorded LFPs in very brief time windows throughout the successive stages of task processing. It was demonstrated that these models capture important dynamic properties of the LFP data[15,16]. Spectral coherence was measured from the models for all pairs of LFP recording sites in all time windows. Because spectral coherence measures the relative phase concentration of LFP signals, it was used as an index of the coordination of activity from different cortical sites (Box 2).

Cortical coordination dynamics was studied by observing the temporal evolution of the spectral coherence between LFPs from different cortical sites. In Fig. IIb of Box 2, the peak at 12 Hz in the coherence spectrum of striate and inferotemporal cortical sites indicates that the two sites have a high degree of phase concentration at this frequency in a time window centered 130 ms after stimulus onset. Figure 1a shows the modulation of the 12 Hz coherence level between these sites over the entire time course of the task, and demonstrates that this peak value is attained only briefly. The rapid transition from low to high coherence, and back again, is indicative of the relative coordination of these sites – their ability to partially synchronize their oscillatory activity without becoming locked into global synchronization. The central value of relative phase concentration, shown in Fig. 1b, is modulated over the time of the task. Although the relative phase takes on a wide range of values, it stabilizes for a short period around 130 ms, when the coherence is at its peak.

Convergence of the 12 Hz relative phase relationship between these two sites to a consistent value, repeatedly over a large number of trials, as demonstrated by the elevation of coherence in Fig. 1, is indicative of functional involvement of the sites in this stage of task processing. Although the nature of that involvement is still uncertain, the extended duration of the episode of elevated coherence suggests that it does not simply reflect first-pass feedforward transmission of pulse activity from the striate to inferotemporal site. In fact, recent findings suggest that during the time of elevated coherence, both feedforward and feedback causal influences are exerted between these two areas[27].

Box 1. Principles of coordination dynamics

A theoretical model of coordinative interaction in a relatively simple two-component system was originally introduced by Haken, Kelso and Bunz (Ref. a) as a theoretical account of phase transitions in interlimb coordination discovered earlier[b]. This account is referred to in the literature as the HKB model. The HKB model was extended to include the impact of microscopically generated stochastic fluctuations (the noise term ξ_t of strength $Q^{1/2}$ in Eqn 1)[c] and frequency differences among interacting components ($\Delta\omega$ in Eqn 1)[d]. Eqn 1 is highly informative because it exemplifies a law of coordination that has been found to be independent of the specifics of system structure. That is, Equation 1 captures the coordination between behaving components of the same system, between an individual and the environment, and even between two individuals socially interacting[e,f]. All extraneous features of a real world system have been stripped away, leaving the bare dynamics accessible for examination.

Although the system comprises two components, we are primarily interested in their coupled, or coordinated, behavior. Therefore we consider the dynamics in terms of the collective variable Φ, the relative phase between the two interacting components. The phase relationship is an excellent candidate for a collective variable because: (1) it captures the spatiotemporal ordering between the components; (2) it changes more slowly than the variables that describe the components; and (3) it changes abruptly at bifurcations or phase transitions. An essential way to represent the dynamics is to express the relationship between variables and their time derivatives as a family of phase plane or vector field trajectories. In the present case, the relationship is simply between the first time derivative of Φ (i.e. $\dot{\Phi}$) and Φ itself. With this in mind, the coordination dynamics is defined by the equation:

$$\dot{\Phi} = \Delta\omega - a\sin\Phi - 2b\sin 2\Phi + \sqrt{Q}\,\xi_t$$

where a and b are coupling parameters, $\Delta\omega$ represents the intrinsic frequency difference between the uncoupled components, and ξ_t is a stochastic noise term of strength $Q^{1/2}$.

The simplest dynamics occurs when the parameter $\Delta\omega$ is zero, meaning that the intrinsic frequencies of the two components are equal[a]. This is the symmetric case shown in Fig. Ia, which displays the vector field of the relative phase dynamics as a function of the coupling ratio b/a, when $\Delta\omega$ equals zero. Because the behavior of the system is different, sometimes qualitatively different, depending on the coupling ratio b/a, the ratio is referred to as a 'control parameter'.

Transformations in coordination dynamics that result from changing the control parameter are best characterized by observing the values of Φ for which $\dot{\Phi}$ is zero. These are the fixed points of the system. A fixed point can be stable and attracting, or unstable and repelling. When the value of b/a is high, meaning that the frequency of oscillation is low and the period is long (Fig. Ia), two stable fixed points (indicated by black lines and converging arrows) exist at $\Phi = 0$ degrees and $\Phi = 180$ degrees. The fact that the slopes at these points are negative signifies that these represent stable and attracting states, namely the in-phase and out-of-phase attractive coordinative states of the system. Two unstable fixed points surround the stable fixed point at $\Phi = 180$ degrees in Fig. Ia. These points (indicated by gray lines and diverging arrows), at which the slopes are positive, represent unstable, repelling states. Notice that at a critical value of b/a, the stable and unstable fixed points collide in a so-called 'pitchfork bifurcation'. Coordination switches to the only remaining stable fixed point in the system at $\Phi = 0$ degrees and stays there forever. The point, though, is that how the system moves in the parameter space of its dynamics determines the pattern and changes in pattern observed.

