Distinct synaptic mechanisms underlying sustained responses in auditory and visual cortical neurons.

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In cortical neurons, the number and timing of action potentials during sustained responses varies randomly across trials. This randomness is thought to arise from random membrane potential fluctuations around spiking threshold during sustained depolarizations, called UP-states, which have been observed in visual and other cortical areas. The randomness of these fluctuations implies that network activity is temporally uncorrelated on a fine scale. UP-states have never been observed in auditory cortical neurons; evoked responses are typically transient in anesthetized animals, with the membrane potential remaining near rest except for brief high-amplitude excursions (or "bumps") which imply temporally precise coordination. The synaptic mechanisms underlying sustained responses in auditory cortical neurons are therefore unclear. Here we report that sustained responses in auditory cortical neurons in unanesthetized rats consisted of sustained epochs of bumps. These bumps were highly correlated with fluctuations in the simultaneously recorded local field potential, which suggests that these bumps reflect concerted, transient volleys of network activity. In contrast, sustained responses in visual cortical neurons never consisted of bumps, and instead took the form of UP-states of variable duration. These qualitatively different membrane potential and network dynamics suggest that the mode by which information propagates through cortical networks may be fundamentally different in auditory and visual cortex.

Auditory cortical neurons can show sustained spiking responses to sounds in awake animals (Bieser and Muller-Preuss 1996; Brugge and Merzenich 1973; Liang et al. 2002; Lu et al. 2001; Malone et al. 2002; Mickey and Middlebrooks 2003; Recanzone 2000; Wang et al. 2005). The number and timing of individual spikes in these sustained responses varies randomly across trials. How does this randomness arise? One explanation is that neurons receive large numbers of temporally uncorrelated synaptic inputs, which produce a sustained depolarization of the membrane potential to a value near threshold (Anderson et al. 2000; Shadlen and Newsome 1998). Individual spikes are then triggered by random fluctuations around threshold. In this view, information is propagated through the cortical network by the increased firing rates of pre- and postsynaptic neurons. An alternative view is that information is propagated through cortical networks by synchronously arriving volleys of synaptic inputs (Diesmann et al. 1999; Reyes 2003). This view is supported by intracellular recordings from auditory and somatosensory cortical neurons in anesthetized animals, which show that their membrane potentials remain near rest most of the time, except for brief high-amplitude excursions (or "bumps") which reliably generate spikes (DeWeese and Zador 2006; Okun and Lampl 2008). These membrane potential dynamics imply that network activity is highly correlated at a fine time scale. The nature of sustained membrane potential responses, which do not occur in the auditory cortex of anesthetized animals, remains unknown. On one hand, neurons could show sustained, “DC” depolarizations, implying temporally uncorrelated presynaptic inputs. On the other hand, neurons could show a sustained increase in the rate of high-amplitude membrane potential excursions, i.e., “AC” epochs of bumps. This would imply that even sustained spiking responses, for which spike times vary randomly across trials, are generated by synchronously arriving volleys of synaptic inputs.

To investigate the synaptic mechanisms underlying sustained responses to sounds, we recorded from auditory cortical neurons in unanesthetized rats using in vivo whole-cell methods.
Most sounds evoked brief responses similar to those observed in anesthetized animals. For about half of our neurons (24/47, or 51%), however, we observed sustained responses for a subset of stimuli. This is consistent with previous reports that sustained spiking responses are evoked only by preferred stimuli (Wang et al. 2005). These sustained responses typically consisted of epochs of transient membrane potential excursions, or “bumps” (Fig. 1a). Except for stimulus-locked bumps at the onset and termination of the stimulus, these bumps occurred at random times across trials (Fig. 1b). This neuron responded with “AC” sustained epochs of bumps to several other stimuli, including pure tones (Fig. 1c) and white noise. Evoked action potentials occurred exclusively at the peaks of these brief membrane potential excursions, as can be seen from traces aligned to individual spikes (Fig. 1d, gray traces) and from the spike triggered average membrane potential (Fig. 1d, black trace). Thus each spike was triggered, in this neuron, by a large-amplitude (~20 mV) bump rather than by random fluctuations around spiking threshold.

