Published in final edited form as:

Neuroscience. 2016 March 1; 316: 402–419. doi:10.1016/j.neuroscience.2015.12.057.

Functional congruity in local auditory cortical microcircuits

Craig A. Atencio and Christoph E. Schreiner

Coleman Memorial Laboratory UCSF Center for Integrative Neuroscience Kavli Institute for Fundamental Neuroscience Department of Otolaryngology-HNS University of California, San Francisco

Abstract

Functional columns of primary auditory cortex (AI) are arranged in layers, each composed of highly-connected fine-scale networks. The basic response properties and interactions within these local subnetworks have only begun to be assessed. We examined the functional diversity of neurons within the laminar microarchitecture of cat AI to determine the relationship of spectrotemporal processing between neighboring neurons. Neuronal activity was recorded across the cortical layers while presenting a dynamically modulated broadband noise. Spectrotemporal receptive fields (STRFs) and their nonlinear input/output functions (nonlinearities) were constructed for each neuron and compared for pairs of neurons simultaneously recorded at the same contact site. Properties of these local neuron pairs showed greater similarity than non-paired neurons within the same column for all considered parameters including firing rate, envelope-phase precision, preferred spectral and temporal modulation frequency, as well as for the threshold and transition of the response nonlinearity. This higher functional similarity of paired versus non-paired neurons was most apparent in infragranular neuron pairs, and less for local supragranular and granular pairs. The functional similarity of local paired neurons for firing rate, best temporal modulation frequency and two nonlinearity aspects was laminar dependent, with infragranular local pair-wise differences larger than for granular or supragranular layers.

Synchronous spiking events between pairs of neurons revealed that simultaneous ‘Bicellular’ spikes, in addition to carrying higher stimulus information than non-synchronized spikes, encoded faster modulation frequencies. Bicellular functional differences to the best matched of the paired neurons could be substantial. Bicellular nonlinearities showed that synchronous spikes act to transmit stimulus information with higher fidelity and precision than non-synchronous spikes of the individual neurons, thus, likely enhancing stimulus feature selectivity in their target neurons. Overall, the well-correlated and temporally precise processing within local subnetworks of cat AI showed laminar-dependent functional diversity in spectrotemporal processing, despite high intra-columnar congruity in frequency preference.

Corresponding author: Craig Atencio, craig@phy.ucsf.edu, 675 Nelson Rising Lane, Box 0444, Room 535, San Francisco, CA 94158, 415-502-74023.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

local circuits; subnetworks; microarchitecture; microcircuits; fine-scale networks

1. INTRODUCTION

The auditory cortex is composed of circuits at multiple scales, such as inter-areal, inter-columnar, interlaminar, and intralaminar (Mitani and Shimokouchi, 1985, Barbour and Callaway, 2008, Lee and Winer, 2011, Winer, 2011). At the finest scales, local circuits are formed between nearby neurons, resulting in a tapestry of precisely connected subnetworks (Thomson et al., 2002, Holmgren et al., 2003, Oswald and Reyes, 2008, Otsuka and Kawaguchi, 2009). The connections between adjacent cells may be considered a stereotypical cortical circuit (Defelipe, 1997), and the accompanying activation rules can be complex (Krause et al., 2014). This stereotypy produces a microstructure that is anatomically well-organized, and where the connection strength and cell type are precisely regulated (Defelipe, 1997, Silberberg et al., 2002, Douglas and Martin, 2004). Despite the breadth of these small-circuit descriptions, we know little about the functional processing at these fine scales. Consequently, while functional processing varies with layer (Atencio et al., 2009, Atencio and Schreiner, 2010a, b), few studies have examined the layer-dependent functional micro-organization of auditory cortical processing (Bandyopadhyay et al., 2010, Rothschild et al., 2010, Winkowski and Kanold, 2013). This leaves the question: do neurons at the finest scales of spatial relationship within the tonotopic construct have similar or dissimilar spectrotemporal response preferences?

Two lines of evidence suggest that fine-scale networks within a cortical column can display considerable variability within AI layers. First, nearby neurons in the ventral portion of cat AI appear to have a larger scatter of characteristic frequencies (CFs) than in other regions of AI (Schreiner and Sutter, 1992). Multi-unit data, comprised of multiple single units, revealed broad, pure-tone tuning curves in ventral AI, while contributing single-units often had narrower tuning and disparate CFs. This indicated that multi-unit data can mask the tuning variability in local neuron populations.

The second line of evidence comes from recent imaging work in mouse AI, which revealed a fractured micro-tonotopy, at least in the upper cortical layers (Bandyopadhyay et al., 2010, Rothschild et al., 2010). Previously, single unit recordings in mice at large spatial scales showed consistent, and largely continuous, tonotopy (Stiebler et al., 1997, Guo et al., 2012). Two-photon imaging revealed that in supragranular layers, neurons within 50-100 μm of each other may differ in CF by up to 4 octaves (Rothschild et al., 2010). CFs were more similar in granular layers (Winkowski and Kanold, 2013, Kanold et al., 2014). Functional heterogeneity was also observed by imaging the synaptic preference of pyramidal neuron spines. Each synaptic contact appeared to be tuned to relatively different frequencies, implying that nearby neurons provide varying receptive field information (Chen et al., 2011).

Therefore, to examine the functional variability within cortical columns we recorded from pairs of nearby neurons across the laminar extent of cat AI and constructed spectrotemporal

receptive fields (STRFs) and nonlinear input/output functions for each neuron to assess the characteristics of functional processing of cat AI at the finest spatial scales.

Our previous study on local circuit processing established in the cat a precise temporal relationship between the activity of neighboring neurons (Atencio and Schreiner, 2013). We also have demonstrated a high similarity of frequency-preference between neurons in local networks and in the same column (Atencio and Schreiner, 2010a, 2013). Here, we significantly extend this work by addressing (1) whether spectrotemporal processing characteristics, including nonlinear input/output functions, show local diversity, (2) whether local functional variability is similar across different cortical layers, and (3) whether synchronous spiking of local pairs of neurons transmits the same spectrotemporal information as the constituent neurons.

2. Experimental Procedures

2.1. Surgical procedures, stimulation, and recording

The University of California, San Francisco Committee for Animal Research approved all experimental procedures under protocol AN086113. We previously described the experimental procedures that were used in this study (Atencio and Schreiner, 2010a, b). Briefly, young adult cats (N=10) were given an initial dose of ketamine (22 mg/kg) and acepromazine (0.11 mg/kg), and then anesthetized with pentobarbital sodium (Nembutal, 15-30 mg/kg) during the surgical procedure. The animal's temperature was maintained with a thermostatic heating pad. Bupivacaine was applied to incisions and pressure points. Surgery consisted of a tracheotomy, reflection of the soft tissues of the scalp, craniotomy over AI, and durotomy. After surgery pentobarbital sodium was discontinued and, to maintain an areflexive state, the animal received a continuous infusion of ketamine/diazepam (2-5 mg/kg/h ketamine, 0.2-0.5 mg/kg/h diazepam in lactated Ringer solution).

With the animal inside a sound-shielded anechoic chamber (IAC, Bronx, NY), we delivered stimuli via a closed speaker system to the ear contralateral to the exposed cortex (diaphragms from Stax, Japan). We made extracellular recordings with multi-channel silicon recording probes, which were provided by the University of Michigan Center for Neural Communication Technology. The probes contained sixteen linearly spaced recording channels, with each channel separated by 150 μm . We used probes with channel impedances between 2 and 3 M Ω , since these impedances allowed us to resolve single units. Probes were carefully positioned orthogonally to the cortical surface and lowered to depths between 2300 and 2400 μm using a microdrive (David Kopf Instruments, Tujunga, CA).

2.2. Stimulus

For each recording site, pure tones were presented in a random sequence. The amplitudes and frequencies of the tones spanned 0-70 dB (5 dB steps) and 2.5-40 kHz (0.1 octave steps), respectively. All neurons were also probed with a broadband (0.5 – 40 kHz) dynamic moving ripple (DMR) stimulus (Escabí and Schreiner, 2002, Atencio et al., 2008). The maximum spectral modulation frequency of the DMR was 4 cyc/oct, and the maximum temporal modulation frequency was 40 cyc/s (Escabí and Schreiner, 2002). The maximum

modulation depth of the spectrotemporal envelope was 40 dB. Mean intensity was set at 30-50 dB above the average pure tone threshold. For a small subset of sites, we also presented a Ripple Noise (RN) stimulus. The RN is the sum of sixteen independently created DMR stimuli. The spectrotemporal envelopes of the DMR and RN stimuli are dissimilar: the DMR contains local correlations while the RN does not (see Fig. 2A,G).