The condition of particular interest to us in studying cortical dynamics occurs when $\Delta\omega$ is not equal to zero[d] (Figs Ib,c). In this case, the dynamics displays what is called 'broken symmetry', because the two components have different intrinsic frequencies. Broken symmetry is a critical prerequisite for metastable dynamics, which we propose is a crucial feature of brain function. When $\Delta\omega$ is not zero, decreasing the value of b/a causes the stable fixed points near $\Phi =$ 0 degrees and $\Phi = 180$ degrees to shift or adapt to the new conditions (Figs Ib and Ic, bottom). Notice that each stable fixed point is paired to an unstable fixed point (gray lines and open circles). When the stable and unstable fixed points near $\Phi = 180$ degrees collide, a 'saddle-node' (or tangent) bifurcation occurs. As illustrated in Fig. Ic (middle), the function $\dot{\Phi}$ versus Φ no longer intersects the Φ axis (there is no longer a fixed point) near $\Phi = 180$ degrees. Finally, at sufficiently low values of b/a, no fixed points remain at all (Fig. Ic, top). Both previously stable fixed points have now disappeared in saddle-node bifurcations. This is the interesting metastable regime of the coordination dynamics. Even though all the fixed points of Φ have disappeared (i.e. the function no longer intersects the Φ axis), partial attraction to certain phase relationships (around the saddle nodes) remains in the system. This phenomenon of partial attraction, without the existence of attracting fixed points, corresponds to the metastable regime of the coordination dynamics.

Metastability offers a dynamical account of what the behavioral physiologist von Holst called 'relative coordination'[g], and is of great interest to us for understanding cortical function. The reason that this kind of partial or relative coordination occurs is the competitive 'struggle' between the tendency of each component part to maintain its individual spatial and temporal properties, and the tendency of all the interacting parts to harmonize globally as a unified system.

The temporal properties of relative coordination have been studied in terms of 'intermittent dynamics'[h]. As one tracks the behavior of relative phase in a system displaying relative coordination, the degree of coordination can change over time. At times it can be strong, at other times weak. It can remain weak for a considerable time, and then suddenly increase in strength. A statistical distribution of relative phase from a system showing intermittency contains all possible phase values, but with a concentration around a preferred phase relationship (see Box 2).

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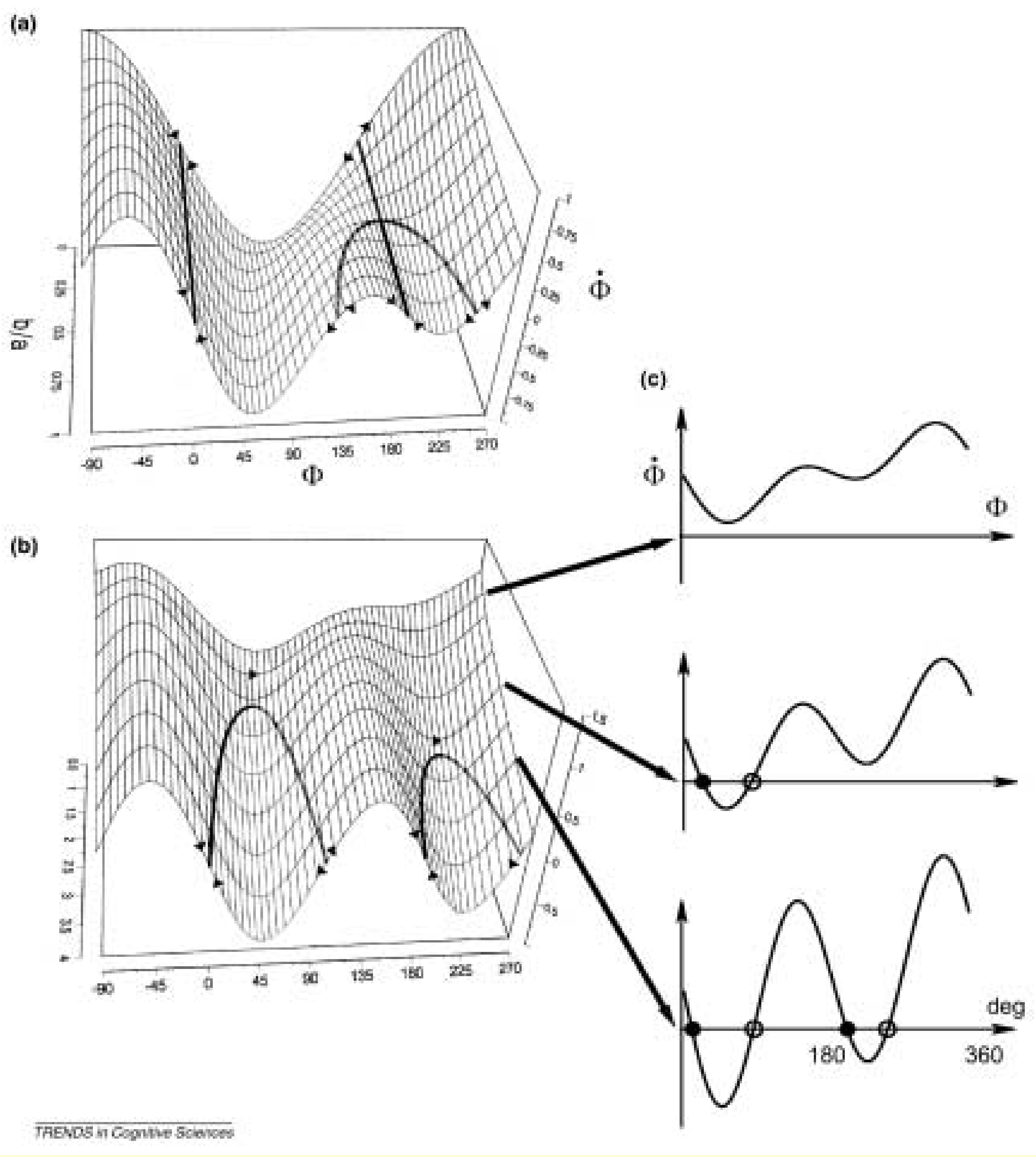