What drives these brief membrane potential excursions? Bumps could be driven mainly by synchronous volleys of synaptic inputs, or alternatively, synaptic inputs could be amplified by postsynaptic nonlinearities such as voltage-dependent sodium or calcium conductances. To distinguish between these two possibilities, we used voltage clamp, which should eliminate any contribution from voltage-dependent conductances. We also included 3 blockers of voltage-dependent conductances in the pipette internal solution (QX-314, which blocks sodium and calcium conductances, and cesium and TEA, which both block potassium conductances). Under these conditions, preferred stimuli could evoke sustained barrages of brief, large-amplitude synaptic currents (Fig. 1e, see Figs. S1-3 for more examples). This suggests that bumps in the membrane potential (or in the membrane current) are driven largely by concerted volleys of synaptic inputs, and do not critically depend on voltage-gated conductances (although this does not rule out some contribution from voltage-gated conductances). When we clamped neurons to hyperpolarized holding potentials, synaptic currents were inward, whereas at depolarized holding potentials they were outward (Fig. 1e). This suggests that individual bumps are driven by a combination of excitatory and inhibitory synaptic inputs, as in anesthetized animals (Okun and Lampl 2008; Wehr and Zador 2003). Because bumps during sustained responses are not stimulus-locked, however, we were not able to determine the balance of excitation and inhibition for individual bumps.

In many neurons, we observed responses that consisted of a sustained “DC” depolarization, during which the membrane potential remained elevated above the resting potential throughout the response (Fig. 2a). On individual trials, brief large-amplitude membrane potential fluctuations were superimposed on the sustained depolarizations; these fluctuations had a time course similar to that of transient responses to brief or non-optimal stimuli (Fig. S4). Many cells showed membrane potential dynamics that were intermediate between the two extremes illustrated in Figs. 1a and 2a. We used two methods to quantify the nature of sustained responses across the population. First, we compared the variance of the membrane potential to its mean for each individual trial (Fig. 2b). For a purely DC sustained response, we expect a high mean but a low variance. In contrast, for an AC sustained response that consists only of bumps, we expect a high variance but a low mean. Across neurons, sustained responses exhibited a wide variation in both mean and variance (Fig. 2b). Responses formed a broad continuum ranging from DC responses (such as those in Fig. 2a, shown by blue dots) to responses consisting only of sustained epochs of bumps (such as those in Fig. 1a-b, shown by red dots). The population showed no apparent segregation into distinct classes of cells or responses. Second, we computed the power spectrum of each individual trial, and compared low-frequency power (0-10 Hz) to high-frequency power (10-80 Hz). For a purely DC sustained response, we expect greater power at low frequencies than at high frequencies. For an AC
sustained response that consists only of bumps, we expect greater power at high frequencies than at low frequencies. As with mean and variance, responses formed a broad continuum across all neurons (Fig. 2c). We conclude that sustained responses occur along a continuum from DC to AC, rather than being segregated into distinct classes of neurons (Lu et al. 2001) or occurring during distinct states (e.g. of arousal or attention).