2.3. Recording

We followed the recording and spike-sorting procedure outlined in (Atencio and Schreiner, 2013). Neural traces were bandpass filtered between 0.6 and 6 kHz and recorded with a Neuralynx Cheetah A/D system at sampling rates between 18 kHz and 27 kHz. After each experiment the traces were sorted off-line with a Bayesian spike sorting algorithm that is conceptually and mathematically described in (Lewicki, 1994, 1998). Only events in the traces that exceeded the DC baseline by 5 RMS noise levels were used in the spike sorting procedure (termed spike events). Most channels of the probe yielded 1-2 well-isolated single units (similar to (Peyrache et al., 2012)). The Bayesian spike sorting allows the proper classification of spikes so long as the peak in one spike waveform does not overlap with the trough of another spike waveform; when spike waveforms overlap, the combined waveform must exceed the 5 RMS threshold to be detected. If an event is detected, and cannot be assigned to a single unit, an overlap decomposition procedure is performed. To resolve a possible overlap, the algorithm uses the single unit waveforms of the neurons on a channel. The waveforms are summed for different temporal relationships, resulting in a set of summed waveforms. Each sum in the set corresponds to one temporal relationship. This set is then compared to the actual event. If there is a significant fit between one of the waveform sums and the possible overlap, then the spike times of the two units are recorded. Detailed mathematical explanations of this procedure may be found in (Lewicki, 1994), while a more conceptual description is provided in (Lewicki, 1998).

All recording locations were in AI, as verified through initial multi-unit mapping and determined by the layout of the tonotopic gradient and bandwidth modules on the crest of the ectosylvian gyrus (Imaizumi and Schreiner, 2007). Pair-wise analysis was restricted to neurons that were identified from a signal electrode contact and did not appear on neighboring contacts (spacing of contacts: 150 μ m), i.e., their spatial separation was likely < 150 μ m.

2.4. Spectrotemporal Receptive Fields

We analyzed the data using the MATLAB (Mathworks, Natick, MA) software environment. For each neuron, we estimated spectrotemporal receptive field (STRF) from the spike-triggered average (STA). STRFs were thresholded so that only significant features ($p < 0.01$) were analyzed.

2.5. Modulation Transfer Function

Modulation properties were derived by computing the two-dimensional Fourier transform of each STRF (Atencio and Schreiner, 2010b). The FFT is a function of temporal (cycles/s, Hz) and spectral modulation rate (cycles/octave). We folded the magnitude of this function along the vertical midline (temporal modulation frequency = 0) to obtain the Ripple Transfer

Function (RTF). Since the Fourier transform is sensitive to periodicities in the STRF, the RTF reflects the spectral and temporal relationship of excitatory (ON) and suppressive (OFF) STRF subfields. Thus, if the STRF contains a single excitatory peak, the RTF will tend to be lowpass in both the temporal and the spectral modulation domains. Strong flanking suppression in frequency and/or in time will produce RTFs that are bandpass in the spectral and/or temporal domain.

We used RTFs to obtain temporal and spectral modulation transfer functions (tMTFs, sMTFs). Summing the RTF along the spectral modulation axis yields the temporal modulation transfer function (tMTF), and summing along the temporal modulation axis yields the spectral modulation transfer function (sMTF). We classified MTFs as bandpass if, after identifying the peak in the MTF, values at lower and higher modulation rates decreased by at least 3 dB. If the MTF amplitude did not decrease at low modulation rates the MTF was classified as lowpass. We did not encounter highpass MTFs. For bandpass MTFs, the best modulation rate was the rate corresponding to the peak value in the MTF; for lowpass MTFs, it was the mean between the zero modulation frequency value and the 3 dB high side cutoff. For bandpass MTFs, the width was the difference between the high and low 3 dB cutoff values, while for lowpass MTFs the width was the difference between the high side 3 dB cutoff rate and the zero modulation rate.

2.6. Response Precision

Using previously described methodologies, we computed a Response Precision Index (RPI) for each neuron using the relation $RPI = (\max(STRF) - \min(STRF)) / (r \cdot 8)$, where $\max(STRF)$ and $\min(STRF)$ are the maximum and minimum values in the STRF, and r is the average firing rate (Escabí and Schreiner, 2002, Atencio and Schreiner, 2012, Atencio et al., 2012). Dividing by r and the square root of 8 allows the RPI to range from 0 (not precise) to 1 (very precise). Here, precision refers to how well the spikes align to different parts of the ripple envelope. If the spikes always align to ripple envelope values that have large magnitudes, then the RPI will be closer to 1, since the difference between the maximum and minimum will be great. When spikes are not as precisely aligned, the maximum in the STRF will decrease, and thus the RPI will decrease in value.

2.7. Nonlinearity

For each STRF, we computed the nonlinear input/output function (nonlinearity) that relates the stimulus to the probability of spike occurrence (Atencio and Schreiner, 2012). We calculated the nonlinearity using the following steps. (1) Each ripple stimulus segment, s , that elicited a spike, was correlated with the STRF by projecting it onto the STRF via the inner product $z = s \cdot STRF$. These projections, or stimulus-filter similarities, characterize the probability distribution $P(z | spike)$. (2) We then projected a large number of randomly-selected stimulus segments onto the STRF, and formed the prior stimulus distribution, $P(z)$. (3) The mean and standard deviation of $P(z)$, μ and σ , were then calculated. (4) $P(z | spike)$ and $P(z)$ were transformed to units of standard deviation by using $x = (z - \mu) / \sigma$, to obtain the distributions $P(x | spike)$ and $P(x)$. Because of the transformation, the values of x are now in units of standard deviation (SD). (5) The nonlinearity for the STRF was then computed as

$P(\text{spike} | x) = P(\text{spike}) \frac{P(x | \text{spike})}{P(x)}$, where $P(\text{spike})$ is the average firing rate of the neuron. Thus, the nonlinearity describes the likelihood of a spike occurrence given the similarity between the STRF and the stimulus. High x values indicate STRF-stimulus correlations that would not be expected from a randomly spiking neuron, while values near 0 would be expected if the neuron fired indiscriminately. Thus, if nonlinearity values increase as the x values increase, then the firing rate will increase as the stimulus becomes more similar to the STRF.

We assessed nonlinearity structure using an Asymmetry Index (ASI) (Atencio et al., 2008). The ASI is defined as $ASI = (R - L)/(R + L)$, where R represents the nonlinearity values that correspond to projection values that are greater than 0, while L represents the nonlinearity values that correspond to projection values that are less than 0 (Atencio et al., 2008).

We also analyzed the shape of nonlinearities using a parametric approach. The applied function has wide theoretical and experimental support (Hansel and van Vreeswijk, 2002, Miller and Troyer, 2002, Atencio and Schreiner, 2012). The function has the following form:

$$f(x | A, \theta, \sigma) = \left[\frac{A(x - \theta)}{2} \right] \left[1 + \text{erf} \left(\frac{x - \theta}{\sigma \sqrt{2}} \right) \right] + \frac{A\sigma}{\sqrt{2\pi}} \exp \left(-\frac{(x - \theta)^2}{2\sigma^2} \right)$$

Here, A is a gain term, θ is the threshold to response, and σ is the transition smoothness in the nonlinearity. $\text{erf}(x)$ is the error function. For analysis, we only used fits that gave normalized mean squared errors less than 0.15, and coefficient of determination values greater than 0.85. θ and σ are the most significant parameters in the fit: θ determines the threshold, while σ determines how smooth the transition is when the responses become greater than the average firing rate. When σ is 0, the function describes hard rectification. When σ increases, the transition in the nonlinearity smoothly varies.

2.8. Connectivity

To analyze the functional connectivity between neurons, we followed standard cross-covariance procedures (Rosenberg et al., 1989, Halliday and Rosenberg, 1999, Atencio and Schreiner, 2010a, 2013). First, we obtained spike trains by binning the spike times with 0.5 ms resolution. For a single spike train $A(n)$, n is the bin number and $A(n)$ is either 1 (spike) or 0 (no spike). For two spike trains $A(n)$ and $B(n)$, the mean intensities, P_A and P_B , for a sample of duration D bins, are estimated as $P_A = N_A/D$ and $P_B = N_B/D$, where N_A and N_B are the total number of spikes in trains A and B , respectively. For the spike trains in our study, the stimulus duration was either 15 or 20 minutes, giving $D = 1,800,000$ or $2,400,000$ bins.

We estimated the cross-correlation function, or correlogram, for spike trains $A(n)$ and $B(n)$ as

$$C_{AB}(m) = \sum_{n=0}^{D-m} A(n+m) B(n)$$

We then estimated $P_{AB}(m)$, the second order cross-product density, from $C_{AB}(m)$ using

$$P_{AB}(m) = \frac{C_{AB}(m)}{\Delta \cdot D}$$

where Δ is the bin size of the spike train, in milliseconds. We then estimated the cross-covariance function, $Q_{AB}(m)$, from

$$Q_{AB}(m) = P_{AB}(m) - P_A \cdot P_B$$

Thus, the cross-covariance function is a scaled version of the cross-correlation function, with the mean background activity removed. This allows excitatory and suppressive interactions to be more easily visualized. Cross-covariance values that are approximately zero represent chance coincidences between the two spike trains. Deflections from zero represent how the activity of one neuron influences the firing of the other neuron. Note that

$\lim_{|m| \rightarrow \infty} Q_{AB}(m) = 0$. The cross-covariance function $Q_{AB}(m)$ has an asymptotic distribution from which its variance may be estimated (Halliday and Rosenberg, 1999). Under the assumption of independent Poisson spike trains, the variance of $Q_{AB}(m)$ may be approximated as

$$\text{Var}(Q_{AB}(m)) \cong \frac{P_A \cdot P_B}{\Delta \cdot D}$$

Thus, upper and lower 99% confidence limits (CL) for $Q_{AB}(m)$ can be set at

$$CL = \pm 3 \left(\frac{P_A \cdot P_B}{\Delta \cdot D} \right)^{1/2}$$

We only analyzed cross-covariance functions with two consecutive bins satisfying the 99% confidence limits.