Fig. I. Coordination dynamics of a coupled two-component system. The coordination dynamics expressed by Eqn 1 is represented by the relationship between the relative phase of the two coupled components, Φ, and its first time derivative, $\dot{\Phi}$. Arrows indicate the direction of flow. Black and gray lines correspond to attractive and repelling fixed points of the dynamics. (a) The symmetric condition with parameter $\Delta\omega = 0$. (b) The broken symmetry condition with parameter $\Delta\omega \neq 0$ (see text for details). (c) Slices through the surface in (b) are shown for three different values of the control parameter, *b/a*: (bottom) high value of *b/a*, representing a low frequency (long period) of oscillation; (middle) intermediate value of *b/a*; and (top) low value of *b/a*. The bottom slice contains two stable fixed points (closed circles) near Φ = 0 degrees and Φ = 180 degrees, and two unstable fixed points (open circles). As the control parameter is continuously changed, first one stable fixed point (middle slice), then the other (top slice), disappears in saddle-node (or tangent) bifurcations. Metastable, intermittent dynamics is observed in the top slice: although there are no longer stable fixed points, there is still attraction to the remnants of the previously stable states. (Modified figure reproduced, with permission, from Ref. f.)

Evidence for differentiation in coordination dynamics across sites within an area comes from those cases in which LFPs were recorded from multiple sites in the same area. It was found that the coordination dynamics could vary considerably for different pairs of sites involving the same two areas. The coherence level between the two cortical sites in Fig. 1, both considered to be primarily visual in function, reached a high value during early visual processing and then declined. Other site pairs, involving both the same and different cortical areas, had different temporal patterns of coordination, presumably reflecting differential involvement in task processing. Also, the fact that many site pairs remained uncoordinated during the entire task emphasizes the selective nature of the cortical coordination dynamics. In the next section, we consider the question of large-scale patterning of inter-area coordination in the cortex and its possible relationship to cognitive functioning.

Large-scale cortical coordination dynamics

Coordination in any complex system is an emergent property of groups of components rather than of individual component pairs (except from the perspective of the sub-components one level below). In walking, for example, not only the muscles of the legs, but also muscle groups throughout the entire body, must be coordinated. It is widely believed that the multifaceted nature of most cognitive functions requires the active participation of multiple cortical areas[28–33]. We propose that a crucial aspect of cognitive function, which can both integrate and segregate the activities of multiple distributed areas, is large-scale relative coordination governed by way of metastable dynamics. The anatomical foundation for large-scale cortical integration is well known: areas of the cerebral cortex are highly interconnected by largely bi-directional, high velocity pathways[34] and by subcortical pathways[35–37]. Large-scale cortical segregation has an anatomical basis in the fact that cortical areas are preferentially interconnected with other areas that are part of the same functional systems[38,39]. It is therefore reasonable to suppose that, under conducive conditions, cortical areas have the potential to arrange themselves quickly in coordinated configurations of varying sizes, extending throughout both hemispheres. From what is known of the projection and reception patterns of the axonal pathways, the activity in any cortical area might potentially be coordinated with that of the other areas with which it is connected, either directly or through subcortical structures. This potentiality provides the groundwork for an enormous space of possible configurations in which the cortex might organize itself.

When a collection of cortical areas consistently becomes coordinated at a given stage of cognitive processing, it can be said to comprise a ‘coordinated network’. It is useful to consider that by manifesting one or more coordinated networks at any given instant, the cortical system enters particular ‘coordination states’. For the reasons given above, the awake, normally functioning cortex is thought to operate in a metastable dynamic regime. Therefore, it is to be understood in the following discussion that a coordinated network is a relatively coordinated network whose coordination states are metastable, corresponding to relative, not absolute, coordination (see Box 1).

