

Rapid learning in cortical coding of visual scenes

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Experience-dependent plasticity in adult visual cortex is believed to have important roles in visual coding and perceptual learning. Here we show that repeated stimulation with movies of natural scenes induces a rapid improvement in response reliability in cat visual cortex, whereas stimulation with white noise or flashed bar stimuli does not. The improved reliability can be accounted for by a selective increase in spiking evoked by preferred stimuli, and the magnitude of improvement depends on the sparseness of the response. The increase in reliability persists for at least several minutes in the absence of further movie stimulation. During this period, spontaneous spiking activity shows detectable reverberation of the movie-evoked responses. Thus, repeated exposure to natural stimuli not only induces a rapid improvement in cortical response reliability, but also leaves a ‘memory trace’ in subsequent spontaneous activity.

Visual stimulation can modify the circuitry and response properties of the cortex on multiple timescales. For example, in contrast adaptation, exposure to high-contrast stimuli for seconds or minutes causes a reduction in response amplitude¹ and changes the stimulus selectivity²⁻⁴ of cortical neurons. These changes could be due to reduced neuronal excitability^{5,6} or short-term synaptic depression⁷. On a time-scale of several minutes, synchronous visual stimulation within the receptive field of a neuron and in a surround region to which that neuron does not respond causes the receptive field to expand into the co-stimulated surround⁸, which could be accounted for by Hebbian synaptic plasticity⁹. Recent studies have also shown that shifts in cortical receptive field location and orientation tuning depend on the relative timing of paired conditioning visual stimuli on the order of tens of milliseconds¹⁰⁻¹², consistent with spike-timing-dependent synaptic plasticity (STDP)^{13,14}. These studies have demonstrated that there are multiple forms of rapid plasticity in adult visual cortex. However, it remains unclear how often these mechanisms are invoked by natural stimuli, and how they enhance visual processing under natural conditions.

The importance of natural stimuli in shaping cortical function has been demonstrated on much longer time scales. During development, natural visual experience is crucial for the refinement of cortical circuitry and function over days to months^{15,16}. Although this refinement is most evident in young animals, experience-dependent improvement of visual cortical function can occur throughout life, as revealed by studies of perceptual learning in adults¹⁷⁻²¹. As these events are typically studied over days to months, the immediate effects of natural stimuli on cortical processing remain largely unexplored.

In this study, we describe a form of rapid visual cortical modification that is induced by natural stimuli. A few minutes of repeated stimulation with natural movies, but not with white noise or flashed bars, caused a significant improvement in the response reliability of cortical

neurons. Unlike contrast adaptation, in which repeated stimulation causes a reduction in cortical responses to the adapting stimuli¹, the increased response reliability was mediated by enhanced cortical responses to subsets of the repeated stimuli. Surprisingly, the repeated movie stimulation also left a memory trace in the subsequent spontaneous cortical activity, revealed by an increased similarity between the spontaneous firing patterns and the movie-evoked responses.

RESULTS

Natural stimuli improve response reliability

We made single-unit recordings in the primary visual cortex of anesthetized adult cats (see Methods) to test the effects of repetitive stimulation with time-varying natural scenes (movies). Each movie (30.1-s long; **Fig. 1a**, **Supplementary Video 1** online) was repeated 30 times, and the spike trains of each neuron during different repeats (trials) were compared to assess the reliability of the response and the change in reliability over trials. As shown in **Figure 1b**, natural movies evoked relatively sparse spiking in these cortical neurons^{22,23}, with brief episodes of high spiking probability interspersed among long periods of low spike rate. Within each episode of high spiking probability, there was considerable inter-trial variability in the number of spikes. However, this variability reduced over repeated trials, as quantified by the correlation coefficient between the time-binned firing rate in each trial (41.9 ms per bin, frame rate of the movie) and the firing rate averaged over its four neighboring trials (see Methods). As shown in **Figure 1b** (right), the correlation coefficient for the cell tended to increase over trials. For the population of cells studied (96 cells, 26 movies), the correlation coefficient increased steadily over ~10 trials before reaching saturation (**Fig. 2a**). This effect was observed regardless of the stimulation history (either drifting gratings or blank screen for several minutes before the natural movie) and over a wide range of bin sizes (data not shown). Thus, repeated exposure to the movies induced a

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Received 8 January; accepted 19 March; published online 29 April 2007; doi:10.1038/nn1895