2.9. Bicellular Receptive Field and Nonlinearity Analysis

To determine the stimulus features that elicited synchronous spikes from both neurons, we estimated receptive fields using Bicellular spikes (Atencio and Schreiner, 2013). Bicellular spikes were obtained from the peak in the cross-covariance function and correspond to moments when the spiking of one neuron is temporally closely related to the spiking of the other neuron in the pair. To identify the spikes in the peak, the half-width (HW) of the cross-covariance function was estimated, where HW was the width of the function at half the peak amplitude. The window that was used to obtain Bicellular spikes extended from 1 HW

below the peak delay to 1 HW above the peak delay value (window = $[PD - HW, PD + HW]$). We then estimated the STRF for the Bicellular spike train, resulting in three STRFs: one for each neuron in a pair, and one for the Bicellular spikes. We estimated nonlinearities for the Bicellular spikes using the Bicellular STRF.

2.10. Comparisons between neurons

Throughout this report, we compare the receptive field properties and nonlinearities for each member in a pair of neurons. To provide a principled way in which to plot the values for each pair, the neuron with the shortest spike waveform had its value plotted on the abscissa, while the neuron with the longer waveform had its value plotted on the ordinate (Atencio and Schreiner, 2013). For parameter differences, we used the absolute value of the difference ($abs(V_1 - V_2)$; V_1 = value 1, V_2 = value 2) for latency, firing rate, response precision, best modulation frequency, nonlinearity asymmetry, threshold, and transition. We used the absolute value of the octave difference ($abs(20\log_{10}(V_1/V_2))$; V_1 = value 1, V_2 = value 2) for best frequency and spectral tuning. The similarity between STRFs or nonlinearities was measured using the Pearson correlation coefficient. For laminar analyses, layers were defined following previous work: Supragranular (Supra: 0-600 μm), Granular (Gran: 700-1100 μm), and Infragranular (Infra: 1200-2000 μm) (Atencio and Schreiner, 2010b). Neurons located at depths between these three regions (i.e., between 601-699 μm and 1101-1199 μm) were not considered for the laminar analyses.

Receptive field differences between local pairs of neurons were assessed using random sampling, thus allowing local neuron pair parameter differences to be compared to a baseline value. A proper control cannot simply randomly permute pairs of neurons since it must account for recording location, stimulus presentation, and laminar position. Therefore, we searched for penetrations that contained four or more neurons. For these penetrations, we estimated every possible pairwise combination, and then calculated the pairwise differences for response parameters. For each layer, we aggregated the differences into a distribution, and compared the actual data differences to the “random” differences. $P_D, S_D, G_D,$ and I_D denote Population (P), Supragranular (S), Granular (G), and Infragranular (I) pairwise differences for neurons recorded from the same electrode channel (D = data). $P_R, S_R, G_R,$ and I_R denote pairwise differences obtained through the random pairwise sampling procedure (R = random).

Unless otherwise indicated, values are reported as mean $\pm$ standard error of the mean.

3. RESULTS

3.1. Local distribution of receptive field properties

We examined functional processing within fine-scale networks by recording from pairs of neurons ($N = 670$) obtained from the same electrode contact of a linear, multi-contact array. The probes spanned all layers of AI. Since the neurons in a pair are in close geometric proximity, studying the functional processing of pairs provides a view of the functional variance of local subnetworks within AI. The spatial separation of these local neurons is

likely less than 150 μm since their spiking was not noted on neighboring electrode contacts that were 150 μm away.

The functional characteristics of local subnetworks were determined by first recording from pairs of neurons with differentiable spike waveforms from a single electrode contact (Fig. 1A). Neural spiking events that occur separately in time from each other can be well discriminated. Spikes of two neurons that occur more closely in time produce a superimposed neural signature that is dissimilar from the spike waveforms of either neuron alone (Fig. 1B). By sliding the two individual spike waveforms over time, and summing the waveforms, in many cases it is possible to match the superimposed voltage trace, which then allows the individual spikes of the constituent neurons to be identified (Fig. 1B). The cross-correlation and cross-covariance functions may contain a strong peak near 0 ms delay, which is consistent with synchronous spiking (Fig. 1C,D). Consequently, STRFs for both neurons in the pair can be estimated, since spikes were elicited in response to DMR stimulation (Fig. 1E).

The synchronous spiking between pairs of neurons may be due to either functional connectivity, receptive field similarity, or stimulus influences. Receptive field similarity may explain synchronous spiking because when a stimulus excites pairs of nearby neurons, the stimulus lies within the overlap between the STRFs of the two neuron, and may cause independent spike emission for both neurons. Thus, high correlation between STRFs alone may explain synchronous spiking between neighboring neurons.

To assess whether receptive field overlap can account for synchronous spiking, we correlated the STRFs of pairs of neurons (Fig. 2B-E), and compared the STRF correlations to neural functional connectivity (Fig. 2F). We found that STRF overlap was much broader in time than the width of cross-covariance peaks, and, thus, STRF overlap is not sufficient to account for the temporally precise response coordination observed for local pairs of neurons. This high temporal fidelity for ~10% of the spiking events reveals the influence of precise common input and/or strong functional connectivity between neighboring neurons. It should be noted that the spiking-correlation width for neurons with similar CFs but located > 500 μm from each other corresponds more closely to the STRF correlation width (Atencio and Schreiner, 2010a), suggesting that STRF overlap for more widely separated neurons in the cortical column may become a more dominant aspect than direct synaptic connectivity.

We next considered whether stimulus statistics could influence synchronous spiking. Since the DMR spectrotemporal envelope evolves with time, the changing envelope parameters may influence the shape of functional connectivity (Fig. 2A). Thus, for a subset of neurons we presented a second stimulus, Ripple Noise, that, in contrast to DMR, contained no short-term correlations in its spectrotemporal envelope (Fig. 2G). For both stimuli, we found that the correlation between STRFs could not explain the functional connectivity of local neuron pairs (Fig. 2F,L). The functional connectivity between local pairs was synchronous and highly similar, independent of the two different stimulus statistics (Fig. 2F,L). We further note that since each stimulus was 15 minutes long, the sharp functional connectivity was stable across time (~30 minutes) as well as across stimulus class.

Finally, we compared neural functional connectivity to the stimulus autocorrelation of the DMR to determine if temporal stimulus correlations occurred on the time scale of functional connectivity. We estimated the stimulus correlation of DMRs, and in all cases, the stimulus correlation structure was much broader than the neural correlation width, indicating that the observed sharp spiking synchrony was not a result of entrainment to the stimulus statistics (Fig. 2M). Therefore, the functional connectivity that we observed for local neuron pairs is not dependent on STRF correlation, and it is not explained by stimulus statistics. Instead, it likely indicates unique spiking events due to local and global network activity.

3.2. Response Metrics

The microarchitecture of AI provides a substrate that organizes receptive field processing. This substrate is achieved through the direct and indirect short- and long-range connectivity of neurons. Thus, functional processing within local subnetworks reflects the functional connectivity of the entire network. In subnetworks, if the most basic parameters are dissimilar, then other functional parameters are likely to also be represented in an incongruent manner. In cat AI columns, the frequency preference of neurons is highly conserved ($CF < 0.1$ octaves; Atencio and Schreiner, 2010b, 2013). It does not necessarily follow, though, that other receptive field aspects, such as bandwidth, nonlinearity, or modulation preferences, show the same degree of similarity given the rich parametric structure of cortical neurons (Atencio and Schreiner, 2010a). For all receptive field aspects described in this study, we did not find a significant correlation ($p > 0.1$, t-tests) between aspect differences and best frequency, and thus data were combined across the tonotopic axis.

We first examined the local variance of response strength. We found that pairs of neurons had similar, but not identical, driven firing rates. For the population of neighboring neurons, firing rates differed only by a few Hertz on average (Fig. 3A,C; $r = 0.43$, $p < 0.001$; FR Difference: $P_D = 4.47 \pm 0.21$ Hz). Firing rate difference based on pairwise resampling (see Experimental Procedures) was $P_R = 5.88 \pm 0.12$ Hz, indicating that the firing rate differences between highly synchronous, local neurons were significantly smaller (~23%) than predicted by random sampling (Fig. 3C). A significant firing rate reduction was also seen for granular and infragranular layers alone, with a similar statistical trend in the supragranular layers (Fig. 3C).

The average driven firing rate for the DMR stimulus in cat AI was $\sim 5.6 \pm 0.21$ Hz (Atencio and Schreiner, 2010a, b). The driven firing rate and local pair-differences increased with cortical depth: pairs in infragranular layers had less similar rates than pairs in granular and supragranular layers (Fig. 3B,C; Supra: 2.92 ± 0.68 Hz; Gran: 3.79 ± 0.42 Hz; Infra: 5.65 ± 0.32 Hz; Supra vs. Gran: $p = 0.30$; Supra vs. Infra: $p < 0.001$; Gran vs. Infra: $p < 0.001$, Rank-Sum tests). These layer differences likely reflect the changes in mean and variance of the firing rates between layers (Sakata and Harris, 2009).