From the forgoing discussion, the areas in a coordinated network are expected to exhibit high LFP coherence with one another, but not necessarily at the same frequency or relative phase value. We have found evidence that in the pattern discrimination task, cortical sites do participate in coordinated networks. The networks are observed as sets of distributed sites having coherent LFP oscillations within a common frequency band, but with different relative phase values[15,26]. Recently, we have found additional evidence that two coordinated networks can independently organize at different frequencies at the same time[16]. In addition, direct estimation of phase synchronization[81] in scalp EEG signals during face recognition has revealed a coordination pattern over widely distributed areas lasting about 200 ms[82]. These results afford a stronger interpretation of the functional relationships between cortical areas, in terms of temporally specific coordination states (consistent relative phase relationships), than does the temporally diffuse co-activation of areas observed by metabolic or blood flow imaging techniques. The coordinated large-scale cortical network, in which the participating sites are much more interrelated to one another than to non-network sites, corresponds to the dynamic structure recently described as a functional cluster by Tononi *et al.*[40].

Evidence that the cortex undergoes transitions among metastable coordination states is provided in the pattern discrimination task when the animal switches from the stage of anticipation to that of stimulus processing[16]. In this case, two separate networks, coordinated at different frequencies in the anticipatory stage, are replaced by a new, integrated network, coordinated at a third frequency, during the subsequent stage of stimulus processing. The system remains in each coordination state for approximately 100 ms, and the transition occurs very rapidly within approximately 25–50 ms. In the transition, the cortical system rapidly breaks functional couplings within one set of areas and establishes new couplings within another set. This flexibility, provided by relative coordination understood as metastable dynamics, allows the same area to engage in different functions at different stages of processing. The underlying dynamics also permits the system as a whole to switch rapidly between different functions through the reorganization of its component areas into different coordinated networks.

Box 2. Measurement of relative coordination in the cerebral cortex

Adaptive MultiVariate AutoRegressive (AMVAR) modeling is a technique that allows measurement of the relative coordination of LFPs in short windows by their spectral coherence and phase[a]. Coherence is a normalized quantity between zero and one that is measured as a function of frequency. At each frequency, the value of coherence indicates the degree of phase concentration: values of coherence near one indicate a great degree of concentration and values near zero indicate lack of concentration. Along with the coherence spectrum, the analysis provides a corresponding phase spectrum, indicating for each frequency the value of relative phase around which the concentration occurs.

Figure I shows distributions of relative phase between a site in the striate cortex with another in inferotemporal cortex, computed using the AMVAR method. The two distributions are from 50 ms long time windows centered at 50 ms before onset of the visual stimulus during the task, and 130 ms following stimulus onset when stimulus feature extraction is taking place. Both distributions represent relative phase at a frequency of 12 Hz. In the poststimulus period, LFP oscillations at this frequency are observed at widely distributed cortical sites. The prestimulus distribution shows no tendency for these two cortical locations to coordinate their LFPs at 12 Hz: the LFP relative phase takes on every possible phase value with roughly the same probability. The degree of relative phase concentration, reflecting coordination of the two cortical locations, clearly changes as a result of stimulus presentation. One can see the signature of relative coordination in the poststimulus distribution by the tendency of its LFP relative phase distribution to be concentrated around a preferred value, but not to be completely fixed at it.

Figure IIa displays the coherence and phase spectra corresponding to the prestimulus window of Fig. I. The coherence spectrum has a coherence value of 0.01 at 12 Hz. This is a very low value, corresponding to the lack of concentration in the phase distribution. The value of phase at 12 Hz in the corresponding phase spectrum has very little meaning because there is no phase concentration. The coherence and phase spectra in Fig. IIb correspond to the 130 ms phase distribution of Fig. I. Unlike the prestimulus window, there is a prominent peak in coherence at 12 Hz. The presence of the peak reflects the existence of LFP oscillations in the poststimulus period at this frequency. The large coherence value at this peak (0.79) reflects the large increase in concentration of its phase distribution seen in Fig. I. The corresponding phase spectrum shows that the striate site leads the inferotemporal site in time with a phase value of 54° at 12 Hz. This phase value matches the central phase of the 130 ms phase distribution in Fig. I.

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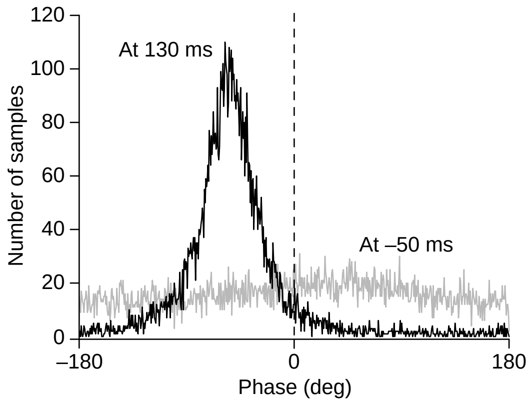

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Fig. I. Distributions of relative phase between local field potentials (LFPs) at striate and inferotemporal cortical sites. At 50 ms before stimulus onset, there is no preferred phase relationship at 12 Hz between these two sites. During stimulus processing, at 130 ms, these sites exhibit a strong tendency to take on a preferred phase relationship, concentrated at –54°, with the striate site leading in time.

