# Cortical state and attention

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Abstract | The brain continuously adapts its processing machinery to behavioural demands. To achieve this, it rapidly modulates the operating mode of cortical circuits, controlling the way that information is transformed and routed. This article will focus on two experimental approaches by which the control of cortical information processing has been investigated: the study of state-dependent cortical processing in rodents and attention in the primate visual system. Both processes involve a modulation of low-frequency activity fluctuations and spiking correlation, and are mediated by common receptor systems. We suggest that selective attention involves processes that are similar to state change, and that operate at a local columnar level to enhance the representation of otherwise non-salient features while suppressing internally generated activity patterns.

Electroencephalogram
An electrical recording made from the scalp, which reflects the global structure of cortical synaptic activity.

Cortical activity, even in primary sensory areas, is not strictly determined by sensory input but reflects an interaction of external stimuli with spontaneous patterns that are produced endogenously[1]. The form of this spontaneous activity — and the way that it shapes sensory responses — is determined by cortical state. Cortical states were first studied as patterns of electroencephalogram (EEG) activity and have more recently been shown to determine patterns of population spiking, neuronal correlation and intracellular potentials. Because cortical spiking patterns can depend as much on state as on sensory inputs, an understanding of state is essential to study how information is processed by neuronal populations.

A classical view holds that cortical state is a function of the sleep cycle: during slow-wave sleep the cortex operates in a 'synchronized' state, characterized by strong low-frequency fluctuations in cortical activity, whereas during waking and rapid eye movement (REM) sleep it operates in a 'desynchronized' state in which low-frequency fluctuations are suppressed[2]. Recent experiments in rodents have indicated a more complex picture, in which cortical state also varies during wakefulness. Although alert or actively behaving animals exhibit a highly desynchronized state, awake quiescent animals can show spontaneous fluctuations in cortical activity that are prominent although smaller than those observed during slow-wave sleep[3–11]. Thus, the classical synchronized and desynchronized states are likely to represent two extremes of a continuum of states corresponding to varying levels of spontaneous fluctuations in neural population activity. As we argue below, the continuum is also likely to be multidimensional: there are several different behavioural and experimental conditions that all cause desynchronization but that can have diverse effects on other variables, such as gamma frequency power and the activity of different cortical cell classes.

Attention refers to an animal's ability to selectively enhance the detection of, and response to, certain stimuli at the expense of others. In this Review, we use the word attention specifically to mean 'top-down' attention, in which enhanced responses are caused by a prior expectation of which stimuli will be important, rather than 'bottom-up' attention, in which the physical properties of an intrinsically salient stimulus itself directs the animal's attention. Primate studies have shown that in multiple cortical regions, attended stimuli produce larger spiking responses than unattended stimuli[12–17]. But this is not the only effect of attention on cortical activity. Intriguingly, many of the other effects of attention — such as decreased low-frequency fluctuations, trial-to-trial variability and correlations — resemble cortical desynchronization, occurring specifically in parts of cortex that represent the attended stimulus[18–23].

In this Review, we first discuss the nature and mechanisms of state-dependent cortical processing in rodents, and then examine how attention modulates processing in primate visual cortex. We argue that attention involves similar processes to those causing cortical desynchronization, but that operate at a local level. We suggest that this local desynchronization arises from a combination of diffuse neuromodulatory inputs and tonic glutamatergic drive focused on the cortical populations that represent the attended stimulus.

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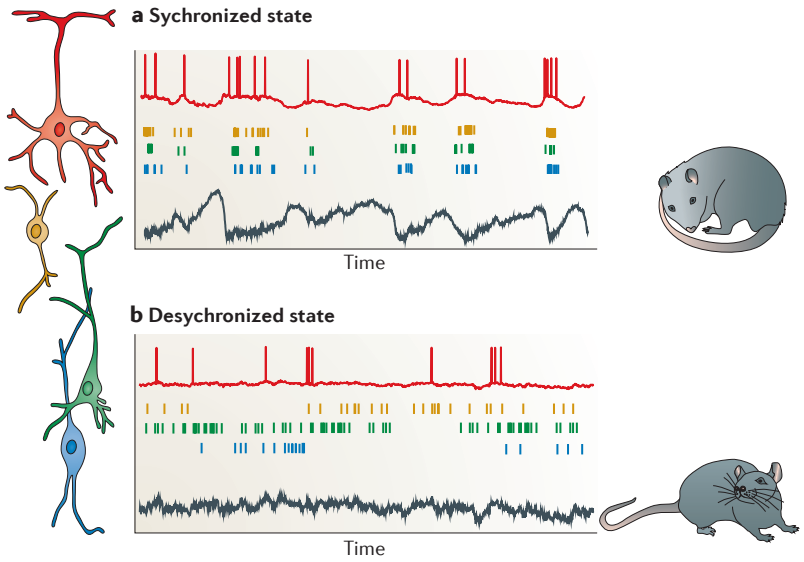



Figure 1 | **Population activity patterns vary with cortical state.** Illustrations of two extremes of a continuum of states seen in awake rodents. **a** | In synchronized states, cortical populations show spontaneous common fluctuations in firing rate. During the up phase, all neuronal classes show a propensity to fire (shown by the coloured raster plots), whereas during the down phase spiking is reduced or absent. These phases are accompanied by corresponding depolarization and hyperpolarization in intracellular potentials (shown by the red trace). The deep-layer cortical local field potential (LFP) (shown by the black trace) shows slow negative waves accompanied by high-frequency activity in the up phase and smooth dome-shaped positive waves in the down phase. This type of activity is seen in drowsy or quiescent animals. **b** | In the desynchronized state, coordinated slow fluctuations in population activity are not seen, and low-frequency fluctuations in the LFP and membrane potentials are suppressed. This type of activity is seen in actively behaving, alert animals. Note that this figure does not show actual recordings from the neurons whose morphology is illustrated to the left, but is a drawing integrating the results of multiple studies.

## State-dependent organization of cortical activity

Modern multi-electrode and optical techniques have shown how the spiking of cortical populations is organized both within individual columns and across the cortical surface. This has provided an understanding of cortical state at the neuronal level. The organization of cortical population activity is best understood for the case of spontaneous activity. Spontaneous activity has been studied using a number of experimental techniques, including optical imaging[3,6,24–28], extracellular population recording[8,9,29–34] and intracellular recording[5,7,11,35–37], all of which paint a broadly consistent picture. Although the largest fluctuations in cortical population activity are seen in sleeping and anaesthetized animals, studies from many laboratories have now shown that spontaneous fluctuations in firing rates and intracellular potentials can also occur during quiet wakefulness[3–11]. Spontaneous cortical population activity in an awake animal does not simply switch between discrete synchronized and desynchronized states but forms a continuum of states characterized by variations in fluctuation depth that correlate at least partially with ongoing behaviours, such as whisking and locomotion[5–7,38].

The defining characteristic of cortical state, for our purposes, is the amount of common fluctuation in population spiking activity (as we argue below, other measurements such as low-frequency local field potential (LFP) power, spiking correlations and variability also relate to this definition). In a synchronized state activity fluctuates between up phases, characterized by firing in multiple neuronal classes, and down phases, in which the whole network is quiet (FIG. 1a; see BOX 1 for a discussion of terminology). In a desynchronized state, spontaneous fluctuations are weaker (FIG. 1b). Cortical state is not bimodal (FIGURE 1 illustrates the extreme ends of a continuum of cortical state in awake rodents), and strong variations in cortical state are also seen during sleep (most notably between slow-wave and REM sleep) and also under certain anaesthetics[31,39–41]. Urethane anaesthesia, under which a continuum of cortical states is seen — ranging from states that are more synchronized than slow-wave sleep to transient desynchronized epochs similar to REM or waking[31,32,41] — is a frequently used experimental model to investigate how state affects cortical processing.

