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Rapid Learning in Cortical Coding of Visual Scenes

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Experience-dependent plasticity in adult visual cortex is believed to play important roles in visual coding and perceptual learning. Here we show that repeated stimulation with movies of natural scenes induces a rapid improvement of response reliability in cat visual cortex, an effect largely absent with white noise and flashed bar stimuli. 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, there is detectable reverberation of the movie-evoked responses in the spontaneous spiking activity. Thus, repeated exposure to natural stimuli not only induces a rapid improvement of cortical response reliability, but also leaves a "memory trace" in subsequent spontaneous activity.

Visual stimulation can modify cortical circuitry and response properties on multiple time scales. For example, in contrast adaptation, exposure to high-contrast stimuli for seconds to minutes causes a reduction in response amplitude[1] and changes in stimulus selectivity[2–4] of cortical neurons. These changes may be due to reduced neuronal excitability[5,6] or short-term synaptic depression[7]. On the time scale of several minutes, synchronous visual stimulation within the receptive field and in a non-responsive surround region causes an expansion of the receptive field into the co-stimulated surround[8], which could be accounted for by Hebbian synaptic plasticity[9]. Recent studies have also demonstrated shifts in cortical receptive field location and orientation tuning that depend on the relative timing of paired conditioning visual stimuli on the order of tens of milliseconds[10–12], consistent with spike-timing-dependent synaptic plasticity (STDP)[13,14]. Together, these studies have demonstrated 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 functions has been demonstrated on much longer time scales. During development, natural visual experience is known to be 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 the lifetime of the animal, as revealed by studies of perceptual learning in adults[17–21]. Since these effects are typically studied over days to months, the immediate impacts of natural stimuli on cortical processing remain largely unexplored.

In the present study, we demonstrated a form of rapid visual cortical modification induced by natural stimuli. A few minutes of repeated stimulation with natural movies, but not white noise or flashed bars, caused a significant improvement of response reliability of cortical neurons. Unlike contrast adaptation, in which repeated stimulation causes a reduction in cortical responses to the adapting stimuli[1], 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

Improvement of response reliability induced by natural stimuli

Single-unit recordings were made in the primary visual cortex of anesthetized adult cat (**Methods**) to test the effects of repetitive stimulation with time-varying natural scenes (movies). Each movie (30.1 s long; **Fig. 1a**, Supplementary Movie 1) was repeated 30 times, and the spike trains of the neuron in different repeats ("trials") were compared to assess the reliability of the response and the change in reliability over trials. As shown in **Fig. 1b**, spiking of these cortical neurons evoked by natural movies was relatively sparse[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, we also observed a reduction of the variability over repeated trials, as quantified by the correlation coefficient (CC) between the time-binned firing rate in each trial (41.9 ms/bin, frame rate

of the movie) and the firing rate averaged over its four neighboring trials (**Methods**). As shown in **Fig. 1b** (right panel), CC for the cell exhibited a trend of increase over trials. For the population of cells studied (96 cells, 26 different movies), CC increased steadily over ~10 trials before 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 rapid reduction of cortical response variability and hence an improvement in the coding of natural stimuli.

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

Selective increase of spiking

Inspection of the spike trains in response to natural stimuli suggested that the improvement of response reliability was associated with a selective increase of spiking during episodes of high firing probability (**Fig. 3a**, gray shading). To quantify this observation, we divided all the time bins in the PSTH of each cell into two groups, based on a threshold (T) set at a fraction (e.g., 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 ± 1.6%, s.e.m., of all time bins) and the rest as "non-event" bins (gray). When spiking within each group of bins was examined over trials, we found a

marked increase in the number of spikes in the event bins, but much less change in the non-event bins (**Fig. 3c**). The time course of the increase in spiking was similar to that of the CC increase (**Fig. 2a**). To further examine the selective increase in spiking and to reduce the arbitrariness in choosing a single threshold, we repeated the above analysis with four thresholds (*T1* to *T4*), which divided the time bins into five groups (**Fig. 3d**). We found that the percentage increase in spiking increased monotonically with the threshold (**Fig. 3e**, **f**). Thus, repeated presentation of each movie induced a selective increase in the spiking probability in large events, which presumably represent responses to the preferred stimuli of the cell. Notably, repeated presentation of white noise or flashed bar stimuli also induced a preferential increase of spiking in large events, but the level of increase was much lower than that for natural stimuli (**Fig. 3f**, dashed and dotted lines).

Dependence on sparseness

Why are natural stimuli more effective in inducing the improvement in response reliability? 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 bar stimuli, we found higher probability of both near-zero and high firing rates but a lower probability of intermediate firing rates (**Fig. 4a**), indicating a higher level of response sparseness. Since the improved response reliability is associated with a preferential increase of spiking in large events (**Fig. 3**), the effect may 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 $(1-\langle r\rangle^2/\langle r^2\rangle)/(1-1/n)$ (r is firing rate at a given time bin of the PSTH, n is the number of bins, and $\langle\bullet\rangle$ denotes average over all bins)[24], which quantifies the over-representation of high/low firing rates and under-representation of intermediate rates. As shown in **Fig. 4b**, the sparseness of the response to natural stimuli was indeed higher than that for both white noise and flashed bar stimuli. When we plotted the increase in CC against the response sparseness of each cell, we found a significant correlation between them ($p < 0.02$, **Fig. 4c**). In particular, the increase in CC 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 suggests that the effectiveness of natural stimuli in inducing the reliability improvement is at least partly due to the higher response sparseness.