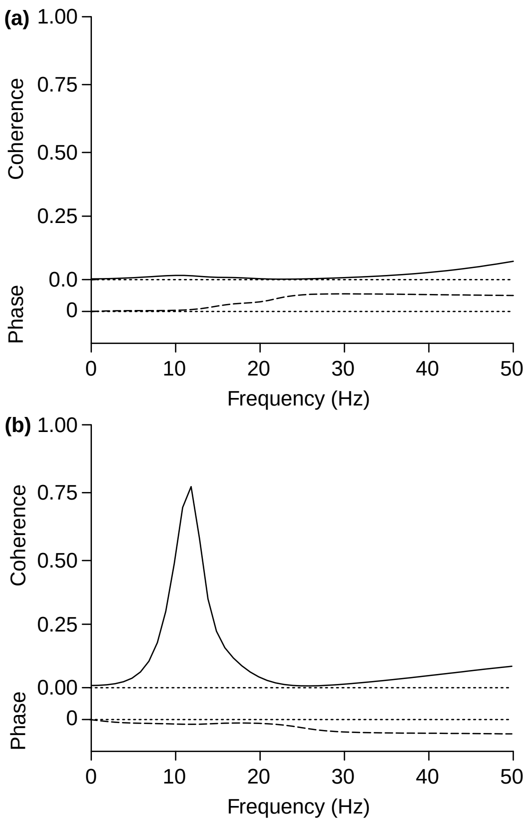

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Fig. II. Coherence and phase spectra. (a) The coherence spectrum corresponding to the distribution of relative phase at –50 ms in Fig. I shows a very low value (0.01) at 12 Hz. The phase spectrum is irrelevant because the coherence values are so low. (b) During stimulus processing, at 130 ms, the coherence spectrum has a distinct peak at 12 Hz with a value of 0.79. The large peak in coherence corresponds to the large degree of phase concentration at this time. The value of the phase spectrum at 12 Hz (–54°) is the center of concentration of the corresponding phase distribution in Fig I. The range of the coherence spectra is from 0.0 to 1.0. The range of the phase spectra is from –360° to 360°.

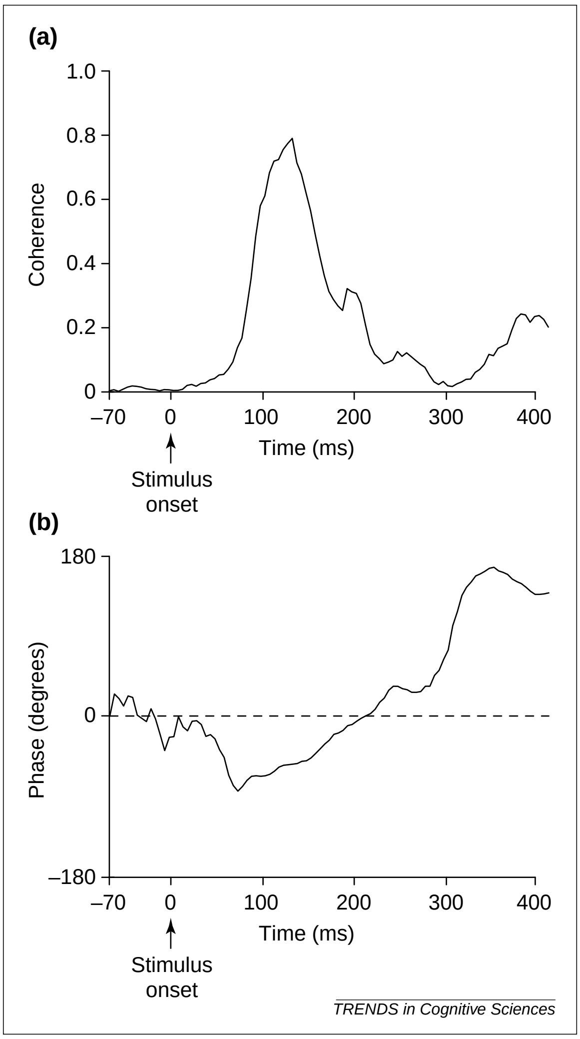

Fig. 1. Task-related modulation of relative coordination. (a)The degree of coherence between local field potentials (LFPs) from two sites, one in the striate cortex and one in the inferotemporal cortex, is variable, changing with time during performance of a visual pattern discrimination task.The large increase in coherence, peaking at 130 ms after onset of the visual stimulus, indicates a corresponding increase in the degree of relative phase concentration at this time between these two parts of the visual cortex. (b)The central value of phase between these sites changes with time during the task.This value becomes negative following stimulus onset, indicating that the inferotemporal activity lags striate activity in time, and briefly stabilizes at around –54° during the peak of coherence. Both coherence and phase correspond to activity in the LFPs at a frequency of 12 Hz, which is the dominant frequency of relative coordination observed during visual stimulus processing.