Spontaneous cortical activity during sleep can display patterns that are slow, regular and rhythmic[42]. By contrast, the spontaneous fluctuations seen in cortex of awake rodents typically have an irregular structure, and the length and depth of the up and down phases vary from one period to the next. These waking patterns are therefore not well described as 'oscillations'. Recordings of different cell types have shown that the firing and membrane potential of most, if not all, cortical neuronal classes increase in the up phase, although differences in the precise timing of neuronal firing relative to the onset of the up phase exist both between and within cortical neuronal classes and layers[10,37,43–45].

***Relation of cortical state to pairwise correlations.*** When the firing rate of a neuronal population is modulated by global fluctuations, the activity of neuronal pairs is generally positively correlated. This idea can be mathematically expressed by describing the relationship between the weighted mean of pairwise correlation coefficients and the variance of the population rate (BOX 2). If more pairs are positively rather than negatively correlated, the mean pairwise correlation is positive, and so the population rate has large variance, which is indicative of coordinated global fluctuations that are typical of a synchronized state. If no neuronal pairs are correlated, the variance of population activity is small and the neuronal population is in a desynchronized state. However, a mean correlation of zero does not require every single pair to be uncorrelated; it is also possible to have a desynchronized state in which positive correlations between neurons exist but are counterbalanced by an equal number of negative correlations[32] (BOX 2).

***Relation of cortical state to local field and intracellular potentials.*** Fluctuations in cortical population activity are strongly correlated with LFP patterns. The LFP can show large differences between sleeping, awake quiescent, and actively exploring animals. Although the physics underlying LFPs is complex, periods of strong firing in a column are generally accompanied by depth-negative waves that are generated by local excitatory

Local field potential
(LFP). An electrical potential measured from extracellular space. LFP primarily reflects synaptic activity rather than action potential waveforms.

Population rate
The mean of the firing rates of all neurons in a population. The population rate does not denote an average over multiple presentations of a stimulus, but denotes the averaged activity of multiple neurons at a single moment in time.

Depth-negative waves
Local field potential (LFP) waves for which a negativity (or in the case of depth-positive waves, positivity) is seen in the subgranular layers. This laminar specification of the polarity of LFP waves is needed because cortical LFPs typically show a reversal around the middle layers.

synapses[46–48]. The down phases of the synchronized state are accompanied by depth-positive LFP waves of smooth appearance, reflecting a lack of spiking and synaptic activity. In synchronized states, alternations between up and down phases in fluctuating population activity therefore give rise to LFP patterns of strong, low-frequency power (FIG. 1a). In desynchronized states, smaller fluctuations in global firing rates are mirrored by less LFP power at low frequencies (FIG. 1b).

Fluctuations in population activity correlate strongly with fluctuations in intracellular voltages of multiple neuronal classes[7,45,49,50]. The strength of membrane potential fluctuations thus also varies with cortical state, with periods of strong low-frequency LFP showing large intracellular fluctuations and periods of LFP desynchronization showing more steady intracellular potentials[5,7,11]. Intracellular recordings in awake rodents also reveal a continuum of states rather than a switch between discrete synchronized and desynchronized states[11].

***Relation of cortical state to gamma oscillations.*** Cortical desynchronization has often been linked with an increase in the power of gamma frequency oscillations (25–100 Hz), which have in turn been proposed to assemble neurons into synchronous groups that are capable of strongly driving their targets[51]. Gamma power increases when cortical desynchronization occurs during active behaviour in rodents[38] or after electrical stimulation of basal forebrain, brainstem cholinergic and non-specific thalamic nuclei[52–55]. However, the correlation between desynchronization and gamma power is not absolute. For example, in rats, stimulation of dorsal Raphe nuclei causes a decrease in low-frequency LFP power and a simultaneous decrease in gamma power[56]. Moreover, selective attention in primates uniformly decreases low-frequency power but can either raise or lower gamma power, depending on cortical area and task[18,21,22]. Finally, although local gamma power in visual cortex is typically increased by visual stimuli, the correlation between gamma power and firing rate is also complex, with certain stimuli being able to increase gamma power without changing or even decreasing neuronal firing rates[57,58].

***Coordination of spontaneous population activity across areas.*** Electrical recordings have shown that neuronal correlations and LFP coherence decay as the lateral distance between recording sites increases[33,34,59,60]. Recent results have revealed a spatiotemporal picture of cortical activity that can explain these findings. In synchronized states, cortical activity often takes the form of spatially extended travelling waves[6,9,27,61–65]. Despite variations in trajectory from one wave to the next, these waves share a number of characteristic features, such as timescales of the order 10–100 ms and remarkable bilateral symmetry[66]. The passage of a wave through a cortical column initiates a local spiking pattern that is independent of the wave direction[9]. The correlated fluctuations that are seen in any one column during synchronized states are thus part of much larger patterns that spread out across the cortical surface.

Fluctuating spontaneous activity is not restricted to cortex but is also found, among other areas, in the thalamus[67,68], basal ganglia[69,70], cerebellum[71] and hippocampus. Spontaneous activity in the hippocampus has been particularly well studied and is similar to that in neocortex, with a few key differences. The hippocampal equivalent of the synchronized state — the 'large irregular activity' (LIA) that is seen during immobility and sleep — consists of periods of near silence punctuated by 'sharp waves' of strong population activity whose occurrence is correlated with the timing of cortical up phases[72,73]. Unlike in cortex, however, hippocampal sharp waves are accompanied by a 150–200-Hz 'ripple' oscillation[74]. In the hippocampal equivalent of desynchronization, known as the 'theta state', sharp-wave fluctuations are suppressed, leading

Box 1 | **What's in a name?**

The study of cortical state suffers from confusing terminology. Some terms have different meanings according to different authors, and in some cases multiple terms are used to refer to a single phenomenon. Here, we provide definitions for terms according to how they are used in this Review.

**Cortical state**
The dynamics of network activity on a timescale of seconds or more. For our purposes, the defining characteristic of cortical state is the amount of slow fluctuation in the summed activity of a set of local neurons. Cortical state is not bimodal; however, for linguistic convenience we refer to synchronized and desynchronized states to describe relative positions along a continuum.

**Desynchronized state**
A situation in which the population rate in a cortical column fluctuates only weakly. In such a state, low-frequency local field potential (LFP) power is also comparatively small. However, neuronal coherence at gamma frequencies often increases in the desynchronized state[52], leading some authors to question the use of this term. The terms asynchronous state and activated state are largely synonymous with the term desynchronized state, although it should be remembered that 'activated' does not refer to an increase in firing rates, as the firing rate of some neurons may go down in desynchronized states.

**Synchronized state**
A situation in which the average population firing rate in a cortical column fluctuates strongly at a timescale of ~100 ms or slower. In such a state, low-frequency LFP power is high, although power at gamma frequencies may decrease. Other terms that are used for this state include deactivated and inactivated. Once again this does not necessarily imply lower firing rates or ion channel inactivation.

**Up phase and down phase**
The terms up state and down state were originally used to refer to the two modes of the bimodal distribution of membrane potentials that are seen in intracellular recordings of striatal and cortical neurons *in vivo*[198]. Subsequently, however, the usage of these terms has widened to include any periods of spontaneous depolarization and hyperpolarization, even when the histogram of membrane potentials is not bimodal. Furthermore, as intracellular up and down states occur during phases of strong local network spiking and silence, respectively, the terms are now also used to refer to spiking and silent phases of population activity, even in the absence of intracellular recordings. Spontaneous depolarizations and spiking periods also go by other names, such as population bursts[199] or bumps[4].