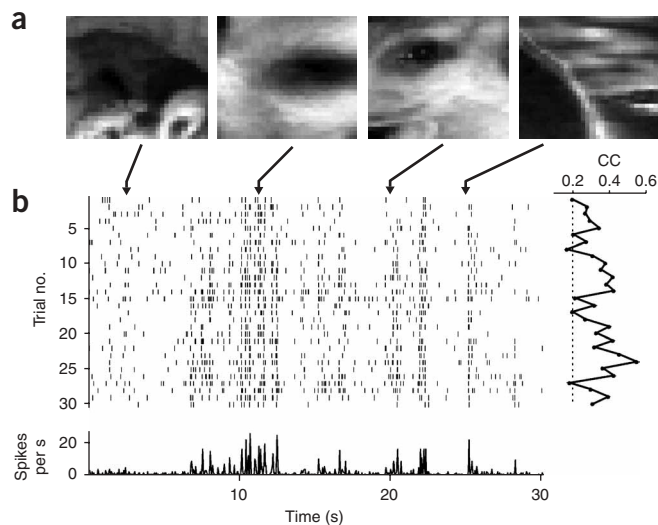


Figure 1 Improvement in cortical response reliability over repeated trials of natural movie. **(a)** Example images from a movie. Arrow, timing of each image. **(b)** Left, Responses of a V1 cell to 30 trials of the movie (raster plot and PSTH). Right, correlation coefficient (CC) between response in each trial (binned at 41.9 ms) and mean response of its neighboring four trials.

rapid reduction in cortical response variability and hence an improvement in the coding of natural stimuli.

To test whether this effect is specific to natural stimuli, we also measured cortical responses to repeated sequences of white noise and flashed bars (at the preferred orientation of each cell). These two types of stimulus did not induce a consistent increase in correlation coefficient over the 30 trials (Fig. 2b,c), indicating that the increase in response reliability (Fig. 2a) is relatively specific to natural stimuli.

Selective increase in spiking

Inspection of the spike trains that were evoked by natural stimuli indicated that the improvement in response reliability was associated with a selective increase in spiking during episodes of high firing probability (Fig. 3a, gray shading). To quantify this observation, we divided all the time bins in the peristimulus time histogram (PSTH) of each cell into two groups, based on a threshold (T) set at a fraction (for example, 20%) of the highest amplitude of the PSTH (Fig. 3b, dashed red line). The time bins in which the PSTH exceeded T were defined as ‘event’ bins (red; $14.2 \pm 1.6\%$ (s.e.m.) of all time bins) and the rest as ‘non-event’ bins (gray). When we examined spiking within each group of bins over trials, we found a marked increase in the number of spikes in the event bins, but much less change in spiking in the non-event bins (Fig. 3c). The time course of the increase in spiking was similar to that of the increase in correlation coefficient (Fig. 2a). To further investigate the selective increase in spiking and to reduce the arbitrariness inherent in choosing a single threshold, we repeated the above analysis with four thresholds (T_1 – T_4), which divided the time bins into five groups (Fig. 3d). The percentage increase in spiking increased monotonically with the threshold

(Fig. 3e,f). Thus, repeated presentation of each movie induced a selective increase in spiking probability during large events, which presumably represent responses to the preferred stimuli of the cell. Notably, repeated presentation of white noise or flashed bars also induced a preferential increase in spiking during large events, but the increase was much less than that for natural stimuli (Fig. 3f, dashed and dotted lines).

Dependence on sparseness

Why do natural stimuli induce an improvement in response reliability more efficiently than bars or white noise? The cortical responses to natural stimuli typically consist of brief episodes of high spiking probability separated by periods of low firing rate (Figs. 1b, 3b), consistent with the notion of sparse coding^{22,23}. When we compared the distribution of firing rates in response to natural stimuli with the distributions for white noise and random bars, we found that natural stimuli produced a higher probability of both near-zero and high firing rates but a lower probability of intermediate firing rates (Fig. 4a), indicating greater response sparseness. As the improved response reliability is associated with a preferential increase in spiking during large events (Fig. 3), the effect might depend on a relative abundance of these events (Fig. 4a, lower plot) and therefore on response sparseness. We measured the sparseness of each cell as $(1 - \langle r \rangle^2 / \langle r^2 \rangle) / (1 - 1/n)$, where r is firing rate at a given time bin of the PSTH, n is the number of bins, and $\langle \bullet \rangle$ denotes the average over all bins²⁴. This quantifies the over-representation of high and low firing rates and the under-representation of intermediate rates. The sparseness of the response to natural stimuli was higher than that for both white noise and flashed bar stimuli (Fig. 4b). When we plotted the increase in correlation coefficient against the response sparseness of each cell, we found a significant correlation between them ($P < 0.02$, Fig. 4c). In particular, the increase in correlation coefficient was most consistent for cells with sparseness > 0.8 (gray box), but with white noise and flashed bar stimuli the response sparseness rarely reached this level. This indicates that the effectiveness of natural stimuli at inducing the improvement in reliability might be related to the higher response sparseness.