Persistence of the effect

The improvement of reliability induced by the first few repeats of the movie persisted for at least several minutes in the absence of further stimulation by the same movie. In the experiment shown in **Fig. 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 CC 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 distinct firing patterns of the cortical neuron (**Fig. 5b**), also did not diminish the increase in CC induced by the first 6 repeats of movie 1 (**Fig. 5d**), suggesting that the "memory" of movie 1 was not washed out by a different movie of 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 during sensory stimulation[29] or learning-related behavioral tasks[26–28,31]. In our study, since 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 exhibit similarity 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 ~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 **Fig. 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 (i.e., 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 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 rank test, n = 78) and medium-length (7.8 – 15.3 s, $p < 0.02$, n = 541) movies, although not for long movies (30.1s, $p > 0.5$, n = 209). This indicates that the temporal patterns of spontaneous activity exhibit higher similarity to the movie-evoked response after repeated movie stimulation. This is different from the previously reported similarity between the spatial patterns of spontaneous and evoked cortical activity, which is independent of stimulus history[29].

To test whether the increase in CC after movie stimulation is due to changes in the general statistical properties of the spontaneous spike trains (e.g., firing rate, refractory period, burstiness), we performed additional control analyses. First, we generated large numbers of surrogate spontaneous signals ($R_{blank1\_control}$ and $R_{blank2\_control}$) for each cell by random sampling (**Fig. 7a**) of the spike trains in Blank1 or Blank2, respectively. Since random sampling disrupts signals that reverberate at the rate of movie repetition but preserves the general spiking statistics, any change in CC due to changes in the spontaneous spiking statistics should be reflected in the different distributions of CC ($R_{blank1\_control}$, R_{movie}) and CC ($R_{blank2\_control}$, R_{movie}). When CC (R_{blank1}, R_{movie}) and CC (R_{blank2}, R_{movie}) were converted into *Z* scores based on their control CC distributions[28] (**Methods**), which should eliminate the difference in CC 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 CC is not due to changes in the general statistics of spontaneous firing. To further exclude the possibility that the increase in CC 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%). We found that the Z score was higher for Blank2 than for Blank1 in all three groups, with no correlation between the changes in Z score and 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**), suggesting that the increase in similarity following the movie stimulation depends on the effectiveness of the movie in driving 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[17,18,20,21,32]. Our study reveals a new form of learning in cortical coding of natural stimuli that occurs within minutes, similar in rapidity to the learning in locust antennal lobe induced by repeated odor stimulation[33]. The improvement in response reliability as measured by CC increase 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 may contribute to visual priming, in which recent exposure to a given visual stimulus facilitates its perception in subsequent encounters[34]. Note that our study has only provided the first demonstration of this phenomenon in the primary visual cortex. In future studies, it would be important to determine whether such rapid learning occurs in

awake animals under natural visual behavior, during which the same stimulus pattern is rarely repeated multiple times.

The observed effect is likely to be distinct from contrast adaptation[1], in which repeated exposure to given stimuli (e.g., sinusoidal gratings) reduces the cortical responses to the adapting stimuli[2,35]. Instead, repeated stimulation with natural movies induced an increase of 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 adaptation[6], which is thought to be mediated by a reduction in neuronal excitability[5,6] or short-term synaptic depression[7].

A potential mechanism for the observed effect is 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 of response 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 in both superficial[36] and deep[37] 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 measured with gratings[29]. In our study, similarity between spontaneous and evoked activity was found in the temporal patterns of single neuron firing. A major difference between these findings is that, while the spatial similarity appears to be present in the adult visual cortex independent of the stimulus history, the temporal similarity we have observed emerges

after repeated movie stimulation (**Fig. 6**). It is possible that both types of similarity result from experience-dependent cortical modification at different time scales: Whereas the temporal similarity represents reverberation of the most recent visual experience, the spatial similarity reflects the long-term impact of visual experience on intracortical connectivity patterns.

The stimulus-induced similarity between spontaneous and visually evoked cortical activity (**Figs. 6** and **7**) is reminiscent of the "replay" of learning-related activity in neural circuits mediating episodic[26,28,31] and sensorimotor[27] learning. In these studies, temporal firing patterns of single or multiple neurons recorded during the learning period are observed in the neural circuit afterwards, either during sleep[26–28] or in the awake state immediately after the experience (in this case with reversed sequence)[31]. However, there is an important difference between these previously reported replays and the phenomenon shown in the current study. In both the hippocampus and the bird song circuit, replay appears 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] time scales. Our analysis, on the other hand, only identifies patterns recurring at the same rate as the movie repetition, since the probability of matching at arbitrary temporal shifts is represented in the randomly sampled surrogate signals and therefore discounted when CC is converted into the Z score (**Fig. 7**).

The mechanism for such periodic replay may involve oscillations in the cortex. For example, slow wave oscillation (0.1 – 1Hz) in the neocortex[38] has been implicated in visual perceptual learning[39–41]. Such slow oscillations may be well suited for

reverberating temporal sequences lasting for several seconds, the length of replayed sequences we observed in the visual cortex (up to ~15s). 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]. Experimentally, learning of temporal patterns has been demonstrated in cultured neuronal networks, which is thought to be mediated by STDP[44]. In our study, the repeated movie presentation may selectively strengthen synaptic pathways that propagate spatiotemporal signals matching the visually evoked responses.