To add further confusion, the up state and down state are not, in our usage, actually cortical states. A cortical state (as the term is used in this Review) refers to a global pattern of cortical dynamics — such as the desynchronized or synchronized state — that changes over a time course of seconds or more and is defined by fluctuation magnitudes or power spectra that can only be computed from several seconds of data. Up and down states occur at timescales of ~100 ms, and are thus not states but phases of an ongoing fluctuation. For the sake of clarity, we therefore use the terms up phase and down phase in this Review.

to a steadier spiking pattern; but unlike in neocortex, this relatively steady activity is superimposed with a rhythmic 6–10-Hz theta oscillation. The character of the hippocampal theta oscillation is also fundamentally different to the fluctuations of cortex in the synchronized state. In the latter, all neurons show increases in firing in the up phase and decreases in the down phase, resulting in a strongly fluctuating population rate during the synchronized state. By contrast, individual hippocampal pyramidal cells show phase relationships to the theta rhythm that vary between neurons, and even within individual cells, from moment to moment[75–77]. This results in a pyramidal cell population with a summed firing rate that is only weakly modulated by theta phase[78] (BOX 2).

***How does state correlate with ongoing behaviour?*** The behaviour dependence of brain state has been best studied in the hippocampus. In the rat hippocampus, the theta state occurs during behaviours such as walking, running, rearing and exploratory sniffing, whereas LIA occurs during behaviours such as waking immobility,

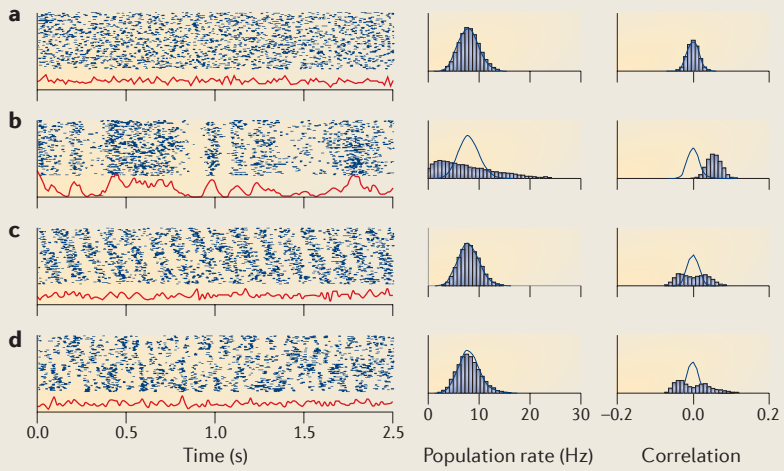
Box 2 | **Mathematical relationship between fluctuation and correlation**

Intuitively, it would be expected that if a set of neurons show a common fluctuation in firing rate, their activity will in general be positively correlated. To clarify this idea, consider a population of $N$ neurons and let $x_i$ refer to the instantaneous firing rate of the $i^{th}$ neuron, as could be measured by counting spikes in some time-bin. Then $\frac{1}{N}\Sigma_i \times_i$ is the population rate in the corresponding time-bin. For any set of random variables $x_i$ it holds that:

$$Var\,(\Sigma_i x_i) = \Sigma_i Var\,(x_i) + \Sigma_{i\neq j}\, Cov(x_i, x_j)$$
$$= \Sigma_i Var\,(x_i) + \Sigma_{i\neq j}\, \alpha_{ij} Corr(x_i, x_j) \quad \text{where} \quad \alpha_{ij} = \sqrt{Var\,(x_i)\, Var\,(x_j)}$$

This equation therefore implies that the variance of the population is dominated by a weighted mean of the correlation coefficient of all cell pairs. If the population rate does not fluctuate and has small variance then the mean correlation must be close to zero. This could happen either when all neurons fire independently or when positively correlated cell pairs are counterbalanced by an equal number of negative correlations. Conversely, when mean correlations are non-zero, this implies that there are large fluctuations in population rate even if the correlations are themselves of moderate order (for example, <0.1).

Four illustrations of this relationship are shown for simulated spike trains of 128 neurons of equal firing rate (see the figure). In each row, the left panel shows 2 s of simulated data, with the blue raster plots representing the spikes of all cells and the red traces representing the instantaneous population rate. The middle panel in each row shows a histogram of population rates over 50 s of simulated data and the right panel shows the histogram of correlation coefficients over all cell pairs. The blue curves in the right two histograms correspond to outlines of the histograms for independent Poisson neurons. In the first example, the neurons fire as independent Poisson processes (see the figure, part **a**). The population rate has low variance and the mean correlation is zero. The width of the correlation histogram reflects the expected size of statistically insignificant correlation coefficients arising from random fluctuations. In the second example, the neurons fire as inhomogeneous Poisson processes, modulated by a single fluctuating rate function (see the figure, part **b**). The population rate has high variance and the mean correlation is positive but small. The data resemble cortical activity in a synchronized state. In the third example, the neurons are modulated by a common sinusoidal oscillation but with phases distributed evenly across the population (see the figure, part **c**). Similar to the independent cells in the first example (part **a**), the population rate has low variance and the mean correlation is close to zero. In this case, however, the correlation histogram is wider than in part **a**, indicating an equal number of significantly positively and negatively correlated pairs. This pattern shows how it is possible for a population to be modulated by a common oscillation (such as hippocampal theta) while remaining in a desynchronized state. In the fourth example, the neurons display a more complex pattern of cell assembly activity (see the figure, part **d**). However, population activity has low variance because positive correlations among neurons that are frequently joining in one assembly are counterbalanced by negative correlations among neurons that only rarely do so (see REF. 200). Similar to the neurons in the third example (part **c**), the population rate has low variance and the mean correlation is close to zero, but the distribution of correlations is wide, indicating an equal number of significantly positively and negatively correlated pairs.



eating, grooming and defecation[79]. Although various terms have been used to characterize the circumstances under which these states are seen in rats (for example, 'voluntary' or 'exploratory' for theta, 'automatic' or 'consummatory' for LIA), the precise list of behaviours for each state is species-dependent[80,81]. The mechanisms and implications of these species differences are still poorly understood.

In the rodent neocortex, variations in state during waking are more subtle than in the hippocampus and were not detected in early studies that were based on visual inspection of pen-chart EEG recordings[82] (FIG. 2a). However, spectral analysis later revealed a suppression of low-frequency LFP power in actively behaving awake rats compared with awake but immobile rats[83]. In head-fixed mice, cortical activity becomes desynchronized during behaviours such as whisking or ball-running[5,7,38] (FIG. 2b). The effect of behaviour on cortical state can be greatly amplified by pharmacological treatments: for example, after delivery of the muscarinic antagonist atropine, large, slow, sleep-like cortical activity occurs during quiet rest, but this activity is suppressed during locomotion[84] (FIG. 2a,c).

## Mechanisms controlling cortical state

What are the mechanisms responsible for the control and maintenance of cortical states? We will divide this question into three: how can a cortical area maintain a desynchronized state; what produces the fluctuations of the synchronized state; and what causes a cortical area to switch between states?

***How can cortex maintain a desynchronized state?*** As discussed earlier, the level of fluctuation that is exhibited by a neuronal population is related to the mean pairwise correlation of the constituent neurons. It has long been recognized that two neurons can be correlated without having a direct synaptic connection, and that a correlation can also arise from excitatory or inhibitory inputs that are shared between the two cells[85]. Conversely, one might expect that any two neurons that share a large number of inputs — such as neighbouring pyramidal cells of cortex — will necessarily display correlated activity. This is indeed seen in feedforward network models, in which even uncorrelated inputs can lead to synchronous spiking output[86–88]. Furthermore, neuronal pairs in primates frequently have noise correlations of the order 0.1 (REFS 33,89–93); numerically close to those predicted on the basis of anatomically shared connections[86]. It was therefore suggested that such correlations are an inevitable property of cortical shared connections, and that they result in a reduction in coding capacity because shared noise cannot be averaged out efficiently[86,92].