The existence of sustained tone-evoked epochs of bumps (Fig. 1a) suggests that sustained spiking responses can be generated by epochs of synchronous volleys of inputs, which we refer to as an "AC" mode of cortical operation, at least in some neurons. On the other hand, the existence of sustained depolarizations (Fig. 2a) can be interpreted in two ways. It could be taken as evidence for the existence of a "DC" mode, in which sustained depolarizations and spiking responses are driven by temporally uncorrelated synaptic inputs (Shadlen and Newsome 1998). This would suggest that both AC and DC modes exist in a continuum across the population. This is consistent with our population data (Fig. 2b-c). Alternatively, sustained DC depolarizations could be driven not by uncorrelated synaptic inputs, but by a rapid succession of synchronous volleys which arrive close enough in time to temporally summate. In this scenario, a single mode of information propagation (highly correlated volleys of synaptic inputs) could account for both for bumps in the membrane potential and for sustained DC depolarizations, depending on the rate at which stimuli evoke synchronous volleys of inputs. We cannot distinguish between these two scenarios based on the dynamics of sustained DC depolarizations, because both scenarios result in similar membrane potential dynamics. Nevertheless, the underlying mechanisms are fundamentally distinct: in one case, presynaptic inputs are uncorrelated with each other, whereas in the other case, they are organized into synchronous volleys and are therefore highly correlated with each other. In order to distinguish between these two possibilities, we simultaneously recorded the local field potential along with the membrane potential. The local field potential, which reflects the summed activity of the local cortical network, was highly correlated with the membrane potential during sustained responses (Fig. 3a). For responses that consisted of sustained epochs of bumps, each bump in the membrane potential coincided with a downward bump in the field. This was also true for the fluctuations during DC sustained responses (Fig. 3b, see Figs. S5-S7 for more examples). Close inspection of individual trials (Fig. 3b, inset) reveals that fluctuations in the membrane potential and local field potential were negatively correlated with each other. Cross-correlation analysis between the membrane potential and the local field potential (Fig. 3c) revealed a sharp negative peak with a width of 50-100 ms for both the AC example shown in Fig. 3a (blue line) and the DC example shown in Fig. 3b (orange line). This suggests that, even during sustained DC depolarizations, apparently random membrane potential fluctuations are due to highly correlated activity among presynaptic inputs. This implies that precise temporal coordination of presynaptic inputs is responsible for sustained spike trains for which the spike timing appears random across trials.

Is this mode of operation specific to auditory cortex? We wondered whether sustained spiking responses in visual cortical neurons might also be driven by sustained epochs of brief, stereotyped large-amplitude bumps. We therefore used whole-cell methods to record from neurons in rat visual cortex in both anesthetized and unanesthetized animals, and presented full-field high-contrast sinusoidal gratings. We observed sustained responses in many neurons, but in striking contrast to auditory cortical neurons, these responses never consisted of sustained epochs of bumps. Instead, sustained responses consisted of sustained depolarizations of variable duration, i.e. UP-states (Fig. 4a, see Figs. S8-S10 for more examples). This suggests that spikes in the sustained responses of visual neurons are driven by prolonged depolarizations, rather than epochs of brief, stereotyped bumps. These sustained depolarizations are consistent with previous reports of stimulus-evoked UP-states in visual
cortical neurons in anesthetized cats (Anderson et al., 2000). Similar UP-states have been reported in other cortical areas in both anesthetized (Haider et al. 2006; Petersen et al. 2003; Steriade et al. 1993) and unanesthetized (Steriade et al. 2001) animals, but never in auditory cortex. The UP-states that we observed in visual cortical neurons appeared to be qualitatively different from the sustained DC depolarizations that we observed in some auditory cortical neurons. The membrane potential histogram averaged across all visual neurons was prominently bimodal (Fig. 4b), unlike that for auditory neurons. The fast correlations between simultaneously recorded membrane and local field potentials seen in auditory cortex (Fig. 3) were absent in visual cortex (Fig. 4, S8). Consistent with this, the temporal dynamics of visual cortical neurons were significantly slower than auditory cortical neurons at the population level. Cross-covariance analysis between the membrane potential and the simultaneously recorded local field potential revealed that the covariance width was significantly greater in visual neurons (269 ± 120 ms, mean ± s.d.) than in auditory neurons (251 ± 115 ms, p<10^{-4}). The spike-triggered average of the membrane potential was also significantly wider in visual neurons (74 ± 54 ms) than in auditory neurons (47 ± 36 ms, p<10^{-4}). Spectral analysis of the membrane potential on individual trials (Fig. 4c) revealed that visual neurons had significantly greater power than auditory neurons between 0-10 Hz (p<10^{-4}), but that auditory neurons had significantly greater power than visual neurons between 10-80 Hz (p<10^{-4}).