In Hebb's postulate[9], reverberating activity embodying transient memory facilitates the formation of permanent memory through long-term synaptic modification. In our study, the rapid improvement of response reliability following repetitive natural stimulation may represent a first step in the learning of the stimuli. Subsequent reverberation of the activity patterns may facilitate consolidation of the effect by long-lasting modifications of cortical connectivity. Given its specificity to natural stimuli (**Fig. 2**), the effect we observed may contribute to 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 previously described[48] and approved by the Animal Care and Use Committee at the University of California, Berkeley. A total of 33 adult cats (2 – 6.5 kg) were used. 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 only included cells if their response correlations between different repeats of the natural movie were above chance level ($\langle \mathrm{CC}(r_i, \langle r_j \rangle_{j \neq i}) \rangle \geq 0.05$, where i and j represent trial numbers, n is the total number of trials, and $\langle \bullet \rangle$ denotes average across trials); no other criteria were used to select cells. A total of 1274 cells were included in this study (**Figs. 1 – 4**, n = 218; **Fig. 5**, n = 228; **Figs. 6 – 7**, n = 828).

Visual stimulation Visual stimuli were generated with a PC computer with a Leadtek Winfast 3D L3100 graphics board and presented with a Viewsonic PT813 monitor (RGB short persistence phosphor, size 40 × 30 cm, refresh rate 119 Hz, maximum luminance 80 cd m^{-2}). Luminance nonlinearities were corrected through software. Each natural movie (720, 365, 265, 186, and 73 consecutive images, for 30.1s, 15.3s, 11.2s, 7.8s, and 3.1s movies, respectively) was selected randomly from a natural scene database[49]; a total of 94 movies were used. Each image (32 × 32 or 64 × 64 pixels, 7 × 7^o – 16 × 16^o, 2× to 5× receptive field diameter) were updated every 5 refresh frames, corresponding to an effective frame rate of 24 Hz (41.9 ms/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 (30.1s). In the blank movie (**Figs. 5 – 7**) a gray screen (16 cd m^{-2}) was shown in all frames. For the experiment shown in **Figs. 6** and **7** using 30.1s, 15.3s, 11.2s, 7.8s, or 3.1s 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 15.3s or 30.1s long movie) may contain multiple segments of continuous shots (see Supplementary Movie 1). The stimulus discontinuity between segments could potentially evoke strong transient responses in cortical neurons that contribute to the "events" shown in Fig. 3. However, analyses of these discontinuities showed that this is not the case. The number of event bins in the PSTH (**Fig. 3**) attributable to the stimulus discontinuities is only ~ 1%. Thus, the artificial discontinuities in the movies should not cause significant distortion of 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 4 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.

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**); 10,000 surrogate signals were generated 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 (e.g., due to refractory period or bursting). Thus, although in principle changes in the general statistics of spontaneous spike trains following movie stimulation may contribute to the difference between CC (R_{blank1}, R_{movie}) and CC (R_{blank2}, R_{movie}), converting these CC values to their Z scores based on the distributions of CC ($R_{blank1\_control}$, R_{movie}) and CC ($R_{blank2\_control}$, R_{movie}) should eliminate these effects. Note that the match between the recorded and surrogate signals in their general statistical properties is critical for the analysis of non-random patterns in spontaneous activity. Failure to preserve these properties may lead to under-estimation[50] of CC ($R_{blank1\_control}$, R_{movie}) and CC ($R_{blank2\_control}$, R_{movie}) and thus over-estimation of the Z scores.

References

1. Maffei, L., Fiorentini, A. & Bisti, S. Neural correlate of perceptual adaptation to gratings. *Science* **182**, 1036-1038 (1973).
2. Movshon, J. A. & Lennie, P. Pattern-selective adaptation in visual cortical neurones. *Nature* **278**, 850-852 (1979).
3. Muller, J. R., Metha, A. B., Krauskopf, J. & Lennie, P. Rapid adaptation in visual cortex to the structure of images. *Science* **285**, 1405-1408 (1999).
4. Dragoi, V., Sharma, J. & Sur, M. Adaptation-induced plasticity of orientation tuning in adult visual cortex. *Neuron* **28**, 287-298 (2000).
5. Carandini, M. & Ferster, D. A tonic hyperpolarization underlying contrast adaptation in cat visual cortex. *Science* **276**, 949-52 (1997).

6. Sanchez-Vives, M. V., Nowak, L. G. & McCormick, D. A. Membrane mechanisms underlying contrast adaptation in cat area 17 in vivo. *J Neurosci* **20**, 4267-85 (2000).

7. Chance, F. S., Nelson, S. B. & Abbott, L. F. Synaptic depression and the temporal response characteristics of V1 cells. *J Neurosci* **18**, 4785-99 (1998).

8. Eysel, U. T., Eyding, D. & Schweigart, G. Repetitive optical stimulation elicits fast receptive field changes in mature visual cortex. *Neuroreport* **9**, 949-954 (1998).

9. Hebb, D. O. *The Organization of Behavior* (Wiley, New York, 1949).

10. Fu, Y. X., Djupsund, K., Gao, H., Hayden, B., Shen, K. & Dan, Y. Temporal specificity in the cortical plasticity of visual space representation. *Science* **296**, 1999-2003 (2002).

11. Yao, H. & Dan, Y. Stimulus timing-dependent plasticity in cortical processing of orientation. *Neuron* **32**, 315-23 (2001).

12. Yao, H., Shen, Y. & Dan, Y. Intracortical mechanism of stimulus-timing-dependent plasticity in visual cortical orientation tuning. *Proc Natl Acad Sci U S A* **101**, 5081-6 (2004).

13. Markram, H., Lubke, J., Frotscher, M. & Sakmann, B. Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. *Science* **275**, 213-215 (1997).