Although a correlation of 0.1 between any two neurons is small, this level in fact indicates prominent global fluctuations in population firing (BOX 2). If such correlations were inevitable, a truly desynchronized state would be impossible. However, recent studies have shown that mean correlations very close to zero can occur in primary visual cortex (V1) of behaving primates[94] and in somatosensory and auditory cortices of rats in the

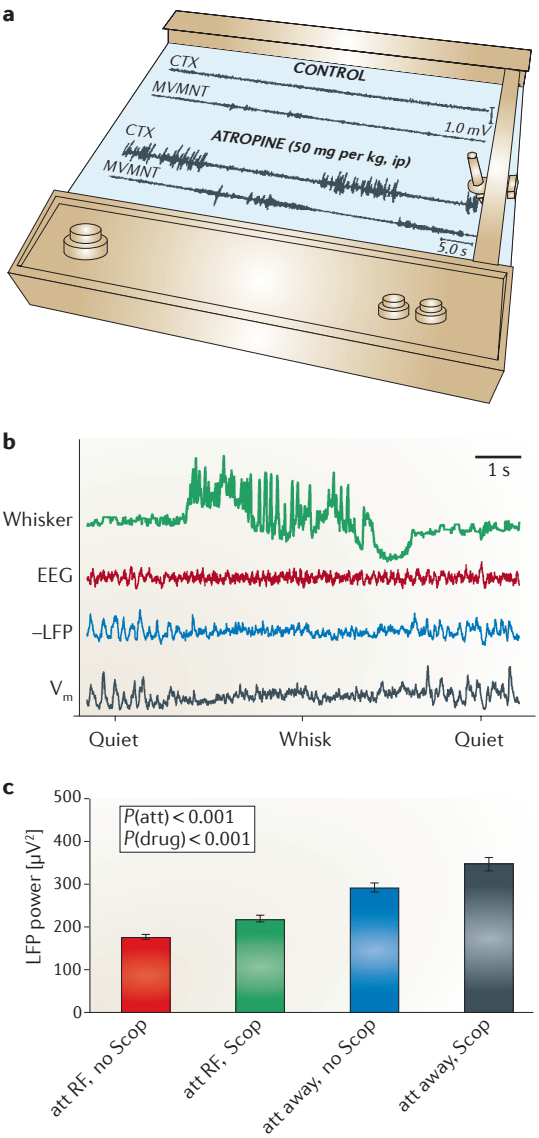



Figure 2 | **Cortical local field potential and behaviour.** **a** | In classical pen-chart recordings, the correlation between behaviour and the cortical electroencephalogram (EEG) is difficult to detect visually under control conditions (shown by the top two traces; the cortical EEG (CTX) and movement (MVMNT)) but is greatly amplified by intraperitoneal (ip) application of 50 mg per kg of the muscarinic antagonist atropine (shown by the bottom two traces). **b** | A recent study showed a reduction of spontaneous fluctuations during whisking behaviour, clearly visible in intracranial local field potential (LFP) and membrane potential but more difficult to detect visually in the surface EEG. **c** | In monkey primary visual cortex (V1), low-frequency (2–10-Hz) power is reduced when attention is directed into the receptive field corresponding to the electrode site (att RF; shown in red and green) and is increased by application of the muscarinic antagonist scopolamine (Scop; shown in green and black) or when attention is directed to a different location (att away; shown in blue and black). $V_m$, membrane potential. Part **a** is reproduced, with permission, from REF. 82 © (2003) Kluwer Academic Publishers. Part **b** is reproduced, with permission, from REF. 7 © (2008) Macmillan Publishers Ltd. All rights reserved. Data in part **c** are from recordings in the laboratory of A.T. (unpublished observations; see REF. 183 for methods).

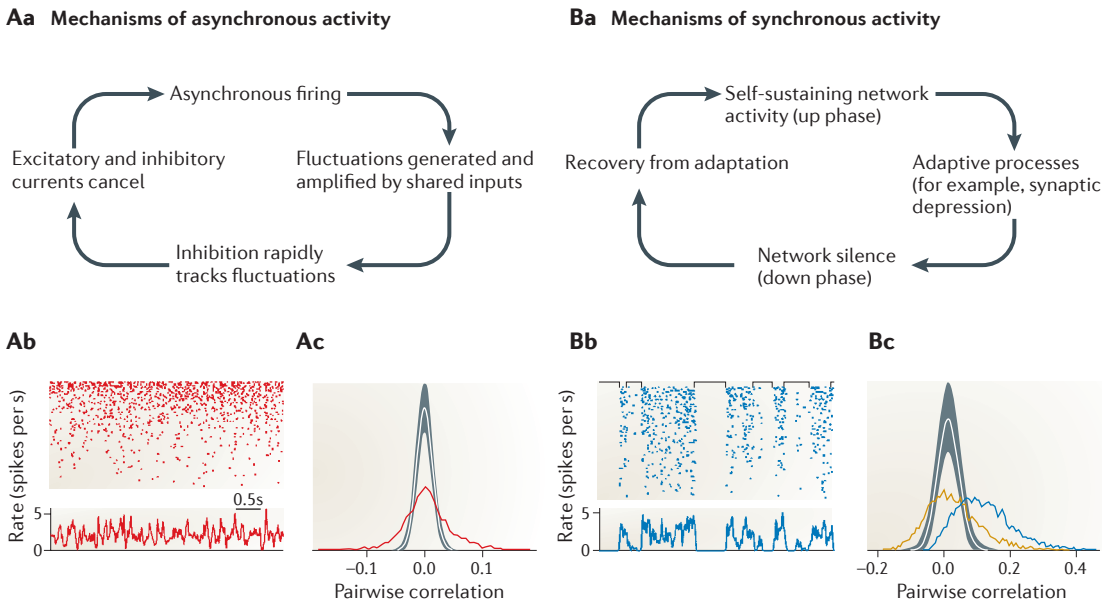



Figure 3 | **Possible mechanisms of asynchronous and synchronous activity. Aa** | Correlations that are generated by shared excitatory input may be cancelled by rapid recurrent inhibition. **Ab** | A raster plot showing spontaneous activity of a simultaneously recorded population of neurons in rat somatosensory cortex in a desynchronized state. The bottom trace plots the population rate as a function of time, showing a small degree of fluctuation. **Ac** | A histogram of pairwise correlations in the same population of neurons as in **Ab** (shown by the red trace). The mean is close to zero but the long tails indicate an approximately equal number of significant positively and negatively correlated pairs. The grey curve shows the distribution of correlations that would be expected by chance. **Ba** | An excitable system model of slow fluctuations in cortical activity in which up phases are generated and sustained by recurrent synaptic activity before being overcome by adaptive processes. **Bb** | A raster plot showing spontaneous activity of the same population of neurons as in **Ab** but now in a synchronized state. **Bc** | A histogram of pairwise correlations in the same population of neurons as in **Ab**, showing a positive mean for the whole data set (shown in blue) but a mean that is close to zero when considering up phases only (shown in yellow). Panels **Ab**, **Ac**, **Bb** and **Bc** are reproduced, with permission, from REF. 32 © (2010) American Association for the Advancement of Science.

desynchronized state under urethane anaesthesia[32]. The cortex must therefore have some mechanism to enforce decorrelation, even when there are multiple shared inputs.