Non-participating areas in one coordination state might be recruited into, or selectively engaged in, a coordinated network during the transition to another coordination state. Each recruited area affords the possibility of further transitions to new states because it can engage or disengage other areas with which it is connected[41].

Coordination dynamics and information processing

The cortical system has the potential to manifest an extremely large number of coordinated networks. However, this potential is limited by several factors. Extracortical influences, originating in the external environment, the body, and subcortical brain structures, act over subcortical–cortical projection pathways to constrain activity in recipient cortical areas. In addition, cortical areas constrain each other's activity by inter-area influences acting over cortico-cortical pathways. Finally, the activity in each cortical area is constrained by its own intra-area synaptic matrix. All of these factors can be seen as breaking symmetry in the coordination dynamics of the interacting cortical areas. Moreover, brainstem neuromodulatory influences, acting as control parameters, are capable of moving the cortex through a broad range of metastable coordination states.

To be effective in ongoing dynamic computation, the cortex must resolve the large number of competing constraints acting on its component areas in a rapid manner. Several authors have suggested that the cortex does this by a relaxation process in which it settles into a globally consistent state that satisfies the multiple constraints on its interacting component areas[28,29,33,42]. A relaxation process in artificial neural networks is one in which the network converges to a global result on the basis of local interactions, where the network units have access to each other's responses and adjust their own responses accordingly[43]. A problem with many current artificial networks, however, is that they typically settle into a stable state (fixed point or limit cycle) and stay there. In other words, the network dynamics becomes trapped in a stable fixed point or orbit. We propose that the cortex avoids this problem because cortical areas can reconcile their competing constraints through increased relative coordination without the need for relaxation. Because relative coordination is characterized by the *tendency* of areas to coordinate without ever becoming fully coordinated, it prevents the cortical system from becoming locked in any single coordination state[1,2].

In this interpretation, coordinated networks are dynamic structures that emerge as the cortex's adaptive 'response' to the current constraints placed on its component areas. From a functional perspective, the participation of cortical areas in coordinated networks is a sign of their facilitated cooperation, and the formation of coordinated networks is a means by which the cortical system can rapidly perform functions that depend on the combined and coordinated actions of large numbers of distributed areas. Through relative coordination, the cortical system is free to perform one or more functions using one or more coordinated networks at a given stage of processing, and then to move on to other functions at the next stage. The system is thereby endowed with a flexibility that allows it to undergo transitions rapidly and adaptively from one cognitive process to the next in a series that, if properly constrained, can lead to a behavioral goal.

The manifestation of one or more coordinated networks may be interpretated as a selection from the vast number of possible networks the cortex could manifest. In terms of information theory, this selection process constitutes the reduction of uncertainty[44,45]. With the emergence of a coordinated network at a particular stage of task processing, the cortical system becomes committed to performance of one function to the exclusion of other possible functions. Information, in this sense, resides at the level of the large-scale network. There is a further sense, however, in which the coordination state could specify information at the more microscopic level of the local area. Considerable evidence exists that cortical areas can be viewed as quasi-independent information domains[35,39]. Other research suggests that information is expressed topographically in the local area as spatial activity patterns[46–49]. If we assume, following Tononi *et al.*[40], that coordinated areas undergo re-entrant processing, then it follows that re-entrant interactions will constrain the local spatial activity patterns in these areas, thereby defining their local expression of information.

Re-entrant transmissions among the cortical areas of a coordinated network might thus be particularly important in defining the expression of local information in the participating areas. The constraint of local spatial activity patterns offers a means by which the content of cognitive function, as well as the form, can be expressed neurally. As areas interact over reciprocal pathways, they continually impose spatially patterned pulse densities on one another. The spatial pattern of activity in each area is constrained by the multiple imposed pulse patterns that it receives; likewise its projected pulse patterns serve to constrain the patterning of activity in target areas. At times, according to the present view, some areas reach a state of consensus through the process of large-scale relative coordination, in which those areas temporarily manifest consistent local spatial activity patterns.

A distinct advantage of this mechanism is that it dynamically creates a ‘context’ for the local information expressed in each area of a coordinated network by interactions with other coordinated areas[50]. The dynamic creation of local context is a way for the cortex to function in a highly adaptive manner. It is well known, for example, that cortical neurons in the visual system are modulated by a number of contextual and saliency factors[50,51], and this mechanism could enable the spontaneous formation of novel groupings that vision requires[52]. Re-entrant processing among the constituent areas of a coordinated large-scale network thus provides a way for the neurons in each area to adapt rapidly to a wide range of external and internal processing contingencies. Furthermore, as large-scale coordinated networks dynamically evolve with ongoing cognitive processing, re-entrant interactions allow adaptation at the neuronal level to evolve dynamically according to changing task contingencies.