Persistence of the effect

The improvement in reliability that was induced by the first few repeats of the movie persisted for at least several minutes in the absence of

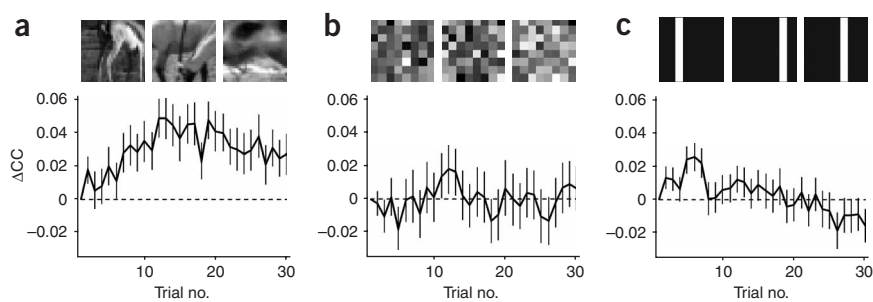


Figure 2 Improvement in response reliability is specific to natural stimuli. **(a)** Change in correlation coefficient induced by natural stimuli, averaged across 96 cells (26 movies). Δ CC: correlation coefficient in each trial minus correlation coefficient in the first trial. Error bar, \pm s.e.m. Spike trains were binned at the stimulus frame rate (41.9 ms). Increase in correlation coefficient (Δ CC averaged over trials 11–30) was highly significant ($P < 0.0001$, Wilcoxon signed rank test) for the population of cells; for individual cells, 59/96 showed significant increase ($P < 0.05$, non-parametric bootstrap), and 24/96 showed significant decrease. Top panel, example images in the stimuli. **(b)** Change in correlation coefficient induced by white noise, averaged across 46 cells (15 movies). Increase in correlation coefficient was not significant ($P > 0.5$). **(c)** Change in correlation coefficient induced by flashed bars, averaged across 76 cells (10 movies). Increase in correlation coefficient was not significant ($P > 0.5$).

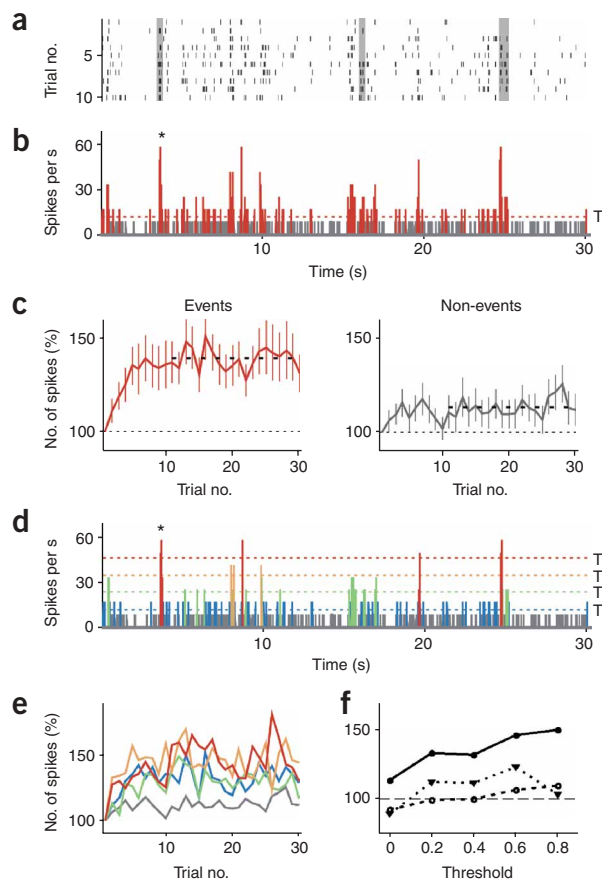


Figure 3 Selective increase in spiking induced by natural stimuli. **(a)** Raster plot of responses of an example cell for the first 10 trials of a natural movie. Gray shading, high firing rate episodes in which spiking reliability improved over trials. **(b)** PSTH of the same cell (averaged over 30 trials). Dashed horizontal line, threshold (T) at 20% of highest amplitude of PSTH (star). Red and gray, event and non-event bins, respectively. **(c)** Number of spikes normalized by that in the first trial for event (left) and non-event (right) bins, averaged from the 96 cells used for **Figure 2a**. Error bar shows \pm s.e.m. Black dashed line, average across trials 11–30. **(d)** Classification of five groups of event bins on the basis of four thresholds. Dashed lines indicate thresholds at 80%, 60%, 40% and 20% of highest PSTH amplitude. Each group of bins is indicated by a distinct color. **(e)** Normalized spike number over trials in each group of bins (indicated by color) for the 96 cells. **(f)** Normalized spike number averaged across trials 11–30, plotted against threshold for each group, for natural (filled circle), white noise (triangle), and flashed bar (open circle) stimuli (the same populations of cells as used for **Fig. 2**).

further stimulation by the same movie (**Fig. 5**). In the experiment shown in **Figure 5a**, we inserted a 6-min resting period (12 repeats of 'blank movie', with blank screen in all frames) after the first 12 repeats of a natural movie. The increase in correlation coefficient over the first 12 trials did not decay significantly over the resting period (**Fig. 5c**). Furthermore, inserting 12 repeats of a different movie (movie 2), which evoked different firing patterns in the cortical neuron (**Fig. 5b**), also did not diminish the increase in correlation coefficient induced by the first 6 repeats of movie 1 (**Fig. 5d**), indicating that the 'memory' of movie 1 was not washed out by a different movie of a similar duration.