The answer to this conundrum may lie with inhibition (FIG. 3a). Although shared inhibitory inputs lead to positive correlations[95], this effect can be cancelled if the excitatory and inhibitory inputs to a pair of neurons are themselves correlated. Theoretical analysis suggests that if inhibition is sufficiently fast and strong, recurrent networks self-organize into a state in which the fluctuations that are produced by shared connections are rapidly 'tracked' by inhibitory interneurons, leading to extremely small mean correlations in large networks[32]. This analysis also predicts that even when the mean correlation is close to zero, a substantial number of neuronal pairs should remain correlated, with approximately equal numbers of positively and negatively correlated cell pairs. This prediction is substantiated in rat cortex, both in the desynchronized state and within up phases of the synchronized state[32].

***What causes fluctuations during synchronized states?*** If positive correlations do not inevitably arise from shared inputs, why are they so frequently observed? The relationship between mean pairwise correlation and the variance of population rate allows us to ask the same question in a different way: why does the activity of neural populations exhibit spontaneous fluctuations in population rate, and why do sensory stimuli induce responses with population rates that vary from one presentation to the next? We address the question of spontaneous fluctuations here and discuss sensory-evoked correlations in the next section.

The fact that fluctuating spontaneous activity occurs even in isolated cortical slices and slabs[96,97] suggests that intracortical mechanisms may have a primary role in generating them. Many cellular and synaptic processes have been implicated in the generation of these fluctuations, but all these processes can be understood within a single conceptual framework, known as the theory of excitable systems (FIG. 3b). In this framework, spiking in the up phase is sustained by recurrent synaptic activity[96,98]. But after a period of prolonged firing, a number of adaptive processes occur that steadily reduce the excitability of the network, such as synaptic depression[99,100], a build-up of afterhyperpolarizing $K^+$ conductances[96] and decreased ATP levels[101]. When sufficient adaptation has occurred, the network's ability to sustain firing fades, leading to a period of network silence. Subsequently, after sufficient 'rest' the synapses and cells recover, and the network can again sustain recurrent activity. Computational models that are based on these principles are able to produce data very similar to those obtained *in vivo* and *in vitro*[31,102–105]. A key feature

Excitable systems
A class of dynamical system models that are used to describe various physical, chemical and biological phenomena. These systems reflect a combination of fast positive feedback that amplifies small perturbations and slower negative feedback that brings the system back to baseline once fluctuations become large.

of this mechanism is that the down phase is caused not by synaptic inhibition but by disfacilitation — that is, the temporary absence of synaptic drive[49,106]. Both *in vitro* and *in vivo* studies suggest that within a cortical column, the up phase is generated in layer V, from where it can (but does not always) spread to superficial layers[10,96].

This scenario also explains why spontaneous cortical fluctuations spread as travelling waves. Once a certain region of cortex has entered an up phase, lateral excitation from this region can spark an activity in neighbouring cortex, but a second wave cannot pass until there has been sufficient time for the recovery of synaptic and cellular adaptation. Models of spatially coupled excitable systems are known as excitable media and have been used to describe diverse phenomena including forest fires, wave propagation in cardiac tissue and stadium waves at sporting events[107].

***What causes changes in cortical state?*** Several mechanisms have been implicated in cortical state shifts, including increased activity of subcortical cholinergic and monoaminergic nuclei, as well as sustained glutamatergic inputs from thalamus and possibly other cortical regions[82,108]. Much of the work that we review here is classical but, despite its relevance, it is rarely discussed in the modern literature.

The cholinergic system plays an important, though not exclusive, part in controlling cortical state. Lesions of the basal forebrain — the primary source of cholinergic input to cortex — increases low-frequency LFP power[83], whereas electrical or pharmacological stimulation of basal forebrain or cholinergic brainstem nuclei causes cortical desynchronization that is blocked by systemic or cortically applied muscarinic antagonists such as atropine[52,53,83,109]. Cholinergic basal forebrain and brainstem neurons show increased firing during cortical desynchronization[109–112]. Nevertheless, cholinergic input is not necessary for cortical desynchronization: although atropine causes a strongly synchronized state in awake immobile rats, actively behaving rats show atropine-resistant desynchronization[82,84] (FIG. 2a). Moreover, selective lesions of cholinergic neurons in the basal forebrain are not sufficient to abolish cortical desynchronization[113].

What might be responsible for acetylcholine-independent desynchronization? Stimulation of other neuromodulatory systems can cause desynchronization, although in some cases this occurs through their effects on the basal forebrain[114–117]. Serotonin may play an important part in acetylcholine-independent desynchronization, as suggested by the atropine resistance of desynchronization that is induced by dorsal Raphe stimulation and by the ability of serotonin depletors combined with atropine to block desynchronization even during active behaviour[115,118,119]. Cortical noradrenaline release has an important role in reducing spontaneous fluctuations as rats wake from anaesthesia, at least in layer IV of primary somatosensory cortex[120]. Neurons in cholinergic and other neuromodulatory nuclei show diverse and rapid modulation of firing rate in response to salient sensory stimuli, behavioural events and cognitive factors such as attention and expected reward, which is consistent with the cortical state being controlled on a moment-to-moment basis[121–129].

An additional mechanism that is implicated in cortical desynchronization involves increased tonic firing of glutamatergic afferents from the thalamus and perhaps elsewhere. Tonic thalamic firing increases under several conditions that are associated with cortical desynchronization[130–134]. This may in turn reflect thalamic neuromodulation; the thalamus receives strong cholinergic input from the brainstem and this depolarizes thalamic relay cells and can shift them to a mode of steady tonic firing, both through direct excitation of relay cells and through disinhibition resulting from cholinergic inhibition of thalamic reticular neurons[135–137]. Increasing tonic relay cell firing (by microdialysis of the non-specific cholinergic agonist carbachol into somatosensory thalamus) causes desynchronization of barrel cortex[138], suggesting that tonic glutamatergic input from the thalamus is sufficient to desynchronize barrel cortex.

How could neuromodulatory and tonic glutamatergic inputs suppress fluctuations in cortical activity? Neuromodulatory systems and metabotropic glutamate receptors have diverse effects on different classes of cortical neurons and synapses, in a manner that may vary further as a function of cortical area and age[139–150]. These multiple receptor systems probably allow fine-tuning in a high-dimensional space of cortical operating modes. Nevertheless, their effects also have several similarities, which paint a basic picture of how these systems can reduce cortical fluctuations. First, multiple neuromodulatory systems and metabotropic glutamate receptors affect the firing mode of pyramidal cells, reducing bursting, afterhyperpolarization and adaptation, and promoting tonic firing[141,143,148,150–158]. Second, multiple neuromodulatory systems cause a reduction in the strength of recurrent excitatory synapses within cortex, with a concomitant reduction in synaptic depression[146,159–161]. Third, metabotropic glutamate and multiple neuromodulatory systems cause tonic depolarization of pyramidal cells in cortical layer V, where cortical fluctuations are thought to be generated[150,162,163]. These three processes should switch the cortex from a mode in which bursting and recurrent excitation lead to rapid increases in population rate that are subsequently dampened, through adaptation, to a mode in which tonic depolarization causes neurons to maintain relatively steady activity. Simulations that are based on both detailed biophysical models and simple dynamical systems support this picture[31,102,104,105].