14. Bi, G. Q. & Poo, M. M. Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type. *J Neurosci* **18**, 10464-10472 (1998).

15. Chapman, B. & Stryker, M. P. Development of orientation selectivity in ferret visual cortex and effects of deprivation. *J Neurosci* **13**, 5251-5262 (1993).

16. Li, Y., Fitzpatrick, D. & White, L. E. The development of direction selectivity in ferret visual cortex requires early visual experience. *Nat Neurosci* **9**, 676-81 (2006).

17. Crist, R. E., Li, W. & Gilbert, C. D. Learning to see: experience and attention in primary visual cortex. *Nat Neurosci* **4**, 519-525 (2001).

18. Schoups, A., Vogels, R., Qian, N. & Orban, G. Practising orientation identification improves orientation coding in V1 neurons. *Nature* **412**, 549-553 (2001).

19. Fahle, M. & Poggio, T. *Perceptual learning* (MIT Press, Cambridge, 2002).

20. Furmanski, C. S., Schluppeck, D. & Engel, S. A. Learning strengthens the response of primary visual cortex to simple patterns. *Curr Biol* **14**, 573-8 (2004).

21. Li, W., Piech, V. & Gilbert, C. D. Perceptual learning and top-down influences in primary visual cortex. *Nat Neurosci* **7**, 651-7 (2004).

22. Barlow, H. B. in *Sensory Communication* (ed. Rosenblith, W. A.) 217-234 (MIT Press, Cambridge, MA, 1961).

23. Olshausen, B. A. & Field, D. J. Emergence of simple-cell receptive field properties by learning a sparse code for natural images. *Nature* **381**, 607-9 (1996).

24. Vinje, W. E. & Gallant, J. L. Sparse coding and decorrelation in primary visual cortex during natural vision. *Science* **287**, 1273-6 (2000).

25. Abeles, M. & Gerstein, G. L. Detecting spatiotemporal firing patterns among simultaneously recorded single neurons. *J Neurophysiol* **60**, 909-924 (1988).

26. Nadasdy, Z., Hirase, H., Czurko, A., Csicsvari, J. & Buzsaki, G. Replay and time compression of recurring spike sequences in the hippocampus. *J Neurosci* **19**, 9497-9507 (1999).

27. Dave, A. S. & Margoliash, D. Song replay during sleep and computational rules for sensorimotor vocal learning. *Science* **290**, 812-816 (2000).

28. Louie, K. & Wilson, M. A. Temporally structured replay of awake hippocampal ensemble activity during rapid eye movement sleep. *Neuron* **29**, 145-156 (2001).

29. Kenet, T., Bibitchkov, D., Tsodyks, M., Grinvald, A. & Arieli, A. Spontaneously emerging cortical representations of visual attributes. *Nature* **425**, 954-956 (2003).

30. Ikegaya, Y. et al. Synfire chains and cortical songs: temporal modules of cortical activity. *Science* **304**, 559-564 (2004).

31. Foster, D. J. & Wilson, M. A. Reverse replay of behavioural sequences in hippocampal place cells during the awake state. *Nature* **440**, 680-3 (2006).

32. Frenkel, M. Y., Sawtell, N. B., Diogo, A. C., Yoon, B., Neve, R. L. & Bear, M. F. Instructive effect of visual experience in mouse visual cortex. *Neuron* **51**, 339-49 (2006).

33. Stopfer, M. & Laurent, G. Short-term memory in olfactory network dynamics. *Nature* **402**, 664-668 (1999).

34. Tulving, E. & Schacter, D. L. Priming and human memory systems. *Science* **247**, 301-6 (1990).

35. Saul, A. B. & Cynader, M. S. Adaptation in single units in visual cortex: the tuning of aftereffects in the spatial domain. *Vis Neurosci* **2**, 593-607 (1989).

36. Froemke, R. C. & Dan, Y. Spike-timing-dependent synaptic modification induced by natural spike trains. *Nature* **416**, 433-8 (2002).

37. Sjostrom, P. J. & Nelson, S. B. Spike timing, calcium signals and synaptic plasticity. *Curr Opin Neurobiol* **12**, 305-14 (2002).

38. Steriade, M., Nunez, A. & Amzica, F. A novel slow (< 1 Hz) oscillation of neocortical neurons in vivo: depolarizing and hyperpolarizing components. *J Neurosci* **13**, 3252-65 (1993).

39. Gais, S., Plihal, W., Wagner, U. & Born, J. Early sleep triggers memory for early visual discrimination skills. *Nat Neurosci* **3**, 1335-9 (2000).

40. Stickgold, R., James, L. & Hobson, J. A. Visual discrimination learning requires sleep after training. *Nat Neurosci* **3**, 1237-8 (2000).

41. Steriade, M. & Timofeev, I. Neuronal plasticity in thalamocortical networks during sleep and waking oscillations. *Neuron* **37**, 563-76 (2003).

42. Abbott, L. F. & Blum, K. I. Functional significance of long-term potentiation for sequence learning and prediction. *Cereb Cortex* **6**, 406-16 (1996).

43. Rao, R. P. N. & Sejnowski, T. J. (eds.) *Predictive sequence learning in recurrent neocortical circuits* (MIT Press, 2000).

44. Bi, G. & Poo, M. Distributed synaptic modification in neural networks induced by patterned stimulation. *Nature* **401**, 792-6 (1999).

45. Attneave. Some informational aspects of visual perception. *Psychological Review* **51**, 183-193 (1954).

46. Simoncelli, E. P. & Olshausen, B. A. Natural image statistics and neural representation. *Annu Rev Neurosci* **24**, 1193-1216 (2001).