Reverberation in spontaneous activity

Previous studies in several neural circuits have shown that spontaneous activity exhibits non-random spatiotemporal patterns^{25–31}, some of which resemble the activity patterns that occur during sensory stimulation²⁹ or learning-related behavioral tasks^{26–28,31}. In our study, as the effect of repetitive movie stimulation persisted through a 6-min resting

period (**Fig. 5a,c**), we searched for a 'memory trace' of the movie by testing whether the temporal patterns of spontaneous activity during the resting period were similar to the responses evoked by the movie.

The experiment consisted of three blocks: Blank1—Movie—Blank2. The Movie block contained 12 repeats of a natural movie; the length of each movie varied from 3.1s to 30.1s in different experiments. Blank1 and Blank2 each contained \sim 6 min of blank movie; each blank movie had the same length as the natural movie (3.1s to 30.1s), but the number of repeats in each block ranged from 12 to 120. This experiment is analogous to that shown in **Figure 5a** (with blocks Movie1—Blank—Movie2), except for the difference in the number and sequence of Movie and Blank blocks. We tested the hypothesis that, after (but not before) repetition of the natural movie, temporal patterns of the movie-evoked activity continue to reverberate in the cortical circuit, repeating themselves at the same rate as the movie repetition. To detect these patterns in the spontaneous spike trains, which typically exhibit low firing rates (**Fig. 5a**), we computed the spontaneous rate signals before and after the movie (R_{blank1} and R_{blank2}) by averaging over all repeats of the blank movie (that is, the PSTH) in each block (**Fig. 6a**). We then measured the similarity of R_{blank1} and R_{blank2} to the movie-evoked response R_{movie} (PSTH, averaged over the 12 repeats in the Movie block) by correlation coefficient (CC). For the population of cells (**Fig. 6b**), we found that CC (R_{blank2} , R_{movie}) was significantly higher than CC (R_{blank1} , R_{movie}) for short (3.1 s; $P < 0.001$, Wilcoxon signed

Figure 4 Dependence of reliability improvement on response sparseness. **(a)** Distribution of firing rate in response to natural (red), white noise (blue) and flashed bar (green) stimuli. For each cell, the PSTH was normalized by the mean firing rate, and the histogram (number of bins at each firing rate) was averaged over 96, 46 and 76 cells for natural, white noise, and flashed bar stimuli, respectively (same cells as those used for **Figs. 2, 3**). The distribution at low ($< 6.5 \times$ mean, upper plot) and high ($\geq 6.5 \times$ mean, lower plot) rates are shown separately; vertical scale of lower plot is $100 \times$ that of upper plot. **(b)** Cumulative distribution of response sparseness of cortical neurons. **(c)** Δ CC (averaged across trials 11–30) against response sparseness. Black line, linear fit of the data ($r = 0.17$, $P < 0.02$). Gray box, cells with sparseness > 0.8 .

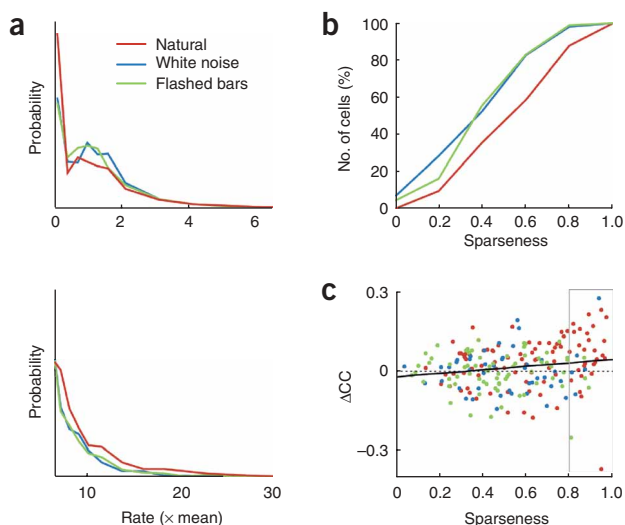
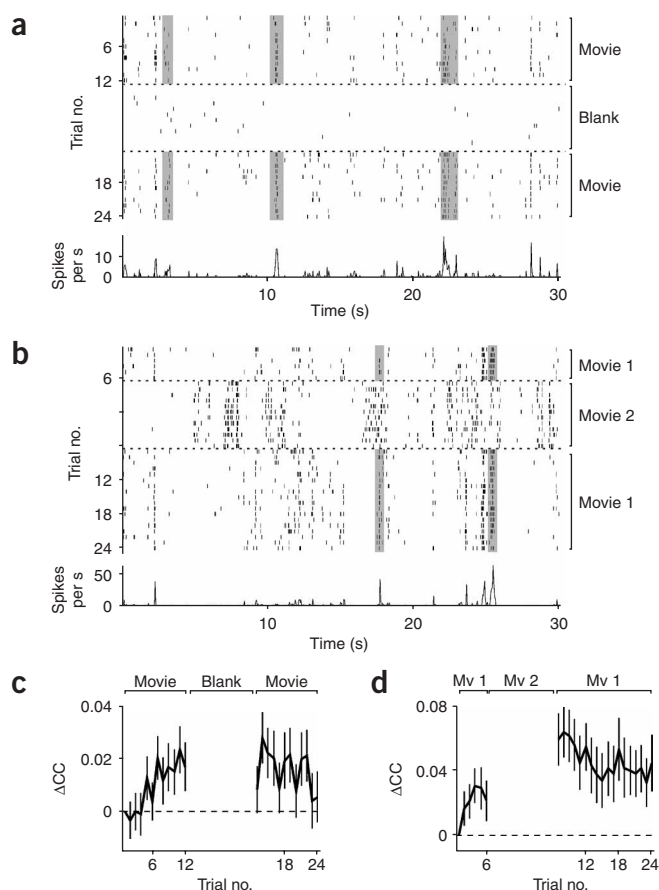