In addition to response strength, local neurons may also differ in response precision. We used a response precision index (RPI) to assess the temporal precision of spiking relative to the stimulus envelope. We obtained the RPI from the STRF by determining the maximum and minimum magnitude values in the STRF, and comparing them to the theoretical values

that we would expect if each spike was perfectly aligned with the stimulus and had no jitter. For the population, local pairs of neurons had RPI differences that were ~20% smaller than unpaired neurons (Fig. 3D,E,F; $r = 0.78$, $p < 0.001$; RPI Difference: $P_D = 0.056 \pm 0.003$; $P_R = 0.068 \pm 0.002$). A significant difference was also seen for infragranular pairs alone. Supragranular layers revealed the smallest differences, followed by infragranular, and then granular layers (Figure 3F; Supra: 0.035 ± 0.004 ; Gran: 0.062 ± 0.005 ; Infra: 0.052 ± 0.004). Supragranular RPI differences did not differ from those of infragranular pairs, though granular layers contained nearby neurons with more variable RPIs (Supra vs. Gran: $p = 0.019$; Supra vs. Infra: $p = 0.357$; Gran vs. Infra: $p = 0.036$, Rank-Sum tests). Therefore, within the local architecture of AI, response precision is well-matched between pairs of neurons in non-granular layers.

3.3. Modulation processing

Within local circuits, more complex acoustic stimulus preferences may also be well-matched. We characterized modulation processing of pairs of neurons, since temporal and spectral modulations carry a substantial portion of auditory signal information (Shannon et al., 1995, Drullman et al., 1996). Temporal modulations describe how the stimulus envelope fluctuates over time, while spectral modulations describe envelope variations along the tonotopic frequency axis. The spacing and structure of excitatory and inhibitory STRF subfields reflects the neuron's envelope modulation preference (Fig. 4A). First, we transformed the STRF using the 2D FFT (Fig. 4B). The magnitude of the 2D FFT is the ripple transfer function (RTF), which is a function of temporal and spectral modulation frequency (Fig. 4B). Second, we summed the RTF across either temporal or spectral frequencies, which produced either the spectral (sMTF) or temporal (tMTF) modulation transfer function, respectively (Fig. 4C,D). From these MTFs we estimated their best modulation frequencies.

For pairs of neurons, the best temporal modulation frequency (bTMF) was moderately correlated (Fig. 4E). The mean bTMF across all neurons was 12.3 ± 0.17 Hz. Neurons in a local pair had bTMFs that were within a few Hz of each other (Fig. 4F; Population bTMF difference: $P_D = 2.91 \pm 0.12$ Hz). Across the population, bTMF differences of local pairs were ~22% smaller than for unpaired neurons (Fig. 4G, black bars; $P_R = 3.72 \pm 0.07$ Hz; $p < 0.001$, rank-sum test). A significant difference was also evident for the infragranular layers alone (Fig. 4G; $p < 0.001$), but not for the granular and supragranular layers. Supragranular pairs had the smallest bTMF differences, with increasing differences in infragranular and granular layers (Supra: 2.16 ± 0.35 Hz; Infra: 2.95 ± 0.17 Hz; Gran: 3.27 ± 0.23 Hz), and were significantly smaller than the other layers (Fig. 4G; Supra vs. Gran: $p = 0.016$; Supra vs. Infra: $p = 0.024$; Gran vs. Infra: $p = 0.62$, t-tests). Therefore, local pairs of neurons have similar temporal modulation preferences with the most similar bTMFs in supragranular layers.

Best spectral modulation frequencies (bSMFs) of paired neurons were tightly centered around the unity relationship (Fig. 4H). Average bSMF values were 0.85 ± 0.02 cyc/oct, and differences were modest for the majority of paired neurons (Population bSMF difference: $P_D = 0.26 \pm 0.01$ cyc/oct), but still significantly smaller (~33%) than for unpaired neurons

(Fig. 4J; $P_R = 0.39 \pm 0.01$; black bars; $p < 0.001$, rank-sum test). A similar, significant difference was seen for infragranular pairs alone, but not for supragranular and not for granular layers. sMTF differences for the layers were not significant (Fig. 4I,J; Supra: 0.21 ± 0.01 cyc/oct; Gran: 0.25 ± 0.02 cyc/oct; Infra: 0.29 ± 0.02 cyc/oct; Supra vs. Gran: $p = 0.90$; Supra vs. Infra: $p = 0.44$; Gran vs. Infra: $p = 0.15$, Rank-Sum tests). Thus, neurons within fine-scale functional networks have closely matched temporal and, especially, spectral modulation preferences.

3.4. Local Microarchitecture of Joint Neuron Receptive Field Properties

Since local neurons often fire synchronously (Atencio and Schreiner, 2013), we examined in more detail the functional conditions under which synchronous spikes occurred.

Synchronous spikes result from stimuli that drive both constituent neurons in a pair to respond in a concerted manner (Fig. 5A). Therefore, synchronous spikes may signal important stimulus-specific information that is not conveyed by the average responses of each individual neuron.

To understand the stimulus features that drive correlated firing, we characterized the stimuli that resulted in synchronous spiking. All receptive field analyses that may be performed for the individual neurons in a pair may be performed for the stimuli that precede synchronous spikes. To differentiate the spikes of individual neurons from synchronous spikes, we term the data corresponding to synchronous spikes the “Bicellular” data.

We first inquired into the relative frequency of synchronous spikes, the Bicellular firing rate. We then found the firing rates of the individual neurons in the pair. By comparing the firing rate of each neuron to the Bicellular rate, we formed two distributions, “Matched” and “Non-Matched.” The firing rate of the neuron in the pair that was nearest the Bicellular firing rate was included in the “Matched” data distribution. The value of the other neuron in the pair was placed in the “Non-Matched” distribution. As expected, the Bicellular firing rate was always less than the rate for the Matched data (Fig. 5B; Match: 3.46 ± 0.13 ; Bicellular: 0.77 ± 0.06 sp/s).

Synchronous spikes represent the correlated firing between pairs of neurons. However, the synchronous spikes do not represent all correlated firing – only the firing in a small time window around the peak in the cross-covariance function. On average, the number of synchronous spikes was much less than the total number of spikes in the cross-covariance function (Fig. 5C; $13.8 \pm 0.4\%$). Previously, we found that although synchronized spikes accounted only for a small proportion of the spikes in the cross-covariance function, they coded for up to twice the information of the spikes in the individual neuron spike trains (Atencio and Schreiner, 2013). Hence, we sought to determine the stimulus characteristics that led to these information bearing, synchronous spikes.

For each spike train (one for each neuron in a pair and one for the Bicellular spikes), we estimated the STRF, and then we determined the similarity of the Bicellular STRF to the STRFs of the individual neurons. STRF similarity varied over a wide range, from having the individual STRFs highly correlated with the Bicellular STRF (Fig. 6A), to having more moderate STRF correlations (Fig. 6B). To compare values over the population, for each pair

of neurons we identified the STRF that was most similar to the Bicellular STRF; this STRF represented the closest match in stimulus processing between the individual neuron spikes and the synchronized spikes (Fig. 6C). Over the population, the STRF similarity was moderate (0.46 ± 0.02). When examined by layers, granular (0.45 ± 0.01) and supragranular (0.48 ± 0.03) layers had Bicellular STRFs that most closely matched the constituent STRFs. Infragranular layers had the least similar STRFs (0.41 ± 0.01). However, across layers, the distributions did not significantly differ (Supra vs. Gran: $p = 0.7$; Supra vs. Infra: $p = 0.07$; Gran vs. Infra: $p = 0.057$; Rank-Sum tests). Therefore, these results imply that synchronous spikes signal special stimulus information, since Bicellular STRFs moderately diverge from constituent neuron STRFs.

For the individual and Bicellular STRFs (Fig. 7A), we estimated ripple transfer functions (RTFs, Fig. 7B). We found that Bicellular RTFs, compared to the RTFs from the individual neurons, could have more energy at higher temporal and spectral modulation frequencies (Fig. 7B). Compared to the constituent neurons, the Bicellular tMTF was shifted toward higher frequencies, indicating that synchronous spikes signal slightly faster temporal modulations (Fig. 7C). The peak in the Bicellular sMTF was also shifted to higher values (Fig. 7D), indicating that more narrowly spaced spectral modulations may be more effective in driving synchronous spiking.

We compared the Bicellular MTF parameters to the parameters from the constituent pair of neurons. Since there are two individual neuron values, and only one Bicellular value, we made conservative comparisons by comparing the best modulation frequencies (BMFs) of constituent neurons to the Bicellular BMF. The value in each pair that was most similar to the Bicellular BMF we placed in a “Matched” distribution. Comparing the Bicellular values to the Matched values provides a lower bound on the difference between the two distributions.

Across the population, Bicellular bTMFs were significantly higher than those of the Matched data (Fig. 8A; Bicellular: 14.5 ± 0.2 Hz; Matched: 12.5 ± 0.2 Hz; $p < 0.001$, Rank-Sum test). While this trend was present in each layer, we found significant differences in Granular layers (Fig. 8C; Bicellular: 15.5 ± 0.5 Hz; Matched: 13.4 ± 0.4 Hz; $p = 0.0034$, Rank-Sum test) and Infragranular layers (Fig. 8D; Bicellular: 14.2 ± 0.3 Hz; Matched: 12.2 ± 0.3 Hz; $p < 0.001$, Rank-Sum test), but not in Supragranular layers (Fig. 8B; Bicellular: 11.3 ± 0.8 Hz; Matched: 9.6 ± 0.5 Hz; $p = 0.23$, Rank-Sum test). Therefore, Bicellular bTMFs are significantly higher than those of the individual neurons that generated the synchronized spikes. Further, since the Bicellular STRFs result from synchronous spikes, the subset of stimuli that induce synchrony in AI local subnetworks do so by having higher temporal modulations than the average stimulus that induces a spike in either neuron alone.