These differences in temporal dynamics were also prominent during spontaneous activity. In auditory cortical neurons, spontaneous activity (in silence) consisted of brief, stereotyped bumps, either in isolation or in epochs (Fig. 4d, see Fig. S11 for more examples). In visual cortical neurons, spontaneous activity (in the presence of a uniformly grey screen) consisted of UP-states of variable duration (Fig. 4e, see Fig. S11 for more examples). Are bumps simply short UP-states? We argue that although bumps share some properties in common with UP-states, their stereotyped nature is qualitatively different from the variability in the duration of UP-states. Taken together, our results suggest that the mode by which information propagates through cortical networks may be fundamentally different in auditory than it is in visual cortex. In auditory cortex, information appears to be transmitted by precisely timed volleys of synchronous action potentials, whereas in visual cortex, information appears to be transmitted by prolonged UP-states of increased, irregular, and temporally uncorrelated spiking. That these dynamics differ, despite the marked similarities in cortical microcircuitry across areas, may reflect divergent adaptations to the different processing tasks faced in vision and audition.

Methods

All procedures were in strict accordance with the National Institutes of Health guidelines as approved by the University of Oregon Animal Care and Use Committee.

Surgery: Rats aged 19-30 days postnatal were anesthetized with either isoflurane (1.75-3%) or 30 mg/kg ketamine and 0.24 mg/kg medetomidine for headpost and chamber implantation. A craniotomy was performed over either auditory or visual cortex, which was then covered with a cylindrical polyethylene chamber and a protective elastomer cap. Animals were given 8 mg/kg dexamethasone and 5 mg/kg ketoprofen after surgery, and 0-8 mg/kg dexamethasone, 0-5 mg/kg ketoprofen, and 0-2 mg/kg atropine as needed before each recording session. After 18-24 hours of recovery, animals were restrained by mounting the headpost in a clamp, and recordings were obtained from unanesthetized animals for 1-2 recording sessions/day (<2 hours each) for up to 5 days. Animals were given a low anxiolytic dose (10-20 mg/kg) of diazepam prior to recording sessions. To verify that diazepam did not affect our results, we obtained 2 whole-cell recordings from animals without diazepam, and 3 from animals with very low (2-5 mg/kg) doses. Results were indistinguishable from those obtained with the standard diazepam.
dosage (see Fig. S12 for an example) except that recording durations were typically shorter. It is possible that animals were occasionally asleep during some recordings, although animals often yawned, stretched, chewed, or groomed during recordings, which in some cases terminated the recording. We recorded from both auditory and visual cortical neurons in unanesthetized animals; in addition we recorded from 14 visual cortical neurons in ketamine-medetomidine anesthetized animals. Spontaneous and evoked activity in visual cortical neurons in anesthetized animals was indistinguishable from that in unanesthetized animals.

**Physiology:** We obtained whole-cell recordings using standard blind patch clamp methods (Scholl and Wehr 2008). Internal solution contained, in mM, Cs- or K-glucconate 140, HEPES 10, MgCl$_2$ 2, CaCl$_2$ 0.05, MgATP 4, NaGTP 0.4, Na$_2$Phosphocreatine 10, BAPTA 10, QX-314 0 or 6, TEA 0 or 4, pH 7.25, diluted to 290 mOsm. To record spiking and membrane potential responses, we used current clamp mode (I=0) and used K+ without QX-314 in the internal solution. To record synaptic currents, we used voltage clamp mode and included QX-314, TEA, and Cs+ in the internal solution. To record local field potentials, we used tungsten microelectrodes ~100-200 µm from the patch electrode, ~400-600 µm below the cortical surface. Local field potentials were band-pass filtered (1-5,000 Hz) and amplified with an AC amplifier.

**Acoustic stimuli:** We presented pure tones, white noise bursts, and sinusoidally frequency modulated (FM) tones with durations 25 ms, 400 ms, or 2000 ms, using a free-field calibrated sound delivery system in an acoustic isolation chamber as previously described (Scholl and Wehr 2008). All stimuli had 10 ms 10–90% cosine-squared ramps, except for 25 ms tones which had 3 ms ramps; dB indicates dB SPL. Pure tone frequencies and FM carrier frequencies ranged from 1-40 kHz; FM modulation rates ranged from 2-6 Hz, and interstimulus intervals ranged from 350-2000 ms. Each individual trial of white noise was a different random instantiation. Because sustained responses are evoked only by optimal stimuli (Wang et al. 2005), we employed a combination of systematic pseudorandomly interleaved stimulus sets as well as individual stimuli tailored to particular neuronal preferences.