Figure 5 Persistence of improvement in correlation coefficient induced by natural movies. **(a)** Data from an example cell, stimulated by natural movie (12 trials), blank movie (12 trials) and then the same natural movie (12 trials). PSTH: mean response to all 24 trials of the natural movie. **(b)** Another example cell, stimulated by natural movie 1 (6 trials), natural movie 2 (12 trials), and natural movie 1 (18 trials). PSTH: mean response to 24 trials of movie 1. **(c)** Population summary of ΔCC for natural movie before and after blank movie (experiment in **a**, $n = 148$, 41.9 ms per bin). Error bar shows \pm s.e.m. **(d)** Population summary of ΔCC for movie 1 before and after movie 2 (experiment in **b**, $n = 80$). Data shown here are from a different population of cells from those in **Figures 1–4**, owing to the difference in stimulus sequence.

rank test, $n = 78$) and medium-length (7.8–15.3 s; $P < 0.02$, $n = 541$) movies, although not for long movies (30.1 s; $P > 0.5$, $n = 209$). This indicates that the temporal patterns of spontaneous activity show higher similarity to the movie-evoked response after repeated movie stimulation than before it. This is different from the previously reported similarity between the spatial patterns of spontaneous and evoked cortical activity, which is independent of stimulus history²⁹.

To test whether the increase in correlation coefficient after movie stimulation is due to changes in the general statistical properties of the spontaneous spike trains (for example, firing rate, refractory period or burstiness), we performed additional control analyses. First, we generated large numbers of surrogate spontaneous signals ($R_{\text{blank1_control}}$ and $R_{\text{blank2_control}}$) for each cell by random sampling (Fig. 7a) of the spike trains during Blank1 or Blank2, respectively. As random sampling disrupts signals that reverberate at the rate of movie repetition but preserves the general spiking statistics, any change in correlation coefficient due to changes in the spontaneous spiking statistics should be reflected in the different distributions of CC ($R_{\text{blank1_control}}$, R_{movie}) and CC ($R_{\text{blank2_control}}$, R_{movie}). When CC (R_{blank1} , R_{movie}) and CC (R_{blank2} , R_{movie}) were converted into Z-scores based on their control correlation coefficient distributions²⁸ (see Methods), which should eliminate the difference in correlation coefficient due to non-specific causes, we found that the Z-score of CC (R_{blank2} , R_{movie}) was still significantly higher than that of CC (R_{blank1} , R_{movie}) for short ($P < 0.002$) and medium-length ($P < 0.02$) movies (Fig. 7b). This indicates that the increase in correlation coefficient is not due to

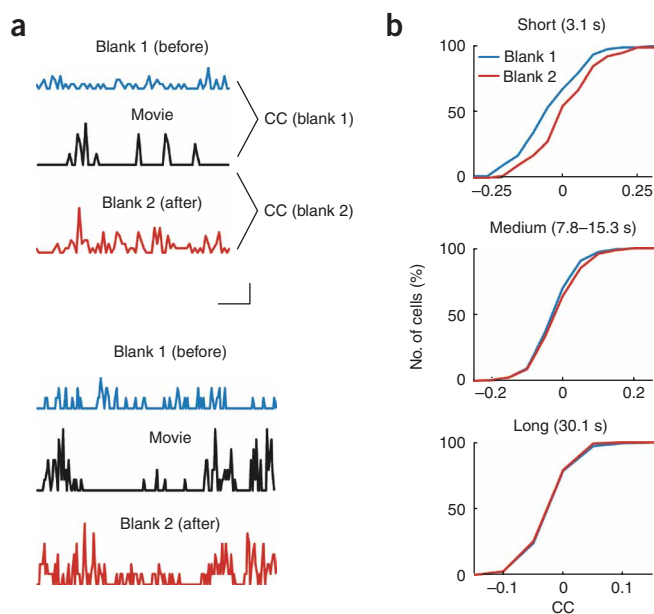


changes in the general statistics of spontaneous firing. To further exclude the possibility that the increase in correlation coefficient is caused by changes in spontaneous firing rate, we divided the cells into three groups based on the difference in mean firing rate between Blank1 and Blank2 ($< -10\%$, between -10% and 10% , and $> 10\%$). The Z-score was higher for Blank2 than for Blank1 in all three groups, with no correlation between the changes in Z-score and the changes in spontaneous firing rate (Fig. 7c; $P > 0.95$, ANOVA). Finally, we found that the difference between Z-scores for Blank1 and Blank2 increased with the reliability of the cortical response to the natural stimuli in the Movie block (Fig. 7d), indicating that the increase in similarity after the movie stimulation depends on how effectively the movie drives the cortical neurons.