Spectral modulation processing followed a similar trend: Bicellular bSMFs exceeded those in the Matched population. Bicellular STRFs had higher bSMFs than the average preferred stimulus feature in either neuron (Fig. 8E; Bicellular: 1.07 ± 0.03 ; Matched: 0.85 ± 0.03 cyc/oct; $p = 0.0002$, Rank-Sum test). The laminar distributions also trended toward higher bSMFs in each layer, though only significantly in Infragranular layers (Fig. 8H; Bicellular: 1.02 ± 0.05 cyc/oct; Matched: 0.83 ± 0.04 cyc/oct; $p = 0.0116$, Rank-Sum test). Granular layer

data showed the next strongest trend (Fig. 8G; Bicellular: 1.12 ± 0.08 ; Matched: 0.85 ± 0.05 cyc/oct; $p = 0.0556$, Rank-Sum test), followed by Supragranular data, which had the weakest trend (Fig. 8F; Bicellular: 1.33 ± 0.17 ; Matched: 1.09 ± 0.09 cyc/oct; $p = 0.4648$, Rank-Sum test). These population and laminar results mirror those for bTMFs, implying that the stimuli that evoke synchronous spikes contain higher modulations, i.e., more narrowly spaced spectral peaks, than the average stimulus that drives the spiking of either of the individual neurons.

3.5. Local Microarchitecture of Individual and Joint Neuron Input/Output Functions

The STRF describes the stimulus preferences of a neuron. By itself the STRF is an incomplete model of neural signal processing, since it does not relate how a response is generated. An additional measure that relates the stimulus to the magnitude of the spiking output is the nonlinearity (Atencio et al., 2008). It describes how stimulus-STRF correlations are translated into a response and can be used to characterize the stimulus selectivity of auditory neurons. It can also be used to characterize the selectivity of synchronous spikes. The nonlinearity, therefore, allows us to determine if the stimulus selectivity of pairs of neurons is similar, and also if synchronous spikes are generated in a similar manner to those of non-synchronous spikes.

To construct nonlinearities, we first computed the projection, or inner product, between each stimulus and the STRF (Fig. 9A). Each projection value represents the similarity between the stimulus and the STRF at a specified time. Positive projection values indicate that the STRF and the stimulus were positively correlated; negative values indicate anti-correlation. Next, the projection values for all stimuli (Fig. 9B), and for those that preceded a spike (Fig. 9D), were grouped into separate distributions, normalized (Fig. 9C,E), and binned (Fig. 9F). The ratio between the two binned distributions is proportional to the nonlinearity (Fig. 9F).

We parametrically described neuronal and Bicellular nonlinearities (Fig. 10) using a fitting process (see Methods). The fitted function had two main parameters: Theta, which describes the threshold of the response, and Sigma, which describes the smoothness of the transition point. A large Theta value, which corresponds to a high threshold, indicates that the neuron does not respond until the stimulus and the STRF are highly correlated (Fig. 10F). Sigma values near 0 indicate hard rectification (Fig. 10B,D,F).

For individual pairs, there could be significant variability with respect to the nonlinearity threshold or the nonlinearity transition. For pairs of neurons, thresholds were only moderately correlated (Fig. 11A; $r = 0.34$, $p < 0.001$, t-test). For the population, threshold differences for paired neurons were significantly smaller (~27%) than for unpaired neurons (Fig. 11C, black bars; $P_D = 1.48 \pm 0.07$; $P_R = 2.04 \pm 0.06$; $p < 0.001$, rank-sum test). A similar difference was seen for infragranular layers alone, but supragranular and granular layers were not statistically significant. Across layers, the threshold differences for paired neurons was highest in infragranular layers but only significantly different between granular and infragranular layers (Fig. 11B,C; $p < 0.05$, KS-test).

For nonlinearity transition, there was a higher correlation between the values for paired neurons (Fig. 11D; $r = 0.44$, $p < 0.001$, t-test). When we compared the differences between

transition values for neurons in a pair, we found for the population that the differences were smaller (~40 %) compared to unpaired neurons in the column (Fig. 11F; black bars; $P_D = 0.73 \pm 0.05$; $P_R = 1.20 \pm 0.05$; $p < 0.001$, rank-sum test). Similar differences between paired and unpaired neurons were seen for supra- and infragranular layers (Fig. 11F). Transition differences in supragranular and granular layers were significantly smaller than those in infragranular neuron pairs (Fig. 11D; $p < 0.05$, KS-test). The findings show that neighboring neurons have nonlinearity properties that are better matched than randomly selected neurons from the same layer and column.

We next compared the neural and Bicellular nonlinearity parameters to determine if synchronous spikes process stimulus information different from individual neurons. We first found the nonlinearity parameter for each neuron in a pair that was most similar to the Bicellular parameter, forming a “Matched” distribution. The remaining parameter value was included in the “Non-Matched” distribution.

Bicellular nonlinearities differed from neuron nonlinearities. First, across the population, the Bicellular nonlinearity thresholds exceeded those for the Matched or Non-Matched populations (Fig. 12A; Matched: 1.22 ± 0.09 ; Non-Matched: 0.23 ± 0.11 ; Bicellular: 2.07 ± 0.08 ; Bicellular vs. Matched or Bicellular vs. Non-Matched: $p < 0.001$, Rank-Sum tests). Since the Matched population values were those that were closest to the Bicellular data, this indicates that Bicellular spikes were generated when the STRF and stimulus were highly correlated. Bicellular thresholds were highest in granular and infragranular cortical layers (Fig. 12C,E,G; Gran Match: 1.31 ± 0.15 ; Gran Bicellular: 2.04 ± 0.15 ; $p < 0.001$; Infra Match: 1.00 ± 0.17 ; Infra Bicellular: 2.14 ± 0.14 ; $p < 0.001$, Rank-Sum tests). The Bicellular and Matched distributions were most similar in supragranular layers, though even at superficial depths they were significantly different (Supra Match: 1.49 ± 0.29 ; Supra Bicellular: 2.01 ± 0.28 ; $p = 0.0466$, Rank-Sum test). Therefore, Bicellular events signal conditions of higher correlation between the stimulus and the STRF, implying increased selectivity. Additionally, the Bicellular spikes have a higher nonlinearity threshold, which effectively reduces transmission noise.

The nonlinearity transition parameters also showed significant differences between the Bicellular and Matched data. Transition values that approach zero characterize hard rectification, while those that deviate from zero imply a noisier, more graded response to acoustic signals. Over the population, the Bicellular transition was significantly lower (Fig. 12B; Match: 1.35 ± 0.05 ; Bicellular: 0.81 ± 0.07 ; $p < 0.001$, Rank-Sum test), implying that Bicellular nonlinearities signal information in a more rectified manner. This trend was present in each cortical layer; Bicellular values were always smaller than the Matched values. Across layers, transition values were also significantly different: Supragranular (Fig. 12D,F,H; Match: 1.09 ± 0.08 ; Bicellular: 0.68 ± 0.14 , $p = 0.0009$), Granular (Match: 1.28 ± 0.09 ; Bicellular: 0.75 ± 0.09 , $p < 0.0001$), and Infragranular (Match: 1.57 ± 0.09 ; Bicellular: 0.96 ± 0.15 ; $p < 0.0001$, Rank-Sum tests). Together, the threshold and transition values imply that Bicellular spikes signal acoustic information that exceeds background stimulation levels, and that, once the response threshold is reached, the spike is transmitted with high fidelity.

4. DISCUSSION

Our main goal in this study was to assess functional relationships within the elements of local circuits in AI. We showed that nearby neurons ($\sim <150\ \mu\text{m}$ separation) have more similar receptive field properties than predicted by the variance of random neurons within the column. We showed that nearby neurons had STRF parameters that were well correlated, with BF the most highly conserved parameter (Atencio and Schreiner, 2013). Local circuits also contained neurons with similar firing rates, modulation preferences, and nonlinearity structure. The high incidence of local functional congruity reflects the strong interconnectivity of local neurons: nearby neurons have higher probabilities of being anatomically connected (Boucsein et al., 2011).

4.1. Laminar Differences

Pairs of neurons in supragranular layers had the most similar receptive field properties, while pairs in infragranular layers had greater differences. In supragranular layers, pairs had the smallest differences between BF, STRF structure, modulation preferences, and nonlinearity similarity, while pairs in infragranular layers had the largest differences. For supragranular layers, smaller differences may result from the precise corticocortical connection patterns within AI and between cortical fields (Lee and Winer, 2005). Within AI, topographic projection are precise between matching spectral tuning modules (Read et al., 2001). Additionally, inter-field connections are specific, even when the fields do not have a clear tonotopic representation (Lee and Winer, 2008b). Hence, the small supragranular parameter differences may reflect a decreased variance of cortical connections.