47. Felsen, G., Touryan, J., Han, F. & Dan, Y. Cortical sensitivity to visual features in natural scenes. *PLoS Biol* **3**, e342 (2005).

48. Touryan, J., Lau, B. & Dan, Y. Isolation of relevant visual features from random stimuli for cortical complex cells. *J Neurosci* **22**, 10811-10818 (2002).

49. van Hateren, J. H. & Ruderman, D. L. Independent component analysis of natural image sequences yields spatio-temporal filters similar to simple cells in primary visual cortex. *Proc. R. So.c Lond. B Biol. Sci.* **265**, 2315-2320 (1998).

50. Mokeichev, A., Okun, M., Barak, O., Katz, Y., Ben-Shahar, O. & Lampl, I. Stochastic emergence of repeating cortical motifs in spontaneous membrane potential fluctuations in vivo. *Neuron* **53**, 413-425 (2007).

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Figure Legends

Figure 1. Improvement of 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*, CC between response in each trial (binned at 41.9 ms) and mean response of its neighboring 4 trials.

Figure 2. Improvement of response reliability is specific to natural stimuli. **a**, Change in CC induced by natural stimuli, averaged across 96 cells (26 movies). ΔCC: CC in each trial minus CC in the first trial. Error bar, ± s.e.m. *S*pike trains were binned at the stimulus frame rate (41.9 ms). Increase in CC (ΔCC 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. **b**, Change in CC induced by white noise, averaged across 46 cells (15 movies). Increase in CC was not significant ($p > 0.5$). **c**, Change in CC induced by flashed bars, averaged across 76 cells (10 movies). Increase in CC was not significant ($p > 0.5$).

Figure 3. Selective increase of spiking induced by natural stimuli. **a**, Raster plot for the first 10 trials of an example cell evoked by natural movies. 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. **c**, Number of spikes normalized by that in the first trial for event (left) and non-event (right) bins, averaged

from the same 96 cells in Fig. 2a. Error bar, ± s.e.m. Black dashed line, average across trials 11 – 30. **d**, Classification of five groups of event bins based on 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 vs. threshold for each group, for natural (filled circle), white noise (triangle), and flashed bar (open circle) stimuli (the same populations of cells shown in **Fig. 2**).

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 in **Figs. 2** and **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**, ΔCC (averaged across trials 11 – 30) vs. 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 CC improvement induced by natural movies. **a**, Data from an example cell, stimulated by natural (12 trials), blank (12 trials), and the same natural (12 trials) movie. 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

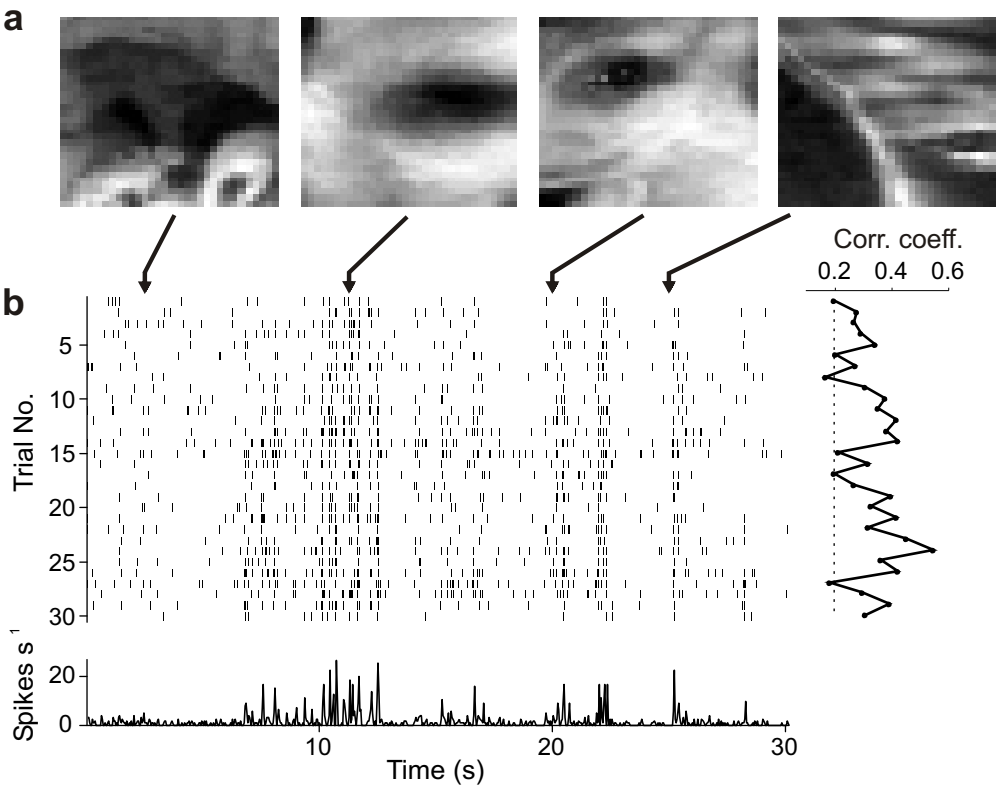
natural movie 1 (18 trials). PSTH: mean response to 24 trials of movie 1. **c**, Population summary of ΔCC for natural movie before and after blank movie (experiment in **a**, n = 148, 41.9ms/bin). Error bar, ± s.e.m. **d**, Population summary of ΔCC for movie 1 before and after movie 2 (experiment in **b**, n = 80). Data shown here are from a different population of cells from those in Figs. 1 – 4, due to difference in stimulus sequence.