**Visual stimuli:** We presented full-field (46x61 degrees) drifting or stationary sinusoidal gratings at 100% contrast on an NEC AccuSync LCD203WXM flat panel display located 33 cm from the contralateral eye. Spatial frequencies ranged from 0.01-1.6 cycles/degree, temporal frequencies ranged from 0-8 cycles/s, and interstimulus intervals ranged from 200-5000 ms. Direction of motion was either pseudorandomly interleaved in sets of 8 or 16 directions, or tailored to particular neuronal preferences. Stimuli were generated using the freely available Psychophysics Toolbox for Matlab; timing of all stimuli was verified with a photodiode during experiments.

**Analysis:**
Resting membrane potential ($V_{\text{rest}}$) was estimated from the point where the membrane potential frequency histogram crossed 10% of its maximal value. Mean, variance, and power spectral density (Figs. 2,4) of the membrane potential (with $V_{\text{rest}}$ subtracted) were computed over the time window defined by stimulus presentation on each individual trial (i.e. they were not computed across trials) for all stimuli 400 ms and longer. Power spectral density was averaged in two frequency bands: DC-10 Hz ($P_{0-10}$), and 10-80 Hz ($P_{10-80}$); the 10 Hz cutoff was chosen to correspond to a bump width of order 100 ms. Cross-covariance (Fig. 3c), which is equivalent to cross-correlation of signals with means removed, was computed between membrane potentials and field potentials across the entire duration of the recording. We defined cross-covariance width as the width of the central negative peak in the cross-covariance function at half of its maximally negative value. Cells without a well-defined cross-covariance peak were excluded.
from this width analysis (specifically, we excluded cells without a cross-covariance peak more negative than -1; varying this threshold over a wide range did not affect the results). Membrane potential frequency histograms were computed across 10 s windows in both the presence and absence of stimuli, with 0.2 ms bins, $V_{rest}$ subtracted. To assess the fraction of auditory cortical neurons that exhibited sustained responses for at least one stimulus, we identified sustained responses by eye and then asked whether (a) the mean membrane potential (or current) computed over the time window defined by the initial 33% of stimulus presentation, and (b) the mean membrane potential (or current) computed over the time window defined by the final 33% of stimulus presentation, on each individual trial were both significantly greater than a pre-stimulus time window with the same duration (one-sided paired t-test). This criterion excluded several cells with responses that were prolonged (compared to transient responses typical of anesthetized animals) but not sustained throughout the entire stimulus duration. Presumably, the fraction of neurons for which we observed sustained responses reflects the limits of our ability to identify an optimal stimulus during brief whole-cell recordings, rather than the ability of cortical neurons to respond in a sustained fashion.

Because we recorded from multiple cortical areas with different recording configurations and under different conditions, we summarize here our sample size for each group. We obtained whole-cell recordings from a total of 77 neurons, 47 in auditory cortex and 30 in visual cortex. Of the 47 auditory cortical neurons, all were from unanesthetized animals, 31 were recorded in current clamp (I=0) mode, 11 of these 31 included a simultaneous field potential recording, and 16 were recorded in voltage clamp mode. All 30 visual cortical neurons were recorded in current clamp (I=0) mode, 14 of these were recorded in ketamine-anesthetized animals (12 of these 14 included a simultaneous field potential recording), and 16 were recorded in unanesthetized animals (4 of these 16 included a simultaneous field potential recording).