Recent results suggest that cortical state is in fact a multidimensional continuum, with different forms of desynchronization reflecting non-identical changes in cortical operating mode. As mentioned above, gamma power may either increase or decrease during desynchronization. Furthermore, the firing rates of individual neuronal classes can differ between desynchronizing conditions: putative fast-spiking interneurons fire faster during locomotion[38], in more difficult discrimination tasks[164] and after artificial elevation of thalamic firing[138]. Conversely, during rodent whisking, fast-spiking interneurons fire slower, whereas non-fast-spiking interneurons fire faster[45]. Many non-fast-spiking

interneurons are excited ionotropically by acetylcholine and serotonin receptors[165] and inhibit fast-spiking interneurons[166], whereas fast-spiking interneurons receive strong glutamatergic drive from thalamus[167]. It is therefore possible to speculate that these two types of desynchronization exhibit a different balance in neuromodulatory versus tonic glutamatergic drive. Modern techniques, such as optogenetics and enzyme-linked electrochemistry[168], may help to resolve the full space of cortical states and the roles of different afferent systems in state and information processing.

## Cortical state and sensory responses

Cortical sensory responses correlate strongly with state. However, the way in which cortical state shapes sensory processing is complex: one cannot simply ask whether responses are larger or smaller in one state or another; instead, the effect of cortical state on neuronal responses seems to depend on the specific type of stimulus that the system is confronted with. Nevertheless, some commonalities are beginning to emerge from studies of multiple sensory areas. In particular, it seems that isolated punctuate stimuli (which could also be labelled as salient, unexpected brief stimuli) are able to generate substantial responses regardless of cortical state, whereas temporally extended or rapidly repeated stimuli are 'filtered out' in synchronized states but are efficiently processed in the desynchronized state (FIG. 4).

Responses to simple punctuate stimuli (for example, whisker deflections and auditory clicks) have been well studied in barrel and auditory cortices in rodents. When discussing how a sensory response is modulated by state we must consider how the response differs between synchronized and desynchronized states, and between the up and down phases within the synchronized state. In rat auditory and somatosensory cortices, the initial response (up to ~50 ms) to a punctuate stimulus is larger in synchronized states and in quiescent animals than in desynchronized states and in actively engaged animals[130,169,170]; larger auditory onset responses are also seen in passive compared with behaviourally engaged ferrets, with smaller onset responses for more difficult detection tasks[171]. Within the synchronized state, the initial response does not depend strongly on phase, with stimuli that arrive in the up and down phases evoking initial responses of approximately equal magnitude[31,172] — a phenomenon that may be related to the suppression of firing variability by stimulus onsets[173]. The later stimulus response period (after ~50 ms) shows more complex dependence on state and phase[31,172]: in synchronized states, punctuate stimuli can trigger long-lasting up phases that can spread over the cortical surface[6,61] — a phenomenon that may be related to observations that receptive fields of sensory cortex neurons are often wider in synchronized states than in desynchronized states[40,174]. In the desynchronized state, the response to a single punctuate stimulus is typically simpler, consisting of a brief response followed by a transient ~100-ms suppression below baseline and a depth-positive LFP wave in all but the most desynchronized conditions[31,175]. Despite the apparent complexity of these results, such state-dependent sensory responses can be quantitatively predicted on a trial-by-trial basis by a simple excitable

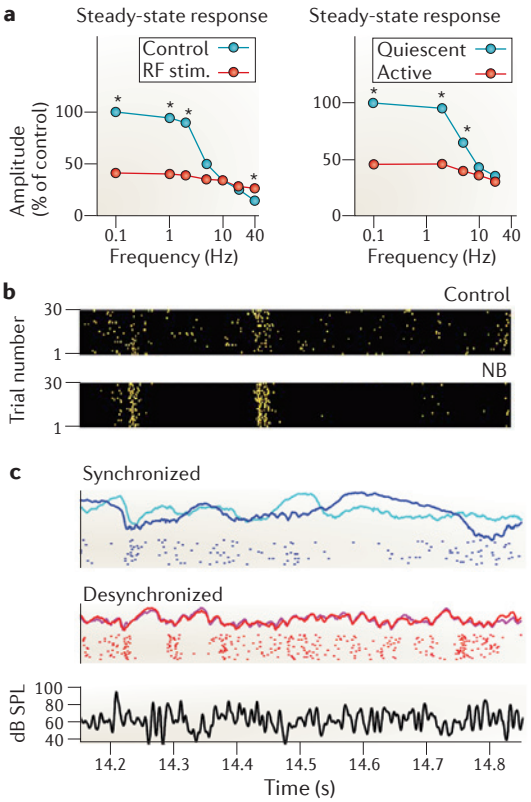



Figure 4 | **State-dependent responses to punctuate and extended stimuli. a** | State-dependent responses of anaesthetized rats (left panel) and awake rats (right panel) to stimulus trains in barrel cortex. In synchronized states under anaesthesia and in quiescent awake animals (shown by blue circles), responses to rare punctuate stimuli are large, but responses adapt strongly at high repetition frequencies. After electrical stimulation of the reticular formation (RF stim.) or during active behaviour (shown by red circles), responses to rare stimuli are smaller and adaptation is reduced. **b** | A raster representation of a visual cortical unit response to repeated presentations of a temporally extended natural scene movie. Stimulation of the nucleus basalis (NB) increases the reliability of responses from trial to trial. **c** | The response in auditory cortex to repeated presentations of a temporally extended amplitude-modulated noise stimulus. Evoked local field potentials (LFPs) from two presentations of the same stimulus in synchronized states (shown by dark and light blue traces) and desynchronized states (shown by red and purple traces), as well as the raster representation of spikes from one cell in response to repeated presentations of the stimulus in each state. The black curve (bottom panel) shows the stimulus envelope. LFP and spiking responses are more reliable in desynchronized states. SPL, sound pressure level. Part **a** is reproduced, with permission, from REF. 170 © (2004) Cell Press. Part **b** is reproduced, with permission, from REF. 132 © (2009) Macmillan Publishers Ltd. All rights reserved. Part **c** is reproduced, with permission, from REF. 176 © (2011) Society for Neuroscience.

Table 1 | **Similarities between desynchronization in rodents and attention in primates**

| Measurement | Effect of desynchronization or active behaviour in rodents | Effect of attention in primates |
|---|---|---|
| Low-frequency LFP power | Reduced[7,38,53,83] | Reduced[18,21,22] |
| Gamma LFP power | Increased (running, cholinergic stimulation and thalamic stimulation)[38,52–55]; decreased (dorsal Raphe stimulation)[56] | Increased (V4)[18]; decreased (V1)[21] |
| Trial-to-trial variability | Reduced[31,132,176] | Reduced[19,20] |
| Noise correlation | Reduced[32,132] | Reduced[19,20] |
| Response size | Reduced (sudden punctuate stimuli)[130,170]; unchanged or enhanced (rapidly repeated or temporally extended stimuli)[132,170,176] | Reduced (unattended stimuli)[208]; enhanced (attended stimuli)[12,13,16] |

LFP, local field potential; V1, primary visual cortex.

system model, using parameters derived from the spontaneous activity preceding the stimulus[31].

The presentation of repeated or temporally extended stimuli reveals another aspect of state dependence. Although the response to the first stimulus in a train of rapidly repeated punctuate stimuli is larger in synchronized than in desynchronized states, response adaptation is stronger in the synchronized state, so that by the end of the train responses are equal between states or smaller in the synchronized state[130,170] (FIG. 4a). In rat visual cortex, temporally extended movies of natural scenes are more faithfully represented after basal forebrain stimulation[132] (FIG. 4b), and responses to continuously drifting gratings are larger in visual cortex of running mice than stationary mice[38]. These data might seem to conflict with the smaller responses to isolated punctuate stimuli in desynchronized somatosensory and auditory cortex. However, it seems unlikely that this is due to a difference between sensory modalities, as the representation of temporally extended amplitude-modulated noise stimuli is also more faithful in desynchronized auditory cortex[176] (FIG. 4c). We therefore suggest that the effects of desynchronization on neuronal responses to sensory stimuli are similar across modalities: onset responses are smaller but adaptation is reduced, leading to an enhanced representation of repeated or temporally extended stimuli.