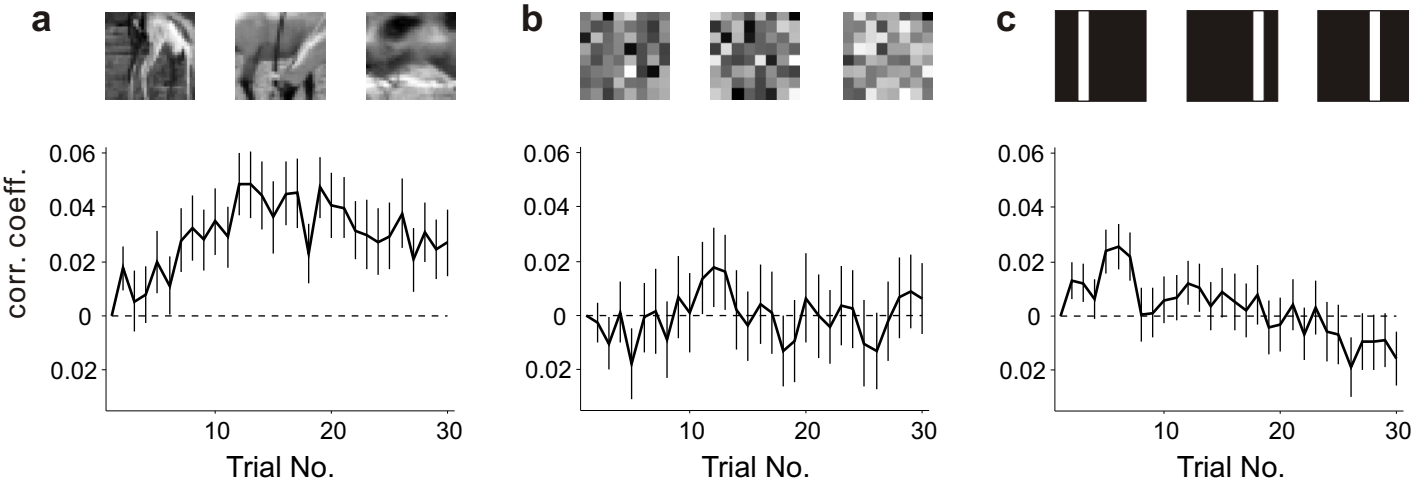
Figure 6. Correlation coefficient between spontaneous and visually evoked spiking patterns. **a**, Data from two example cells, stimulated by a 3.1s movie (upper) and a 7.8s movie (lower). Shown are PSTHs from Blank1, Movie, and Blank2 blocks. Horizontal scale bar: 0.5s (upper cell) and 1s (lower cell). Vertical scale bar: 1 spike/s (Blank1 and Blank2) and 4 spikes/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 – 15.3s, n = 541), and long (30.1s, n = 209) movies.

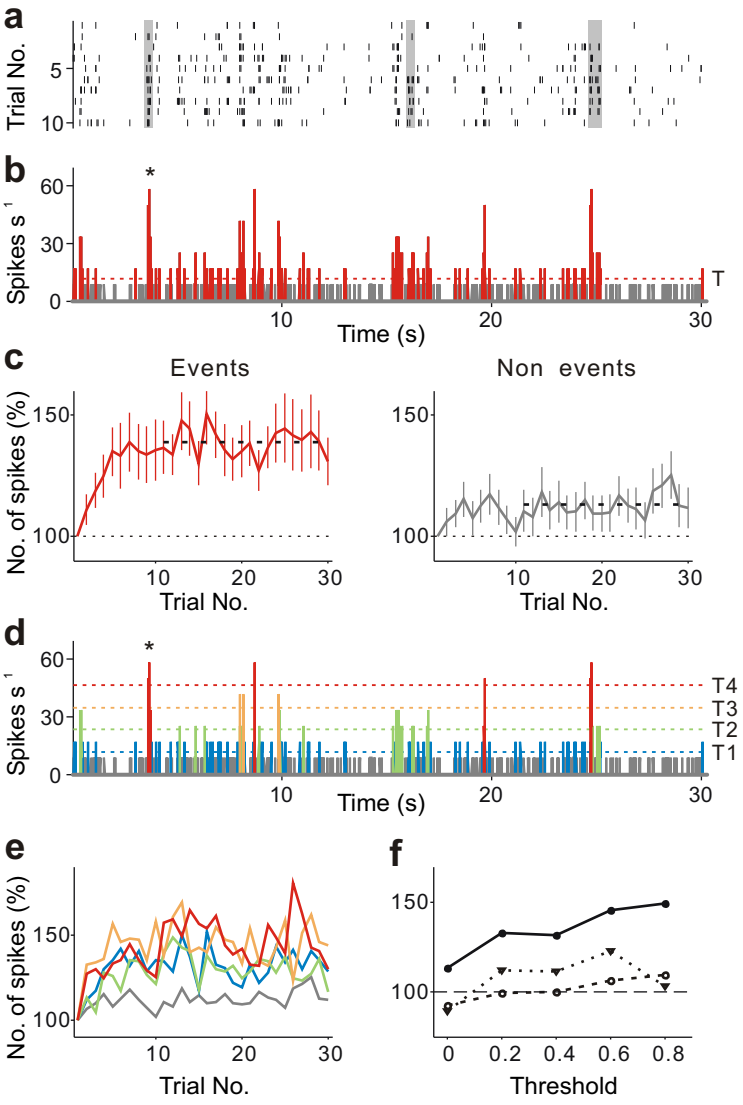
Figure 7. Further analysis of CC between spontaneous and visually evoked spiking patterns. **a**, Schematic illustration of experimental procedure and definitions of spontaneous rate signal (R_{blank2}) and surrogate signals generated by random sampling ($R_{\text{blank2\_control}}$). The distributions of CC ($R_{\text{blank1\_control}}$, R_{movie}) and CC ($R_{\text{blank2\_control}}$, R_{movie}) are used to convert CC (R_{blank1}, R_{movie}) and CC (R_{blank2}, R_{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 (7.8 – 15.3 s, $p < 0.02$, n = 541; for 15.3s movie alone, $p < 0.02$) movies. **c**, Difference between Z scores in Blank1 and Blank2 vs. 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