DISCUSSION

Our study shows that repetitive stimulation with natural scenes not only induces a rapid improvement in cortical response reliability, but also leaves a memory trace in subsequent spontaneous activity. Repeated exposure to given visual stimuli is known to induce perceptual learning in adult animals over periods of days to weeks, mediated in part by functional modifications of early visual circuits such as V1

Figure 6 Correlation coefficient between spontaneous and visually evoked spiking patterns. **(a)** Data from two example cells, stimulated by a 3.1-s movie (upper) and a 7.8-s movie (lower). Shown are PSTHs from Blank1, Movie and Blank2 blocks. Horizontal scale bar: 0.5 s (upper cell) and 1 s (lower cell). Vertical scale bar: 1 spike per s (Blank1 and Blank2) and 4 spikes per s (Movie) for both cells. **(b)** Cumulative histograms of CC (R_{blank1} , R_{movie}) and CC (R_{blank2} , R_{movie}) for three groups of cells, stimulated by short (3.1 s, $n = 78$), medium (7.8–15.3 s, $n = 541$) and long (30.1 s, $n = 209$) movies.



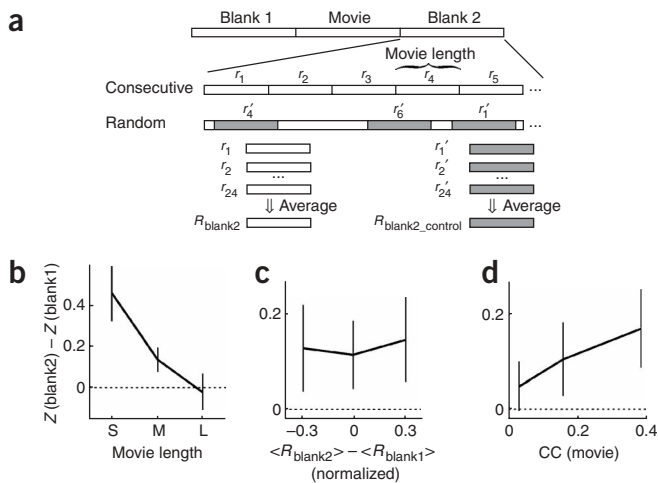


Figure 7 Further analysis of correlation coefficient between spontaneous and visually evoked spiking patterns. **(a)** Schematic illustration of experimental procedure and definitions of spontaneous rate signal (R_{blank2}) and surrogate signals generated by random sampling ($R_{\text{blank2_control}}$). The distributions of CC ($R_{\text{blank1_control}}, R_{\text{movie}}$) and CC ($R_{\text{blank2_control}}, R_{\text{movie}}$) are used to convert CC ($R_{\text{blank1}}, R_{\text{movie}}$) and CC ($R_{\text{blank2}}, R_{\text{movie}}$), respectively, to Z-scores. **(b)** Difference between Z-scores in Blank1 and Blank2 at different movie lengths. The difference is significant for short (3.1 s, $P < 0.001$, $n = 78$) and medium-length movies (7.8–15.3 s, $P < 0.02$, $n = 541$; for 15.3-s movie alone, $P < 0.02$). **(c)** Difference between Z-scores in Blank1 and Blank2 plotted against normalized change in spontaneous firing rate, $(\langle R_{\text{blank1}} \rangle - \langle R_{\text{blank2}} \rangle) / (\langle R_{\text{blank1}} \rangle + \langle R_{\text{blank2}} \rangle)$, where $\langle \cdot \rangle$ represents average over the Blank1 or Blank2 block. **(d)** Difference between Z-scores in Blank1 and Blank2 plotted against reliability of the response to the movie, measured by $\langle \text{CC}(r_i, \langle r_j \rangle_{j \neq i}) \rangle$, where i and j represent trial numbers, and $\langle \cdot \rangle$ denotes average across trials.

(refs. 17,18,20,21,32). We have described a new form of learning in the cortical coding of natural stimuli that occurs within minutes, similar in rapidity to the learning in the locust antennal lobe that is induced by repeated odor stimulation³³. The improvement in response reliability, as measured by the increase in correlation coefficient, is approximately linear over the first ~ 10 trials, and even a single trial causes a small but significant improvement (Fig. 2a; $P < 0.05$, Wilcoxon signed rank test). Such a rapid effect could contribute to visual priming, in which recent exposure to a given visual stimulus facilitates its perception in subsequent encounters³⁴. Of course, our study has only provided the first demonstration of this phenomenon in the primary visual cortex. In future studies, it will be important to determine whether such rapid learning occurs in awake animals during natural visual behavior, in which the same stimulus pattern is unlikely to be repeated multiple times.