In contrast, the greater parameter differences in infragranular layers may reflect the more diverse set of projections and neurons at those depths. Infragranular layers have a much broader range of targets than neurons in supragranular layers. Infragranular layers send projections to intra- and inter-hemispheric cortical fields (Lee and Winer, 2008a), to the thalamus (Winer et al., 2001, Winer, 2005), to the midbrain (Winer et al., 1998, Winer et al., 2002), to the superior olivary complex (Coomes and Schofield, 2004), and even to the cochlear nucleus (Schofield and Coomes, 2005, Schofield et al., 2006). These projections may have to fulfill different requirements to achieve their functional purposes. Additionally, lower layers contain a more diverse population of cell types, such as the multiplicity of pyramidal neurons or the diverse group of inhibitory interneurons (Games and Winer, 1988, Prieto and Winer, 1999, Winer and Prieto, 2001, Yuan et al., 2011). Therefore, the parameter differences in each layer likely reflect each layer's unique cellular composition and output projection patterns.

4.2. Bicellular gain

Another main goal of this study was to determine whether the functional properties of network events, defined as synchronous activity of local neurons, differ from the functional preference of the individual neurons. We had demonstrated the existence of sharply synchronous events previously in our previous study (Atencio and Schreiner, 2013). Here we not only identify Bicellular events, but we also characterize the stimulus properties and information that they represent. Bicellular spikes are a subset of the spikes of both neurons

in a pair and can be interpreted as the expression of the most elementary neural ensemble. If Bicellular spikes were simply a sample from both spike trains, then the stimulus information they represent would be similar to the information gained from each individual spike train of the constituent neurons. We found, however, that for most parameters, Bicellular spikes signaled information regarding stimulus properties and processing capacity that subtly but significantly differed from the individual neurons. STRFs derived from Bicellular spikes had higher modulation content, higher nonlinearity thresholds, and lower nonlinearity transition noise (Fig. 13A-D). Additionally, as earlier reported we also found that Bicellular spikes carried greater stimulus information compared to the spikes of the neurons in a pair (Fig. 13E). The STRF parameter differences for Bicellular events are robust since we made the most conservative assessment by comparing them to the value of the constituent neuron that was most similar. This is a more conservative test than comparing against the mean of the two values for each pair, and yet the Bicellular values were still significantly different from the Matched comparison distributions emphasizing the robustness of the effect.

Bicellular spiking events, then, indicate special stimulus configurations that reflect network activity. Though we were limited to examining local pairs of neurons, Bicellular spikes are likely part of the activity within larger networks. Such larger network events have been identified for synfire chains or for “cell assemblies” (Schrader et al., 2008, Huyck and Passmore, 2013, Palm et al., 2014). In either case, network activity leads to synchronized spiking events across populations of neurons that may be directly connected or indirectly coupled. Bicellular spiking events appear not to be a faithful reflection of the functional preferences of the individual neurons. Their enhanced functional specificity may be a reflection of more global population responses. Therefore, Bicellular spikes are likely triggered by specific stimuli, constitute subsets of larger networks, and convey stimulus information with great fidelity to later processing stages.

Bicellular nonlinearity properties reflect the increased information capacity of Bicellular spikes. Therefore, compared to non-synchronous spikes, Bicellular spikes contain more information about the stimulus that elicited them. The increased information is reflected in two ways. First, the increased threshold of Bicellular nonlinearities shows that there must be a significant match between a stimulus and the Bicellular STRF before a Bicellular spike is emitted, thus reducing noise. Second, the decrease in nonlinearity transition noise indicates that once the threshold is reached, spiking occurs with high reliability. Threshold and transition, then, are consistent with an increased information coding capacity of Bicellular events.

Further, the shifts in modulation frequency for Bicellular STRFs are a likely reflection of neural ensemble coding. Any given neuron may be involved in multiple neuronal ensembles. Thus, the spike train of a neuron contains spikes that are associated with different neuronal ensembles. These combined spikes produce an STRF that will have a lower signal-to-noise ratio than the STRF from the spikes of a single neuronal ensemble. Our approach allowed us to examine the smallest neuronal ensemble, a pair of neurons, and determine receptive field information from this Bicellular STRF. Because the Bicellular STRF is less subject to estimation errors, the obtained modulation frequency is increased.

4.3. Comparisons to earlier work in the cat

Previous work in the cat has focused on large scale organization, such as the spatial distribution of response preferences across cortical fields. One exception is the study of spectral tuning modules in AI. Earlier experiments found that the broad multi-unit tuning of ventral neurons might be the result of local CF scatter in single units (Schreiner and Sutter, 1992).

Our previous results (Atencio and Schreiner, 2013) can be reconciled with this earlier work. We reported that spectral tuning can moderately vary for neighboring neurons, which is consistent with the dissimilar tuning curves seen in cat ventral AI. Our strongest result, however, is that BFs in a column are highly similar throughout AI. Two main possibilities may explain the discrepancy between our report and the earlier study in ventral AI: (1) We estimated BF using dynamic broadband stimuli presented at moderate levels, while the earlier report estimated CF from tones at threshold; and (2) we recorded from primary auditory cortex, while the previous report may have included recordings from the second auditory field, AII. It is challenging to estimate CF from AII cells, since the boundary between ventral AI and AII must be carefully established, and since AII does not have a clear frequency organization (Schreiner and Cynader, 1984).

4.4. Comparisons between mouse and cat auditory cortex

Our results showed that best frequency was highly conserved among nearby neurons. In mouse AI, a global scale tonotopy in middle layers has been reported (Stiebler et al., 1997, Guo et al., 2012). Recent two-photon work has also shown that clear tonotopy is present in middle layers (Winkowski and Kanold, 2013). In supragranular layers, in contrast, two-photon techniques found that neighboring neurons may have widely varying BFs (Bandyopadhyay et al., 2010, Rothschild et al., 2010).

This suggests that mouse and cat cortical organization diverge: mouse auditory cortex contains a fractured tonotopy while cats have a more continuous map with a smooth gradient. Circuitry differences may provide one explanation: preliminary analyses showed that there are differences between the microcircuitry and interlaminar connection patterns in mouse and cat (Mitani et al., 1985, Oviedo et al., 2010). This divergence between cat and rodent does not appear to be restricted to AI, since two-photon imaging in V1 revealed similar results: cat V1 contains local networks with precisely ordered orientation preferences (Ohki et al., 2005) whereas, in rat, neurons had dissimilar orientation preferences, indicating significant species differences (Ohki et al., 2005, Ohki and Reid, 2007).

However, a recent two-photon study by Issa and colleagues (2014) demonstrated both global and local tonotopy within the mouse. By focusing at depths 150-430 microns below the cortical surface, with most neurons in layers 2/3, they found that nearby neurons had similar CFs, and that single neuron CFs were registered to the global AI tonotopy (Issa et al., 2014). Therefore, these results point to a micro-tonotopic organization in the mouse. Clearly, further comparative work is required to delineate these issues and evaluate alternate hypotheses.

5. CONCLUSIONS

Local subnetworks in cat AI contain cells that share highly similar best frequency. Other aspects of STRFs, such as modulation preference, response precision, and input/output function characteristics are also more similar than predicted by random sampling within individual layers. Across cortical layers, cat local networks contained synchronously firing neurons that displayed small to moderate differences in functional similarity. The largest parameter differences were found in infragranular layers. When considering synchronous spiking, the receptive field characteristics represented by Bicellular spiking differed from the most closely-matched constituent neuron. These differences were present in each layer and the magnitude of the differences was similar across layers. Therefore, Bicellular, and in extension multicellular, network activity throughout the cortical column appears to reduce variability, increase feature selectivity, and decrease information processing noise, which enables more precise information transmission over an expanded range of temporal and spectral modulation frequencies. Since Bicellular spikes represent events from the smallest neural ensemble, they represent a baseline to compare population receptive field processing. Further, the unique processing indicated by local two-neuron ensembles indicates that larger neural ensembles may further enhance information specificity and response reliability throughout the auditory cortex.

Acknowledgements

This work was supported by National Institutes of Health grants DC02260, DC011874, the Coleman Memorial Fund, and by Hearing Research Inc. (San Francisco, CA).

REFERENCES

- Atencio CA, Schreiner CE. Columnar connectivity and laminar processing in cat primary auditory cortex. *PLoS One*. 2010a; 5:e9521. [PubMed: 20209092]
- Atencio CA, Schreiner CE. Laminar diversity of dynamic sound processing in cat primary auditory cortex. *J Neurophysiol*. 2010b; 103:192–205. [PubMed: 19864440]
- Atencio CA, Schreiner CE. Spectrotemporal processing in spectral tuning modules of cat primary auditory cortex. *PLoS One*. 2012; 7:e31537. [PubMed: 22384036]
- Atencio CA, Schreiner CE. Auditory cortical local subnetworks are characterized by sharply synchronous activity. *J Neurosci*. 2013; 33:18503–18514. [PubMed: 24259573]
- Atencio CA, Sharpee TO, Schreiner CE. Cooperative nonlinearities in auditory cortical neurons. *Neuron*. 2008; 58:956–966. [PubMed: 18579084]
- Atencio CA, Sharpee TO, Schreiner CE. Hierarchical computation in the canonical auditory cortical circuit. *Proc Natl Acad Sci USA*. 2009; 106:21894–21899. [PubMed: 19918079]
- Atencio CA, Sharpee TO, Schreiner CE. Receptive field dimensionality increases from the auditory midbrain to cortex. *J Neurophysiol*. 2012; 107:2594–2603. [PubMed: 22323634]
- Bandyopadhyay S, Shamma SA, Kanold PO. Dichotomy of functional organization in the mouse auditory cortex. *Nat Neurosci*. 2010; 13:361–368. [PubMed: 20118924]
- Barbour DL, Callaway EM. Excitatory local connections of superficial neurons in rat auditory cortex. *J Neurosci*. 2008; 28:11174–11185. [PubMed: 18971460]
- Boucsein C, Nawrot MP, Schnepel P, Aertsen A. Beyond the cortical column: abundance and physiology of horizontal connections imply a strong role for inputs from the surround. *Front Neurosci*. 2011; 5:32. [PubMed: 21503145]
- Chen X, Leischner U, Rochefort NL, Nelken I, Konnerth A. Functional mapping of single spines in cortical neurons in vivo. *Nature*. 2011; 475:501–505. [PubMed: 21706031]