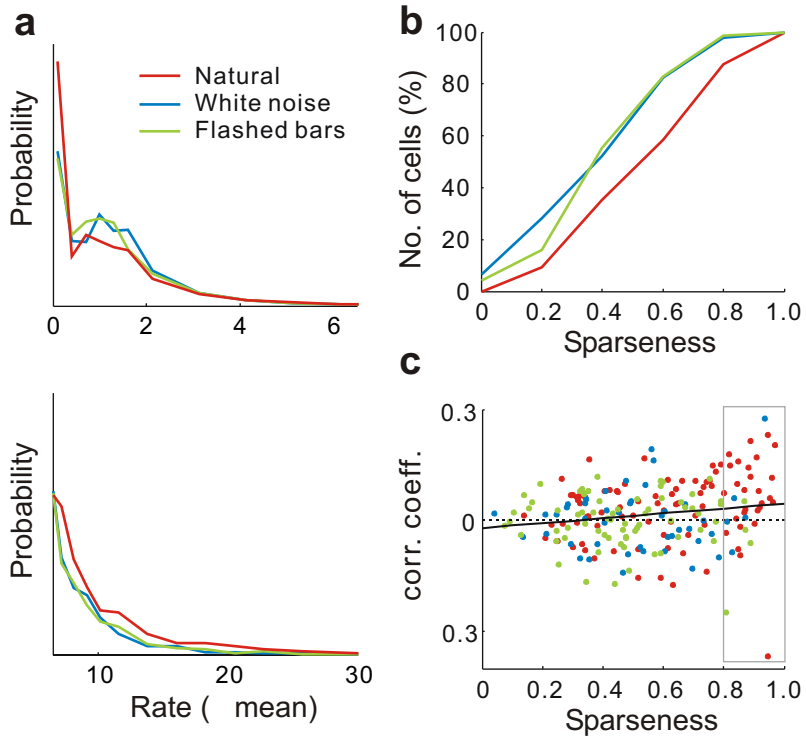
or Blank2 block. **d**, Difference between Z scores in Blank1 and Blank2 vs. reliability of the response to the movie, measured by $\langle \mathrm{CC}(r_i, \langle r_j \rangle_{j \neq i}) \rangle$, where i and j represent trial numbers, n is the total number of trials, and $\langle \bullet \rangle$ denotes average across trials.

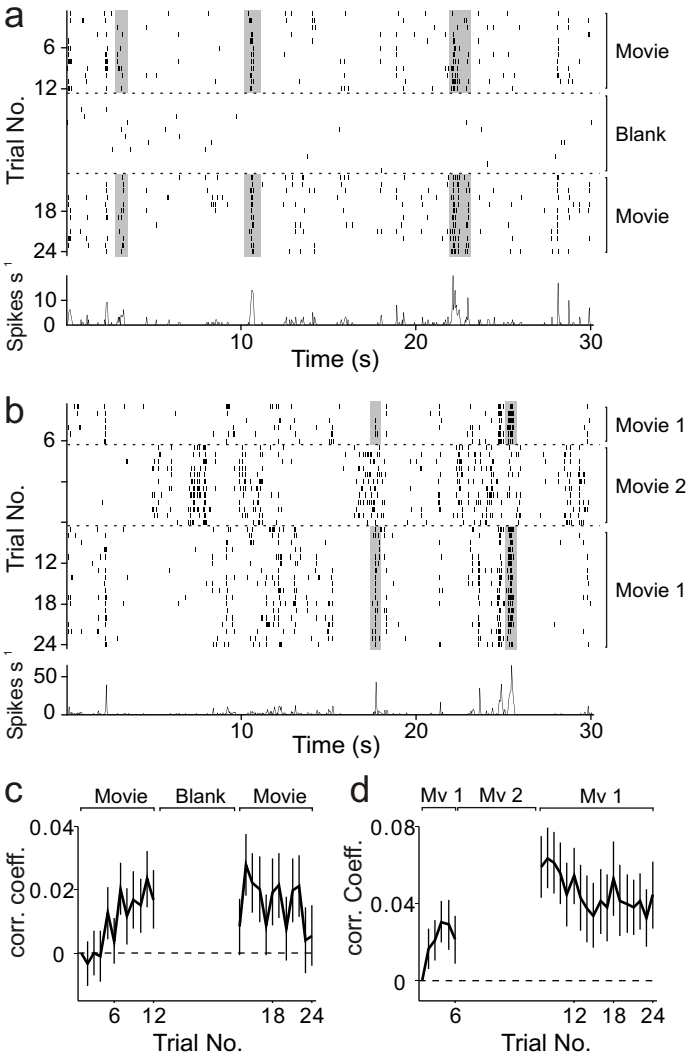
Supplementary Movie 1. This is an example of a 30.1s natural movies used in the experiments.