Adaptive pattern constraint and cognitive function

Computationally, coordination states of the cortex represent ‘solutions’ to the problem of how to adapt to global processing requirements[42]. The coordination state might change from moment to moment because, at each instant, those areas that can resolve their constraints and thereby manifest consistent spatial activity patterns become engaged in a coordinated network, while others that cannot achieve this consistency are temporarily excluded from participation. The ability to make a coherent movement or form a coherent percept might derive from this adaptive pattern-constraint process, because the mutual satisfaction of multiple constraints acts as a powerful determinant of system behavior.

Visual pattern recognition is one function where adaptive local pattern constraint through large-scale relative coordination might play an important role. It is generally assumed that different visual cortical areas provide complementary, and possibly overlapping, constraints in visual scene analysis[39,45,53]. Mutual inter-area pattern constraint among the large number of visual cortical areas might ensure that they act together in a (relatively) coordinated and efficient manner to reach a consistent interpretation of the retinal input, bringing all relevant constraints to bear at each moment during scene analysis[54].

In motor control too, the same general principles of adaptive pattern constraint among motor cortical areas might be important in coordinating the many facets of planning, preparation, and execution. Movement attributes at the extrinsic kinematic, internal kinematic, and dynamic levels have been found to be controlled by locations distributed over several motor cortical areas[55], suggesting that multiple areas must coordinate their activities during normal motor behavior[56]. Evidence further suggests that these areas are integrated into larger sensorimotor networks[57], that the areas in these networks are functionally interdependent[58], and that this interdependence is subserved by large-scale coherence of LFP oscillations[59–62].

Lexical processing is another operation in which contextual effects can be mediated by adaptive pattern constraint. Several authors have proposed that lexical comprehension depends on a constraint satisfaction mechanism[63–66]. Languages have multiple levels of structure, including phonological, morphological, syntactic and conceptual, which simultaneously provide the context that is used to resolve ambiguities in the comprehension of sentences and their components[67,68]. From the present perspective, the structural organization of lexical processing is expected to correspond to the connectional structure of linguistic areas in the cortex. Processing at the different lexical levels can be instantiated by different distributed systems of connected linguistic areas. Lexical comprehension might correspond to the emergence of a coordinated cortical network in which each system provides constraints that jointly determine lexical meaning by causing convergence to a single interpretation. The evolution of these coordinated linguistic networks could provide a temporal flow to linguistic comprehension, with preceding words providing strong context for the interpretation or selection of later ones[69]. Several studies have demonstrated a link between lexical processing and transcortical coherence[70–72].

Subcortical structures might play a key role in perceptuomotor behavior by configuring and coordinating large-scale activity patterns in the cortex. A common path for the control of large-scale cortical network formation by diverse subcortical structures might be the nonspecific thalamic nuclei[73]. These nuclei have been proposed to control the excitability of cortical pyramidal cells by altering their firing thresholds[74]. In dynamical terms, they can be seen as adjusting control parameters that regulate coordination dynamics in the cortex. The pulvinar nucleus in particular might function in visual form perception to regulate dynamically the relative coordination of visual cortical areas[75]. Other thalamic nuclei appear to mediate relative coordination in auditory[76] and somatosensory[77] cortices. In motor control too, subcortical structures might interact with large-scale cortical networks in the planning and execution of goal-directed actions[78]. Subcortical motor systems such as the basal ganglia and cerebellum might interact reciprocally with cortical motor areas to constrain the dynamics of inter-area cortical interactions[32]. The subcortically directed output of cortical networks might in turn coordinate the actions of distributed motor control structures, leading to coherent oscillations across cortical areas, subcortical structures, and even the output musculature[79,80].

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Outstanding questions

- Can the phenomenon of relative coordination be observed in event-related potentials or fields recorded extracranially from humans? If so, what neural mechanisms underlie relative coordination in the human brain?
- How general is relative coordination in cognitive brain function? Does it underlie the (meta)stability and flexibility that are characteristic of perceptual, learning and memory processes?
- Can evidence be found for the mutual constraint of spatial activity patterns in different cortical areas during cognitive function?
- Can large-scale cortical networks be found for complex cognitive functions in humans? And, if found, do they operate predominantly in a relatively coordinated way?
- Which specific transmitter systems act as control parameters for relative coordination in the cortex?
- Is any form of cognitive impairment or disease (e.g. Alzheimer's disease or schizophrenia) directly related to a failure of cortical coordination?
- What are the relative contributions of cortico–cortical and subcortico–cortical mechanisms to coordination in cognition?
- What subcortical structures are involved in coordinating large-scale networks in the cerebral cortex? Do different subcortical structures affect different aspects of cortical coordination?
- How does cortical coordination dynamics influence the encoding and retrieval of information in cortical areas? Does coordination dynamics play a role in the interaction of the hippocampal system with the cerebral cortex in memory processes?
- Are large-scale cortical networks part of global brain networks that coordinate cortical activity with limbic, thalamic, and brainstem activity?