**Figure Legends**

Figure 1. Auditory cortical neurons can show sustained epochs of bumps in response to sound.  
a) Membrane potential responses of an auditory cortical neuron to an FM tone (single trial, 6.7 kHz carrier frequency, 4 Hz sinusoidal frequency modulation, 2 s, 70 dB). Note the large, transient depolarizations that return nearly to the resting membrane potential. b) Four superimposed trials (5.7 and 6.7 kHz carrier frequencies). Timing of bumps varies randomly across trials. c) Sustained epochs of bumps evoked by a pure tone (3.4 kHz, 400 ms, 80 dB) in the same neuron. d) Spike-triggered average membrane potential (black) and individual traces (gray). e) Tone-evoked currents recorded in voltage clamp mode from a different neuron at two holding potentials (red: +1, green: -90 mV), in response to a 1kHz, 80 dB, 400 ms pure tone. a-d: neuron 050708-001, e: neuron 072408-001.

Figure 2. Auditory cortical neurons can show sustained depolarizations in response to sound.  
a) Overlaid membrane potential responses of an auditory cortical neuron to white noise (400 ms, 80 dB) on 5 individual trials (neuron 050108-002). b) Variance vs. mean, and c) mean power spectral density in the 10-80 Hz band vs. the 0-10 Hz band, computed from the membrane potential on individual trials over the time window defined by stimulus presentation. Each dot represents an individual trial, across all stimuli and neurons (n=4652 stimulus presentations across 31 neurons recorded in current clamp mode in auditory cortex). Blue dots indicate the responses shown in (a); red dots indicate the responses shown in Fig. 1a-b. Responses formed a continuum from AC to DC across the population.

Figure 3. Sustained membrane potential responses in auditory cortical neurons were highly
correlated with simultaneously recorded local field potential responses. a) Membrane potential (black) and field potential responses (red) to an FM tone (single trial, 2.8 kHz carrier frequency, 2 Hz sinusoidal frequency modulation, 2 s, 70 dB). Note the simultaneous occurrence of bumps in both membrane and field potentials. b) Membrane potential and field potential responses of a different neuron to white noise (2 s, 70 dB, single trial). Inset, two individual trials during the region enclosed by the dashed line. Note the negative correlation of membrane potential and field potential fluctuations during individual trials. c) Cross covariance between the membrane potential and field potential for the stimuli shown in (a) (blue) and in (b) (orange). Note the negative peak at zero lag for responses to both stimuli. a: neuron 061908-001, b: neuron 091508-001.

Figure 4. Sustained membrane potential responses in auditory and visual cortical neurons were qualitatively different. a) Sustained membrane potential responses in a visual cortical neuron (black) and simultaneously recorded local field potential responses (red) to a full-field stationary grating (single trial, 0.2 cycles/degree, 100% contrast, 500 ms). b) Membrane potential histograms averaged across 31 auditory cortical neurons (blue) and 16 visual cortical neurons (red), calculated from 10 s segments in both the presence and absence of stimuli, all from unanesthetized animals. Shaded region indicates s.e.m. c) Mean power spectral density in the 10-80 Hz band vs. the 0-10 Hz band, computed from the membrane potential on individual trials over the time window defined by stimulus presentation. Each dot (blue: auditory cortical neurons, red: visual cortical neurons) represents an individual trial, across all stimuli and neurons (n=4652 stimulus presentations across 31 neurons recorded in current clamp mode in auditory cortex, n=4234 stimulus presentations across 30 neurons recorded in current clamp mode in visual cortex. Blue dots (auditory) are identical to those in Fig. 2c). d) Spontaneous membrane potential in an auditory cortical neuron (black) and simultaneously recorded local field potential (red), in silence. Spontaneous activity consisted of isolated bumps. e) Spontaneous membrane potential in a visual cortical neuron (black) and simultaneously recorded local field potential (red), in the presence of a uniformly grey screen. Spontaneous activity consisted of UP-states of variable duration. a: neuron 082708-003, d: neuron 091408-004, e: neuron 090208-002.

References


Figure 1

- a: FM tone
- b: FM tone
- c: 3.4 kHz tone
- d: 1 kHz tone
- e: 1 mV, -90 mV
Figure 2
Figure 3
Figure 4
Supplemental Information.

Here we provide 11 figures of additional examples.