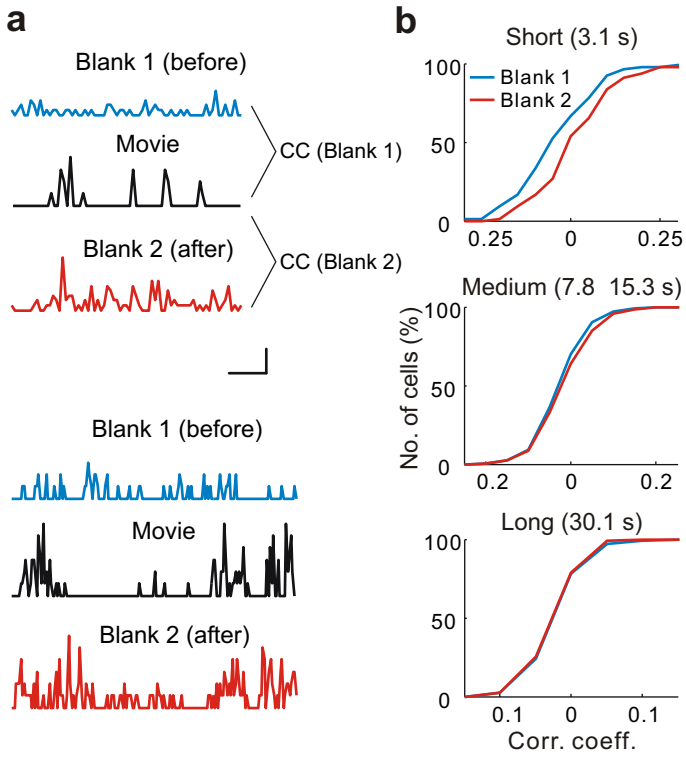

a
b
Corr. coeff.
0.2
0.4
0.6
Trial No.
5
10
15
20
25
30
Spikes s 1
20
0
10
20
30
Time (s)

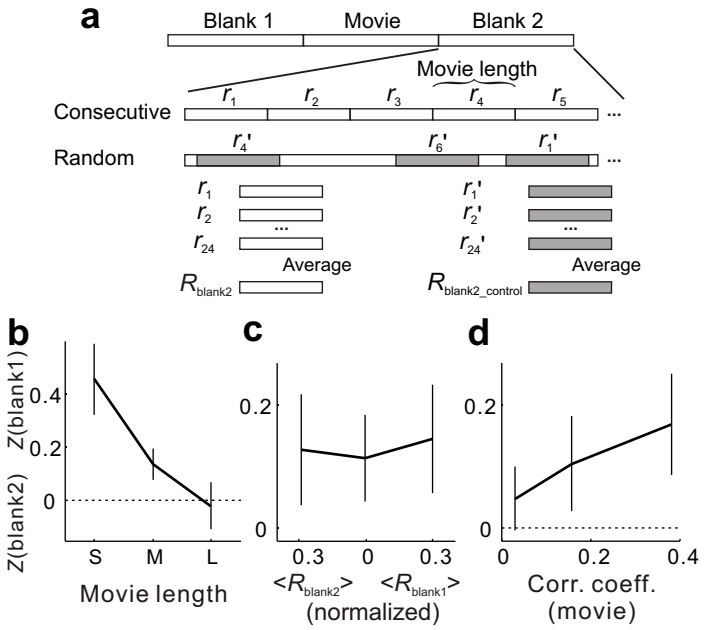

a
b
c
corr. coeff.
0.06
0.04
0.02
0
0.02
10
20
30
Trial No.


a
Trial No.
5
10
b
Spikes s 1
60
30
0
*
T
10
20
30
Time (s)
c
Events
Non events
No. of spikes (%)
150
100
10
20
30
Trial No.
Trial No.
d
Spikes s 1
60
30
0
*
T4
T3
T2
T1
10
Time (s)
20
30
e
No. of spikes (%)
150
100
10
20
30
Trial No.
f
150
100
0
0.2
0.4
0.6
0.8
Threshold


a
Natural
White noise
Flashed bars
Probability
0
2
4
6
Probability
10
20
30
Rate (mean)
b
100
80
60
40
20
0
No. of cells (%)
0
0.2
0.4
0.6
0.8
1.0
Sparseness
c
0.3
0
0.3
corr. coeff.
0
0.2
0.4
0.6
0.8
1.0
Sparseness


a
Trial No.
6
12
18
24
Movie
Blank
Movie
Spikes s⁻¹
10
0
10
20
30
Time (s)
b
Trial No.
6
12
18
24
Movie 1
Movie 2
Movie 1
Spikes s⁻¹
50
0
10
20
30
Time (s)
c
Movie
Blank
Movie
corr. coeff.
0.04
0.02
0
6
12
18
24
Trial No.
d
Mv 1
Mv 2
Mv 1
corr. Coeff.
0.08
0.04
0
6
12
18
24
Trial No.


a
Blank 1 (before)
Movie
CC (Blank 1)
Blank 2 (after)
CC (Blank 2)
Blank 1 (before)
Movie
Blank 2 (after)
b
Short (3.1 s)
Blank 1
Blank 2
100
50
0
0.25
0
0.25
Medium (7.8 15.3 s)
No. of cells (%)
100
50
0
0.2
0
0.2
Long (30.1 s)
100
50
0
0.1
0
0.1
Corr. coeff.


a
Blank 1
Movie
Blank 2
Movie length
Consecutive
Random
Average
Average
b
c
d
Z(blank1)
Z(blank2)
Movie length
S
M
L
(normalized)
Corr. coeff.
(movie)