The effect that we have described is likely to be distinct from contrast adaptation¹, in which repeated exposure to given stimuli (for example, sinusoidal gratings) reduces the cortical responses to the adapting stimuli^{2,35}. Instead, repeated stimulation with natural movies induced an increase in spiking in response to subsets of the repeated stimuli (Fig. 3). In addition, the increased response reliability lasted for at least 6 min in the absence of further stimulation (Fig. 5). This is longer than the time course for recovery from contrast adaptation⁶, which is thought to be mediated by a reduction in neuronal excitability^{5,6} or short-term synaptic depression⁷.

The effect that we have described could be accounted for by Hebbian synaptic plasticity, which is likely to underlie several forms of adult cortical modification induced by minutes of visual stimulation^{8,10–12}. In particular, the selective increase in responses within episodes of high spiking probability (Fig. 3) is consistent with the requirement for postsynaptic spiking in STDP^{13,14}, a robust form of synaptic plasticity that is found in both superficial³⁶ and deep³⁷ layers of the visual cortex.

Previous studies using voltage-sensitive dye imaging have shown that the spatial patterns of ongoing activity in cat V1 resemble the orientation maps that can be measured using grating stimuli²⁹. In our study, we found similarity between spontaneous and evoked activity in the temporal patterns of single neuron firing. There is a major difference between these findings. Although the spatial similarity seems to be present in the adult visual cortex independent of the stimulus history, the temporal similarity that we have observed emerges after repeated movie stimulation (Fig. 6). Both types of similarity might result from experience-dependent cortical modification at different timescales:

whereas the temporal similarity represents reverberation of the most recent visual experience, the spatial similarity might reflect the long-term influence of visual experience on intracortical connectivity patterns.

The stimulus-induced similarity between spontaneous and visually evoked cortical activity (Figs. 6, 7) is reminiscent of the 'replay' of learning-related activity in neural circuits that mediates episodic^{26,28,31} and sensorimotor²⁷ learning. The temporal firing patterns of single or multiple neurons, recorded during the learning period, are repeated in the neural circuit afterwards, either during sleep^{26–28} or in the awake state (in this case with reversed sequence)³¹. However, there is an important difference between these previously reported replays and the phenomenon shown in our study. In both the hippocampus and the bird-song circuit, replay seems to occur at irregular intervals, and matches between the experience-related and spontaneous activity patterns were searched for at all temporal shifts. In addition, the spike sequences are often replayed on compressed^{26,31} or expanded^{27,28} timescales. Our analysis, on the other hand, only identifies patterns that recur at the same rate as the movie repetition, as the probability of matching at arbitrary temporal shifts is represented in the randomly sampled surrogate signals and therefore discounted when the correlation coefficient is converted into the Z-score (Fig. 7).

The mechanism for such periodic replay might involve oscillations in the cortex. For example, slow-wave oscillation (0.1–1 Hz) in the neocortex³⁸ has been implicated in visual perceptual learning^{39–41}. Such slow oscillations might be well suited for reverberating temporal sequences lasting for several seconds, the length of replayed sequences we observed in the visual cortex (up to ~ 15 s). Another potential mechanism is synaptic modification through STDP^{13,14,36,37}. Theoretical studies indicate that STDP is a powerful mechanism for learning temporal sequences^{42,43}. The learning of temporal patterns that has been demonstrated in cultured neuronal networks is thought to be mediated by STDP⁴⁴. In our study, the repeated movie presentation could selectively strengthen synaptic pathways that propagate spatio-temporal signals that match the visually evoked responses.

In Hebb's postulate⁹, reverberating activity embodying transient memory facilitates the formation of permanent memory through long-term synaptic modification. The rapid improvement in response reliability following repetitive natural stimulation might represent a first step in the learning of the stimuli. Subsequent reverberation of the activity patterns might facilitate consolidation of the effect by long-lasting modification of cortical connectivity. Given its specificity to natural stimuli (Fig. 2), the effect that we have observed might contribute to the experience-dependent fine-tuning of visual cortical circuits that underlies efficient coding of natural scenes^{22,45–47}.

Furthermore, the finding of reverberating activity in an early sensory circuit such as V1 raises the possibility that reverberation is a prevalent phenomenon in the nervous system that contributes to multiple forms of learning and memory.

METHODS

Recording. Animal use procedures were as described⁴⁸ and approved by the Animal Care and Use Committee at the University of California, Berkeley. We used 33 adult cats (2–6.5 kg). Single-unit recordings were made in area 17 using tungsten electrodes (A-M Systems); unit isolation was based on cluster analysis of waveforms. Cells were sampled randomly at all laminar locations. For all analyses, we included cells only if their response correlations between different repeats of the natural movie were above chance ($\langle CC(r_i, \langle r_j \rangle_{j \neq i}) \rangle \geq 0.05$, where i and j represent trial numbers and $\langle \bullet \rangle$ denotes average across trials); no other criteria were used to select cells. We included 1,274 cells in this study (Figs. 1–4, $n = 218$; Fig. 5, $n = 228$; Figs. 6–7, $n = 828$).