Figure S1: Timing of bumps in the membrane current was irregular across trials. Tone-evoked currents recorded in an auditory cortical neuron in voltage clamp mode at two holding potentials (+1 and -90 mV), in response to a 1kHz, 80 dB, 400 ms pure tone, 3-4 overlayed trials. Note that only the timing of the bump at tone onset is reliable. Neuron 072408-001, same neuron as Fig. 1e.

Figure S2: Tone-evoked currents recorded in an auditory cortical neuron in voltage clamp mode (holding potential: -76 mV), in response to a 2.4 kHz, 80 dB, 400 ms pure tone, individual trial. Neuron 072908-002.

Figure S3: Tone-evoked currents recorded in an auditory cortical neuron in voltage clamp mode (holding potential: -86 mV), in response to white noise, 80 dB, 2000 ms, individual trial. Neuron 080608-003.

Figure S4: Brief or non-optimal stimuli typically evoked transient membrane potential responses (isolated bumps) in auditory cortical neurons. Each trace is the response to a 25 ms tone, with frequency and level indicated along the bottom and left. Means of 3-4 trials. Characteristic frequency for this neuron was 13.9 kHz. Auditory cortex. Neuron 050108-002 (same neuron as Fig. 2a).

Figure S5: Fluctuations during sustained DC membrane potential responses in auditory cortical neurons were highly correlated with fluctuations in simultaneously recorded local field potential responses. Membrane potential (black) and field potential responses (red) to white noise (top), a 5.8 kHz pure tone (middle), and an 8.2 kHz pure tone (bottom), all 80 dB, 2000 ms, individual trials. Neuron 081908-001.

Figure S6: Fluctuations during sustained DC membrane potential responses in auditory cortical neurons were highly correlated with fluctuations in simultaneously recorded local field potential responses. Membrane potential (black) and field potential responses (red) to white noise (70 dB, 2000 ms) on 5 individual trials. Neuron 091508-001 (same neuron as Fig 3b).

Figure S7: Fluctuations during sustained DC membrane potential responses in auditory cortical neurons were highly correlated with fluctuations in simultaneously recorded local field potential responses. Membrane potential (black) and field potential responses (red) to an FM tone (carrier frequency: 32 kHz, 6 Hz sinusoidal frequency modulation, 70 dB, 2000 ms) on 8 individual trials. Field potential high-pass filtered at 5 Hz. Neuron 091508-002.

Figure S8: Sustained responses in visual cortical neurons consisted of DC UP-states of variable duration. Membrane potential fluctuations during UP-states were not well correlated with simultaneously recorded local field potentials. Membrane potential (black) and field potential responses (red) to a full-field drifting grating (5 individual trials, 0.16 cycles/degree, 4 cycles/s, 100% contrast, 500 ms). Neuron 090208-002.

Figure S9: Sustained responses in visual cortical neurons consisted of DC UP-states of variable duration. Membrane potential responses to a full-field drifting grating (8
individual trials, 0.1 cycles/degree, 4 cycles/s, 100% contrast, 1000 ms). Neuron 091108-001.

Figure S10: Sustained responses in visual cortical neurons consisted of DC UP-states of variable duration. Membrane potential responses to a full-field drifting grating (18 individual trials, 0.16 cycles/degree, 4 cycles/s, 100% contrast, 1000 ms). Neuron 091108-001.

Figure S11: Spontaneous activity was qualitatively different in auditory and visual cortical neurons. a) Membrane potential in an auditory cortical neuron during 10s of silence. Spontaneous activity consisted of isolated bumps. b) Membrane potential in a visual cortical neuron during 10s of a uniformly grey screen. Spontaneous activity consisted of UP-states of variable duration. a: neuron 091508-002 (same neuron as Fig S7), b: neuron 090808-003.

Figure S12: Membrane potential responses of an auditory cortical neuron to a 4.8 kHz, 80 dB, 2000 ms pure tone (3 individual trials) in an animal which had not received diazepam.
Figure S1
Figure S2

2.4 kHz tone

-76 mV

50 pA

100 ms
Figure S3

-86 mV

white noise
Figure S4
Figure S5
Figure S6
Figure S7
Figure S8
Figure S9
Figure S11
Figure S12

4.8 kHz tone

20 mV

500 ms