We emphasize that state-dependent changes in cortical representations do not necessarily arise from changes in cortical processing but could also reflect changes in lower structures. Indeed, in synchronized states thalamic relay neurons show an enhanced propensity to fire in 'burst mode'. This enhanced propensity may emphasize the response to the onset of a stimulus train but may interfere with the linear representation of temporally extended stimuli[177]. During desynchronized states, increased baseline (tonic) firing of thalamic relay cells may cause depression of thalamocortical synapses, which would reduce the response to the first stimulus in a stimulus train but would also reduce the potential for further adaptation, because these synapses are already close to being fully depressed[170].

Why would it be beneficial for an animal to enhance responses to sudden punctuate stimuli but suppress responses to temporally extended stimuli in the synchronized state? One suggestion relates to the different behavioural needs of active versus quiescent animals. The fine details of ongoing continuous sensory stimuli may be of little relevance to a resting animal, so nothing is lost by filtering them out and allowing cortex to exhibit the endogenously generated patterns that are typical of a synchronized state. However, a punctuate stimulus such as a sudden unexpected sound or touch may signal the need for an immediate behavioural response. Larger responses to punctuate stimuli in the synchronized state might therefore serve as a 'wake-up call', enabling appropriate motor responses to unexpected events in passive animals[6,178].

## Cortical state and attention in primates

The classical view of cortical states is that they are global, synchronizing or desynchronizing all cortical areas simultaneously. With regard to the sleep cycle this is generally the case (with certain exceptions; for example, in cetaceans[179]). However, a growing body of evidence suggests that in awake primates, selective attention also affects the level of cortical desynchronization at a local level, at a reduced scale compared to the differences between sleep and waking. By this interpretation, the maximum desynchronization is restricted to a small patch of cortical tissue that represents the attended stimulus while cortical tissue that represents non-attended parts of the sensory world would be in a more synchronized state. We argue that such local changes of state can explain the results from many laboratories on attention-related changes in LFP power, response variability and correlation (TABLE 1).

One of the hallmarks of cortical desynchronization is a decrease in low-frequency LFP power. Studies in multiple visual areas in monkeys have shown that when attention is directed to, rather than outside, the receptive field of recorded neurons near the recording electrode, this results in a decrease in low-frequency LFP power[18,21,22] (FIG. 2c). This result implies that attention modulates the size of low-frequency fluctuations at a local level: if attention simply caused desynchronization uniformly across the cortical surface, LFP power would not change depending on the receptive field location. Surprisingly, attention-associated low-frequency desynchronization can be accompanied by either increased or decreased gamma LFP power[18,21], a finding that is reminiscent of the differential effects on gamma power of stimulating

different subcortical structures in rats (discussed above). The circuit mechanisms and implications of these dissociations between low-frequency desynchronization and gamma power are as yet unknown.

Attention reduces trial-to-trial variability and firing rate correlations between neurons, which is also consistent with local desynchronization. Neuronal responses to repeated presentations of an identical stimulus vary from trial to trial, and variations in the responses of neighbouring neurons are typically correlated in cortex of awake primates[90]. These noise correlations typically reduce the information that can be encoded in populations[92,180,181]. Recent studies have shown that in area V4, both variability and noise correlations are reduced when attention is directed to the receptive field of the recorded neurons[19,20,23]. Coherence analysis suggests that these correlations arise from low-frequency (<5-Hz) fluctuations in firing rate that are correlated across the neuronal population[19]; this resembles a more-synchronized state, which is desynchronized by attention. Reduced noise correlations are also found in rodent auditory cortex after spontaneous desynchronization[31], and in visual cortex after basal forebrain stimulation[132], where reduced correlations are mediated by cortical muscarinic mechanisms.

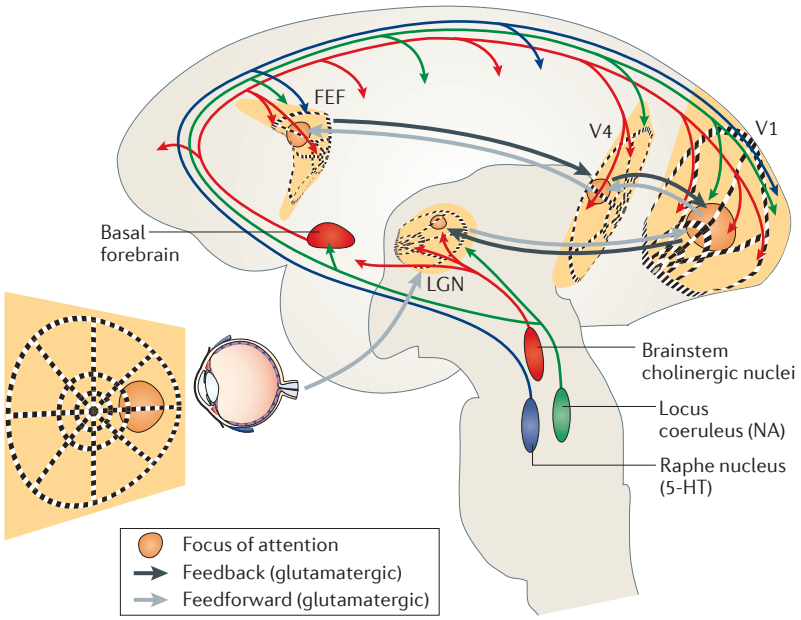



Figure 5 | **Suggested mechanisms for desynchronization during state changes and attention.** An increase in the activity of cortical neuromodulatory afferents, including cholinergic afferents (shown by red arrows), serotonergic afferents (shown by blue arrows) and noradrenergic afferents (shown by green arrows), causes a general desynchronization and reduction in spontaneous fluctuations, but this mechanism may lack the spatial selectivity to desynchronize the patch of cortex that represents the attended stimulus. Focused glutamatergic inputs arising from feedback connections (shown by black arrows) could provide this specificity, causing enhanced desynchronization and sensory responses in the regions of cortex that represent the attended stimulus. The focus of attention (shown by the orange patch in the visual display) affects processing in thalamic and cortical areas at specific locations (shown by the orange patches at different locations). The distorted replication of the visual world in the different areas illustrates the known retinotopic organization of these different areas. 5-HT, 5-hydroxytryptamine (serotonin); FEF, frontal eye field; LGN, lateral geniculate nucleus; NA, noradrenaline; V1, primary visual cortex.

The effects of attention in primates vary throughout the response time course, similar to the effects of cortical state in rats. Immediately after a stimulus appears in the receptive field, spike count variability and correlation in V4 are suppressed regardless of whether the stimulus was attended to. During the sustained response period however, variability and correlation increase in unattended conditions[19,20]. This effect is similar to the effects of state on responses to punctuate stimuli in rat auditory and barrel cortex[31,172], in which the initial response is largely independent of cortical state and phase (and thus not highly variable from trial to trial) but the later response shows strong variability in the synchronized state. Furthermore, attention reduces the adaptation of V4 responses to repeatedly presented visual stimuli, which again is similar to desynchronization in rodents[182].