- Coomes DL, Schofield BR. Projections from the auditory cortex to the superior olivary complex in guinea pigs. *Eur J Neurosci*. 2004; 19:2188–2200. [PubMed: 15090045]
- Defelipe, J. *Biological and Artificial Computation: From Neuroscience to Technology*. Vol. 1240. Springer-Verlag; Berlin: 1997. Microcircuits in the brain; p. 1-14.
- Douglas RJ, Martin KA. Neuronal circuits of the neocortex. *Annu Rev Neurosci*. 2004; 27:419–451. [PubMed: 15217339]
- Drullman R, Festen JM, Houtgast T. Effect of temporal modulation reduction on spectral contrasts in speech. *J Acoust Soc Am*. 1996; 99:2358–2364. [PubMed: 8730082]
- Escabí MA, Schreiner CE. Nonlinear spectrotemporal sound analysis by neurons in the auditory midbrain. *J Neurosci*. 2002; 22:4114–4131. [PubMed: 12019330]
- Games KD, Winer JA. Layer V in rat auditory cortex: projections to the inferior colliculus and contralateral cortex. *Hear Res*. 1988; 34:1–25. [PubMed: 3403382]
- Guo W, Chambers AR, Darrow KN, Hancock KE, Shinn-Cunningham BG, Polley DB. Robustness of cortical topography across fields, laminae, anesthetic states, and neurophysiological signal types. *J Neurosci*. 2012; 32:9159–9172. [PubMed: 22764225]
- Halliday, DM.; Rosenberg, JR. Time and frequency domain analysis of spike train and time series data. In: Windhorst, U.; Johansson, H., editors. *Modern Techniques in Neuroscience Research*. Springer; New York: 1999. p. 503-543.
- Hansel D, van Vreeswijk C. How noise contributes to contrast invariance of orientation tuning in cat visual cortex. *J Neurosci*. 2002; 22:5118–5128. [PubMed: 12077207]
- Holmgren C, Harkany T, Svennenfors B, Zilberter Y. Pyramidal cell communication within local networks in layer 2/3 of rat neocortex. *J Physiol*. 2003; 551:139–153. [PubMed: 12813147]
- Huyck CR, Passmore PJ. A review of cell assemblies. *Biol Cybern*. 2013; 107:263–288. [PubMed: 23559034]
- Imaizumi K, Schreiner CE. Spatial interaction between spectral integration and frequency gradient in primary auditory cortex. *J Neurophysiol*. 2007; 98:2933–2942. [PubMed: 17855587]
- Issa JB, Haeffele BD, Agarwal A, Bergles DE, Young ED, Yue DT. Multiscale optical Ca²⁺ imaging of tonal organization in mouse auditory cortex. *Neuron*. 2014; 83:944–959. [PubMed: 25088366]
- Kanold PO, Nelken I, Polley DB. Local versus global scales of organization in auditory cortex. *Trends Neurosci*. 2014; 37:502–510. [PubMed: 25002236]
- Krause BM, Raz A, Uhlrich DJ, Smith PH, Banks MI. Spiking in auditory cortex following thalamic stimulation is dominated by cortical network activity. *Frontiers in systems neuroscience*. 2014; 8:170. [PubMed: 25285071]
- Lee CC, Winer JA. Principles governing auditory cortex connections. *Cereb Cortex*. 2005; 15:1804–1814. [PubMed: 15800026]
- Lee CC, Winer JA. Connections of cat auditory cortex: II. Commissural system. *J Comp Neurol*. 2008a; 507:1901–1919. [PubMed: 18271027]
- Lee CC, Winer JA. Connections of cat auditory cortex: III. Corticocortical system. *J Comp Neurol*. 2008b; 507:1920–1943. [PubMed: 18271030]
- Lee, CC.; Winer, JA. A synthesis of auditory cortical connections: thalamocortical, commissural and corticocortical systems. In: Winer, JA.; Schreiner, CE., editors. *The Auditory Cortex*. Springer; New York: 2011. p. 147-170.
- Lewicki MS. Bayesian modeling and classification of neural signals. *Neural Comput*. 1994; 6:1005–1030.
- Lewicki MS. A review of methods for spike sorting: the detection and classification of neural action potentials. *Network*. 1998; 9:R53–78. [PubMed: 10221571]
- Miller KD, Troyer TW. Neural noise can explain expansive, power-law nonlinearities in neural response functions. *J Neurophysiol*. 2002; 87:653–659. [PubMed: 11826034]
- Mitani A, Shimokouchi M. Neuronal connections in the primary auditory cortex: an electrophysiological study in the cat. *J Comp Neurol*. 1985; 235:417–429. [PubMed: 2987316]
- Mitani A, Shimokouchi M, Itoh K, Nomura S, Kudo M, Mizuno N. Morphology and laminar organization of electrophysiologically identified neurons in the primary auditory cortex in the cat. *J Comp Neurol*. 1985; 235:430–447. [PubMed: 3998218]

- Ohki K, Chung S, Ch'ng YH, Kara P, Reid RC. Functional imaging with cellular resolution reveals precise micro-architecture in visual cortex. *Nature*. 2005; 433:597–603. [PubMed: 15660108]
- Ohki K, Reid RC. Specificity and randomness in the visual cortex. *Curr Opin Neurobiol*. 2007; 17:401–407. [PubMed: 17720489]
- Oswald AM, Reyes AD. Maturation of intrinsic and synaptic properties of layer 2/3 pyramidal neurons in mouse auditory cortex. *J Neurophysiol*. 2008; 99:2998–3008. [PubMed: 18417631]
- Otsuka T, Kawaguchi Y. Cortical inhibitory cell types differentially form intralaminar and interlaminar subnetworks with excitatory neurons. *J Neurosci*. 2009; 29:10533–10540. [PubMed: 19710306]
- Oviedo HV, Bureau I, Svoboda K, Zador AM. The functional asymmetry of auditory cortex is reflected in the organization of local cortical circuits. *Nat Neurosci*. 2010; 13:1413–1420. [PubMed: 20953193]
- Palm G, Knoblauch A, Hauser F, Schuz A. Cell assemblies in the cerebral cortex. *Biol Cybern*. 2014; 108:559–572. [PubMed: 24692024]
- Peyrache A, Dehghani N, Eskandar EN, Madsen JR, Anderson WS, Donoghue JA, Hochberg LR, Halgren E, Cash SS, Destexhe A. Spatiotemporal dynamics of neocortical excitation and inhibition during human sleep. *Proc Natl Acad Sci U S A*. 2012; 109:1731–1736. [PubMed: 22307639]
- Prieto JJ, Winer JA. Layer VI in cat primary auditory cortex: Golgi study and sublamina origins of projection neurons. *J Comp Neurol*. 1999; 404:332–358. [PubMed: 9952352]
- Read HL, Winer JA, Schreiner CE. Modular organization of intrinsic connections associated with spectral tuning in cat auditory cortex. *Proc Natl Acad Sci U S A*. 2001; 98:8042–8047. [PubMed: 11438747]
- Rosenberg JR, Amjad AM, Breeze P, Brillinger DR, Halliday DM. The Fourier Approach to the Identification of Functional Coupling between Neuronal Spike Trains. *Progress in Biophysics & Molecular Biology*. 1989; 53:1–31. [PubMed: 2682781]
- Rothschild G, Nelken I, Mizrahi A. Functional organization and population dynamics in the mouse primary auditory cortex. *Nat Neurosci*. 2010; 13:353–360. [PubMed: 20118927]
- Sakata S, Harris KD. Laminar structure of spontaneous and sensory-evoked population activity in auditory cortex. *Neuron*. 2009; 64:404–418. [PubMed: 19914188]
- Schofield BR, Coomes DL. Projections from auditory cortex contact cells in the cochlear nucleus that project to the inferior colliculus. *Hear Res*. 2005; 206:3–11. [PubMed: 16080994]
- Schofield BR, Coomes DL, Schofield RM. Cells in auditory cortex that project to the cochlear nucleus in guinea pigs. *J Assoc Res Otolaryngol*. 2006; 7:95–109. [PubMed: 16557424]
- Schrader S, Grun S, Diesmann M, Gerstein GL. Detecting synfire chain activity using massively parallel spike train recording. *J Neurophysiol*. 2008; 100:2165–2176. [PubMed: 18632888]
- Schreiner CE, Cynader MS. Basic functional organization of second auditory cortical field (AII) of the cat. *J Neurophysiol*. 1984; 51:1284–1305. [PubMed: 6737031]
- Schreiner CE, Sutter ML. Topography of excitatory bandwidth in cat primary auditory cortex: single-neuron versus multiple-neuron recordings. *J Neurophysiol*. 1992; 68:1487–1502. [PubMed: 1479426]
- Shannon RV, Zeng FG, Kamath V, Wygonski J, Ekelid M. Speech recognition with primarily temporal cues. *Science*. 1995; 270:303–304. [PubMed: 7569981]
- Silberberg G, Gupta A, Markram H. Stereotypy in neocortical microcircuits. *Trends Neurosci*. 2002; 25:227–230. [PubMed: 11972952]
- Stiebler I, Neulist R, Fichtel I, Ehret G. The auditory cortex of the house mouse: left-right differences, tonotopic organization and quantitative analysis of frequency representation. *Journal of Comparative Physiology a-Sensory Neural and Behavioral Physiology*. 1997; 181:559–571.
- Thomson AM, West DC, Wang Y, Bannister AP. Synaptic connections and small circuits involving excitatory and inhibitory neurons in layers 2-5 of adult rat and cat neocortex: triple intracellular recordings and biocytin labelling in vitro. *Cereb Cortex*. 2002; 12:936–953. [PubMed: 12183393]
- Winer JA. Decoding the auditory corticofugal systems. *Hear Res*. 2005; 207:1–9. [PubMed: 16091301]
- Winer, JA. A Profile of Auditory Forebrain Connections and Circuits. In: Winer, JA.; Schreiner, CE., editors. *The Auditory Cortex*. Springer; New York: 2011. p. 41-74.