Conclusions

The cerebral cortex makes a critical contribution to cognition by performing integrative functions that combine and reconcile information from a multitude of sources. The cortex integrates information from different sensory modalities; sensory information with internally generated information representing goals, plans, memories and emotions; and information of all these types with motor information for the initiation and production of specific actions. In addition, the cortex performs important segregative functions by allocating a diversity of tasks to different areas and regions. Considering that a person's environment can change rapidly and unpredictably, the cortex must be able to maintain currency with that environment by preserving a balance between integrative and segregative functions on a sub-second time scale. We have shown in this review how the cortical system manifests metastability through the organization of large-scale coordinated networks, in which the constituent areas become interdependent without losing their independence. The metastable dynamics of relative coordination endow cognitive functions with the capacity for rapid and fluid change, without ever relaxing into stable states.

This change is highly adaptable: people and animals can repeatedly modify their cognitive processes to produce a course of action that successfully accommodates a variety of time-varying conditions. We have shown how the transient, conjoint coordination of groups of distributed cortical areas comprising large-scale networks can allow individual local-area spatial activity distributions to converge to informationally consistent patterns, thereby satisfying global computational demands. This computational strategy is extremely flexible, allowing each participating local area to act as a unique information source for the large-scale network, and different combinations of areas to combine their information in real time. The context for information processing in each area of the large-scale network is dynamically created by virtue of the combined constraints imposed on it. The result is an enormous computational advantage for perceptual[50] and motor[57] operations. Through the relative coordination of cortical areas, governed by metastable coordination dynamics, these processes are effectively combined with others into coherent, global functions that provide a unity of cognition.

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Mechanisms of synesthesia: cognitive and physiological constraints

Peter G. Grossenbacher and Christopher T. Lovelace

Synesthesia is a conscious experience of systematically induced sensory attributes that are not experienced by most people under comparable conditions. Recent findings from cognitive psychology, functional brain imaging and psychophysiology have shed considerable light on the nature of synesthesia and its neurocognitive underpinnings. These cognitive and physiological findings are discussed with respect to a neuroanatomical framework consisting of hierarchically organized cortical sensory pathways. We advance a neurobiological theory of synesthesia that fits within this neuroanatomical framework.

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Synesthesia is the conscious experience of sensory attributes induced by particular conscious mental events, appearing in addition to any sensations that are normally experienced by most people during such events[1,2]. For example, in one form of synesthesia, perception of a letter induces the phenomenal experience of a color, with each letter inducing its own distinct color. Synesthesia is neither strategy nor attitude; it is an involuntary concrete sensory experience that can be quite vivid. Only a small proportion of people routinely experience synesthesia. Such people ('synesthetes') typically experience synesthesia on a daily basis, beginning in early childhood. Many synesthetes exhibit surprise upon first learning that others do not share the synesthetic part of their perceptual experience.

Although experienced as a unitary whole, synesthesia is composed of two interrelated components. We use the terms 'inducer' and 'concurrent' to refer to the inducing event and the synesthetically induced sensory attribute(s), respectively. For example, one synesthete describes the sound of her crying baby as having an unpleasant yellow color. In her synesthesia, sounds (the inducers) were experienced as having colors (the concurrents) in addition to the customary auditory attributes. For most individuals, synesthesia is unidirectional: if sounds induce the experience of colors, colors typically do not induce the experience of sounds[3]. The relationship between inducers and concurrents is systematic in that each specific concurrent is typically induced by only one inducer[4].

Forms and types of synesthesia

Each form of synesthesia, such as sound inducing color, involves a set of triggering inducers (e.g. sounds) mapped to a corresponding set of synesthetic concurrents (e.g. colors). To avoid ambiguities of phrases like 'colored hearing' we use notation of the general form (I)→(C) where 'I' and 'C' designate inducer and concurrent sets, respectively. Thus '(sound)→(color)' efficiently refers to the form of synesthesia in which sound induces color.

In many forms of synesthesia, the inducer set and concurrent set belong to separate sense modalities. However, not all forms of synesthesia span two sense modalities. Figure 1a shows one relatively common form having visual inducers and visual concurrents[3,5]. In (visual letter)→(color) synesthesia, (visual) colors are induced by (visual) letters of the alphabet that are read by the synesthsete[6]. In addition, some forms of synesthesia involve inducers that are conceptual rather than sensory[1,7-10].

We distinguish between two types of synesthesia, according to whether inducers are sensory or conceptual. In *synesthetic perception*, concurrents are induced by perceiving particular sensory stimuli. In *synesthetic conception*, concurrents are induced by thinking about particular concepts. In (number)→(location) synesthesia, each counting number has a location in space relative to its neighbors[11,12]. Similarly, in the (time period)→(location) form of synesthetic conception, periods of time are conceptualized in a spatial layout (Fig. 1b,c)[10,13].

After several decades of relative neglect, synesthesia is again the subject of increasing interest[14]. In recent years, the field has progressed from seeking objective

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