## Circuit mechanisms of attention in primates

Although the circuit mechanisms of top-down attention are still largely unknown, recent primate experiments have begun to cast light on this question, and in particular on the contribution of different receptor systems. Again, there seem to be strong parallels to cortical state, with an important role for the cholinergic and glutamatergic systems in particular. In behaving primates, iontophoresis of acetylcholine or muscarinic antagonists respectively increases and decreases the effects of attention on spiking patterns in V1 (REF. 183) and V4 (REF. 184). It seems unlikely however, that cholinergic input could be solely responsible for attentional modulation within cortex: despite the topographic organization of basal forebrain projections at the level of cortical lobes and regions[185], it seems improbable that cholinergic afferents have the spatial specificity to target any small patch of cortex that represents an attended stimulus. Thus, although cholinergic mechanisms are involved in attentional modulation in visual cortex, they probably work in interaction with other systems. It may be that cholinergic drive is crucial for setting the network to be maximally responsive to localized glutamatergic feedback from higher cortical areas[186] (FIG. 5).

A role for glutamatergic feedback projections in producing the local effects of attention has been shown by studies of the frontal eye fields (FEFs). FEFs project to extrastriate visual cortices (these feedback projections are glutamatergic), and spiking activity in FEFs is correlated with attention[187]. Elegant studies have shown that microstimulation of appropriate parts of FEFs shift the focus of attention, as measured at the behavioural level[188], and produce a modulation of neuronal coding in V4 that is similar to that seen with attention[189]. As described above, a combination of cholinergic and tonic glutamatergic input is likely to place cortex in a strongly desynchronized state.

The mechanisms by which glutamatergic feedback could increase the gain of visual cortical responses are unknown. However, one intriguing suggestion involves the NMDA receptor (NMDAR). Because of the voltage-dependent nature of NMDAR-mediated glutamate responses, postsynaptic depolarization might multiplicatively increase the excitatory currents that are induced

Box 3 | **Cortical state and resting state networks**

A view of spontaneous cortical activity that complements the one that is described in this Review comes from studies in humans using functional MRI[195,196]. As with electrical recordings, these studies suggest that spontaneous activity is not simply noise but a structured signal that is related to behavioural and cognitive factors. Spontaneous blood oxygen level-dependent (BOLD) activity shows slow (<0.1-Hz) spatiotemporally patterned fluctuations, with positive correlations within a number of resting state networks but weaker or negative correlations between networks[201,202]. The resting state networks consist of groups of functionally and anatomically related cortical areas — for example, sets of regions that are involved in visual or auditory processing as well as a 'default mode network' whose activity is greatest in resting subjects. Fluctuations in the spontaneous activity of these networks correlate with natural fluctuations in task performance[203].

How might these observations relate to the phenomena described in this Review? It seems unlikely that spontaneous fluctuations in BOLD correspond to up and down phases, as their timecourse is at least an order of magnitude slower. Instead, a number of observations suggest that the BOLD signal may be related to local cortical state. BOLD correlates with local field potential (LFP) power, both spontaneously and in response to sensory stimuli, with the strongest correlations seen in the gamma band[204,205]. Visual cortical BOLD increases with visual attention in a topographic manner, with larger increases for more difficult detection tasks[206], and cortical blood flow can be controlled by neuromodulatory activity[207]. These findings would seem to suggest that BOLD should increase during cortical desynchronization. Nevertheless, the exact relationship of BOLD to cortical state is not yet fully clear. Although BOLD reliably correlates with gamma power, the correlation between spontaneous BOLD and lower-frequency LFP power varies between animals and can be positive[204]. This result might seem puzzling, as gamma and low-frequency power are themselves typically anticorrelated. One explanation may be that the space of cortical states is high-dimensional. Under some conditions, gamma and low-frequency power exhibit a positive correlation[21], indicating that different LFP power bands may relate differently to a high-dimensional space of states. Understanding the relationship of the BOLD signal to this space is an important topic of future work.

by other inputs[190]. This proposal is supported by recent results on the effects of NMDA antagonists on responses in macaque V1 during a visual task[191]. In addition, it is possible that focused glutamatergic input could cause localized acetylcholine release, through presynaptic glutamate receptors on cholinergic fibres[192,193] or by activating cholinergic cortical interneurons[194].

## Summary and outlook

Large changes in cortical state are seen between waking and sleep. These changes are controlled by alterations in neuromodulatory and tonic glutamatergic input, which alter the dynamics of cortical networks and their propensity to generate fluctuations. Recent research suggests that similar mechanisms control the more subtle variations in state that are seen in awake animals. Furthermore, it seems that cortical state can be controlled at a local level, with the strongest desynchronization seen in patches of cortex that represent attended stimuli. Computational, *in vitro* and *in vivo* research in anaesthetized animals suggests that these fluctuations are generated by excitable system dynamics, reflecting the interaction of fast recurrent excitation and slower adaptive processes; further research is required to verify that excitable system dynamics also underpin the more subtle spontaneous fluctuations seen in quiescent or inattentive awake animals.

Cortical state seems to be a multidimensional continuum, and variables such as gamma power and interneuron firing rate show diverse changes depending on how desynchronization is induced. Future work using modern techniques such as optogenetics and enzyme-linked electrochemistry may soon reveal how multiple neuromodulatory systems shift the cortical operating mode in a multidimensional space of states.

The effects of cortical state on sensory responses are complex. However, a theme that emerges from work in multiple modalities is that sudden, punctate stimuli are able to generate large cortical responses in all states, whereas temporally extended stimuli are only faithfully represented in cortex during desynchronized states. This could be a manifestation of a more general phenomenon in which stimuli of strong bottom-up salience can produce large responses regardless of state, whereas desynchronization enhances responses to more-subtle stimuli while decreasing responses to unattended and bottom-up salient stimuli. Future work is required to test this hypothesis.

Cortical state does not simply affect sensory responses but also changes the character of cortical spontaneous activity. More-synchronized states are defined by larger low-frequency fluctuations in population firing and LFPs, as well as higher spontaneous and noise correlations. Similar effects are found locally within cortical columns that represent unattended stimuli. What function might these spontaneous fluctuations have, and why would they be preferentially expressed in cortical areas that are not involved in representing attended stimuli? We suggest two, non-exclusive, possibilities. The first is that synchronized states represent a 'power save' mode. Synaptic activity uses a great deal of energy and if fluctuating activity means that a column is electrically active less of the time, this presumably leaves more energy for other functions. The second possibility is that the fluctuations of the synchronized state are themselves a signature of non-sensory information processing. In the absence of sensory input the brain is still active — engaged in processes such as mental imagery and memory recall, which presumably arise from structured cortical activity independent of external stimuli. Human functional MRI studies have revealed complex large-scale fluctuations in blood oxygen level-dependent (BOLD) activity, which are at least partially related to the underlying anatomical connectivity matrix[195,196]. Understanding the relationship between BOLD and cortical state is an important topic for future research (BOX 3).

Although there are many similarities in the structure of spontaneous and sensory-evoked cortical activity patterns, they differ in their laminar profile. Spontaneous up phases are initiated not in the thalamorecipient cortical layers but in the deep cortical layers, which receive feedback projections from higher order cortices[10,197]. In addition, unlike sensory-evoked activity, spontaneous up phases typically cover large areas of cortex and could — for example — reflect coordinated recapitulation of recalled memories, including modality-specific reactivation of appropriate sensory areas.

From this perspective, suppression of spontaneous fluctuations could be interpreted as a form of attention

— not between competing sensory stimuli but between the internal and external worlds. Subjective experience suggests that when we need to detect a subtle stimulus such as a quiet sound, internally generated distractors (such as a tune running through one's head) can be as much of a hindrance as competing external stimuli. Accurate detection of subtle stimuli might therefore require suppression of structured spontaneous activity as well as of non-attended sensory inputs. Systems to control the state of cortical processing in a column-specific manner may provide animals with a toolkit with which to adaptively route sensory and non-sensory information through the brain, to help them survive in a complex and changing world.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**Competing interests statement**
The authors declare no competing financial interests.

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