Visual stimulation. We generated visual stimuli using a PC computer with a Leadtek Winfast 3D L3100 graphics board and presented them with a Viewsonic PT813 monitor (RGB short persistence phosphor, size 40×30 cm, refresh rate 119 Hz, maximum luminance 80 cd m^{-2}). We used software to correct luminance nonlinearities. Each natural movie (720, 365, 265, 186 and 73 consecutive images, for 30.1-s, 15.3-s, 11.2-s, 7.8-s and 3.1-s movies, respectively) was selected randomly from a natural scene database⁴⁹; 94 movies were used. Each image (32×32 or 64×64 pixels, between $7 \times 7^\circ$ and $16 \times 16^\circ$, $2 \times$ to $5 \times$ receptive field diameter) was updated every five refresh frames, corresponding to an effective frame rate of 24 Hz (41.9 ms per frame). Each white noise (8×8 pixels) or flashed bar (16 bar positions, at the preferred orientation of the cell) sequence (Fig. 2) consisted of 720 frames (30.1 s). In the blank movie (Figs. 5–7) a gray screen (16 cd m^{-2}) was shown in all frames. For the experiment shown in Figures 6 and 7 using 30.1-s, 15.3-s, 11.2-s, 7.8-s or 3.1-s natural movies, the Movie block always consisted of 12 repeats of the movie, whereas blocks Blank1 and Blank2 each consisted of 12, 24, 36, 48 or 120 repeats of the corresponding blank movie, respectively.

Note that each natural movie (especially 15.3-s or 30.1-s movies) might contain multiple segments of continuous shots (see Supplementary Video 1). The stimulus discontinuity between segments could potentially evoke strong transient responses in cortical neurons that contribute to the ‘events’ shown in Figure 3. However, analyses of these discontinuities showed that this is not the case. The number of event bins in the PSTH (Fig. 3) that are attributable to the stimulus discontinuities is only $\sim 1\%$. Thus, the artificial discontinuities in the movies should not significantly distort our results.

Reliability measure. To measure the response reliability in each trial, we binned the spike trains at the frame rate of the stimulus (41.9 ms), and computed the correlation coefficient (CC) between each repeat r_i and the average of its neighboring four repeats $(r_{i-2} + r_{i-1} + r_{i+1} + r_{i+2})/4$. The only exceptions were r_1 , r_2 , r_{n-1} and r_n , which were correlated with $(r_2 + r_3 + r_4 + r_5)/4$, $(r_1 + r_3 + r_4 + r_5)/4$, $(r_{n-4} + r_{n-3} + r_{n-2} + r_n)/4$ and $(r_{n-4} + r_{n-3} + r_{n-2} + r_{n-1})/4$, respectively; n is the total number of trials.

Surrogate spontaneous signals. For each cell, we generated two sets of surrogate spontaneous signals ($R_{\text{blank1_control}}$ and $R_{\text{blank2_control}}$) by random sampling. Each surrogate signal was averaged from the same number of spike train segments as R_{blank1} or R_{blank2} , but these segments were selected randomly from the corresponding spike train (Fig. 7a); we generated 10,000 surrogate signals for each cell. This procedure, while disrupting the periodically recurring temporal patterns, ensured that $R_{\text{blank2_control}}$ and $R_{\text{blank1_control}}$ were matched to R_{blank2} and R_{blank1} in mean firing rate, inter-spike interval distribution and local temporal correlations (for example, due to refractory period or bursting). Thus, although in principle changes in the general statistics of spontaneous spike trains following movie stimulation might contribute to the difference between $CC(R_{\text{blank1}}, R_{\text{movie}})$ and $CC(R_{\text{blank2}}, R_{\text{movie}})$, converting these CC values to their Z -scores on the basis of the distributions of $CC(R_{\text{blank1_control}}, R_{\text{movie}})$ and $CC(R_{\text{blank2_control}}, R_{\text{movie}})$ should eliminate these effects. Note that the match between the recorded and surrogate signals in their general statistical properties is essential for the analysis of non-random patterns in spontaneous

activity. Failure to preserve these properties might lead to under-estimation⁵⁰ of $CC(R_{\text{blank1_control}}, R_{\text{movie}})$ and $CC(R_{\text{blank2_control}}, R_{\text{movie}})$ and thus overestimation of the Z -scores.

Note: Supplementary information is available on the Nature Neuroscience website.

ACKNOWLEDGMENTS

We thank H. Sompolinsky for helpful discussions. This work was supported by a grant from the US National Eye Institute (EY 015180).

COMPETING INTERESTS STATEMENT

The authors declare no competing financial interests.

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