- Winer JA, Chernock ML, Larue DT, Cheung SW. Descending projections to the inferior colliculus from the posterior thalamus and the auditory cortex in rat, cat, and monkey. *Hear Res.* 2002; 168:181–195. [PubMed: 12117520]
- Winer JA, Diehl JJ, Larue DT. Projections of auditory cortex to the medial geniculate body of the cat. *J Comp Neurol.* 2001; 430:27–55. [PubMed: 11135244]
- Winer JA, Larue DT, Diehl JJ, Hefti BJ. Auditory cortical projections to the cat inferior colliculus. *J Comp Neurol.* 1998; 400:147–174. [PubMed: 9766397]
- Winer JA, Prieto JJ. Layer V in cat primary auditory cortex (AI): cellular architecture and identification of projection neurons. *J Comp Neurol.* 2001; 434:379–412. [PubMed: 11343289]
- Winkowski DE, Kanold PO. Laminar transformation of frequency organization in auditory cortex. *J Neurosci.* 2013; 33:1498–1508. [PubMed: 23345224]
- Yuan K, Shih JY, Winer JA, Schreiner CE. Functional networks of parvalbuminimmunoreactive neurons in cat auditory cortex. *J Neurosci.* 2011; 31:13333–13342. [PubMed: 21917816]

Highlights

- Local neuron pair receptive fields were more similar than non-paired neurons
- Similarities were greater for rate, modulation processing, and nonlinearity
- Receptive field similarities were layer-dependent
- Synchronous spikes conveyed enhanced receptive field and nonlinearity properties
- Synchronous spikes transmitted stimulus information with high precision

Figure 1.

Spike waveforms, functional connectivity, and spectrotemporal receptive fields (STRFs) for a pair of neurons. (A) Spike waveforms for two neurons recorded from the same electrode channel. (B) Spike waveforms and recording trace. Non-standard events, resulting from overlapping spike waveforms, can be associated with individual spike waveforms by shifting each spike waveform in time and comparing the sum of the waveforms (black) to the recording trace (gray). (C) Cross-correlation (or correlogram) for the two neurons, showing a central peak, indicating synchronous firing. (D) Cross-covariance function derived from the cross-correlation function. Red lines indicate 99% confidence limits. Ordinate = 0 represents baseline coincidences. Deviations from the baseline represent facilitative or suppressive interactions. (E) STRFs for the two neurons, revealing moderate receptive field similarity. Color of STRF title corresponds to color of labelled neurons in (A,B).

Figure 2.

Functional connectivity, receptive field overlap, and stimulus statistics analysis for a pair of recorded neurons. (A) Dynamic moving ripple (DMR) spectrotemporal envelope. (B) STRF for one neuron in the pair. Line indicates a slice through the STRF at the best frequency. (C) STRF for the second neuron in the pair. (D,E) STRF slices from (B,C). (F) Correlation between STRF slices compared to cross-covariance function. The correlation of STRF slices indicates the temporal overlap between receptive fields. The neural functional connectivity is much sharper in time. (G-L) Same analysis as (A-F), except in response to a Ripple Noise (RN) stimulus, which has no spectrotemporal correlations. (L) STRF correlation is broader than functional connectivity for Ripple Noise. Functional connectivity in (F) and (L) is similar despite the dissimilar stimulus statistics. (M) Stimulus correlation compared to neural functional connectivity. The temporal stimulus autocorrelation was calculated when the DMR envelope had temporal modulation frequencies of 5, 10, 20, and 40 Hz and the spectral modulation frequency was 0 cyc/oct. In all cases, synchronous spiking was much sharper than stimulus correlation.

Figure 3.

Response properties of pairs of neurons. (A) Firing rate comparison for pairs of neurons. Each point represents one pair of neurons; points are labelled according to significant (Sync) and non-significant (UnSync) functional connectivity. (B) Firing rate differences over the population of pairs and across layers. (C) Response Precision Index (RPI) for pairs. (D) RPI differences over the population of pairs and across layer. P_D, S_D, G_D , and I_D denote Population (P), Supragranular (S), Granular (G), and Infragranular (I) pairwise differences for neurons recorded from the same electrode channel (D = data). P_R, S_R, G_R , and I_R pairwise differences obtained through the random pairwise sampling procedure (R = random).

Figure 4.

Modulation processing in local circuits. (A-D) Example neuron. (A) STRF for the neuron. (B) Ripple transfer function (RTF) of the STRF. The RTF describes the temporal and spectral modulation frequency (TMF, SMF) content in the STRF. (C) Temporal modulation transfer function for the neuron, obtained by summing the RTF across spectral modulation frequency. (D) Spectral modulation transfer function, obtained by summing the RTF across temporal modulation frequency. (E) Best temporal modulation frequency (bTMTF) for each pair of neurons. Each point represents one pair of neurons; points are labelled according to significant (Sync) and non-significant (UnSync) functional connectivity. (F) bTMTF differences between neuron pairs across the population and layers. (G) Mean bTMTF differences. (H) Best spectral modulation frequency (bSMF) comparison for each pair of neurons. (I) bSMF differences between neuron pairs across the population and layers. (J) Mean bSMF differences. P_D, S_D, G_D , and I_D represent Population (P), Supragranular (S), Granular (G), and Infragranular (I) pairwise data differences, while P_R, S_R, G_R , and I_R represent pairwise differences from random pairwise sampling.

Figure 5.

Bicellular response analysis for pairs of neurons. (A) Identifying Bicellular spikes. From the cross-covariance function for each pair of neurons, the time of the peak (PD) and the half-width (HW) of the peak were identified. Bicellular spikes were those spikes that comprised the peak in the cross-covariance function, and fell within the window = [PD – HW, PD + HW]. (B) Firing rate for Bicellular data compared to Matched/NonMatched data. Bicellular data are the spikes in the peak of the cross-covariance function for each significant cross-covariance function. For each pair, the absolute difference between the rate of each neuron in a pair and the Bicellular rate was estimated. Matched data is the firing rate that was most similar to the Bicellular rate; NonMatched data is the rate that was most dissimilar. (C) Synchronous spikes proportion, which is the number of synchronous, or Bicellular spikes, for each pair of neurons compared to the total number of spikes in the cross-covariance function. On average, synchronized spikes account for $13.8 \pm 0.4 \%$ of the spikes in the covariance function.

Figure 6.

Bicellular STRF similarity. (A,B) STRFs for two example pairs of neurons, and corresponding Bicellular STRFs. The similarity between each constituent STRF and the Bicellular STRF is indicated above the Neuron 1 and Neuron 2 STRFs (example: $SI_{1,BC}$ is the similarity between the Neuron 1 STRF and the Bicellular STRF). (C) Maximum STRF similarity between the Bicellular STRF and constituent neuron STRF. The distribution was formed from the STRF similarity that was highest between each constituent neuron and the Bicellular STRF. The STRF similarity that was least similar to the Bicellular STRF was not included in the distribution. Supragranular and granular layers have Bicellular STRFs that are most similar to the individual neuron STRFs, while the Bicellular STRFs become increasingly dissimilar in infragranular layers.

Figure 7.

Bicellular modulation processing example. (A) STRFs for each neuron in the pair, as well as the Bicellular STRF, which is the STRF estimated from synchronized spikes. (B) Ripple Transfer Functions (RTFs) for each STRF. (C) Temporal modulation transfer functions (RTFs summed across spectral modulation frequency (SMF)) for each STRF. (D) Spectral modulation transfer functions (RTFs summed across temporal modulation frequency (TMF)) for each STRF.

Figure 8.

Bicellular best modulation frequency. Each point represents one pair of neurons. For each Bicellular STRF, the best modulation frequency was estimated. The best modulation frequency for each neuron in a pair was estimated, and the value most similar to the Bicellular data was placed in the Matched data distribution. For temporal modulation, across the (A) population, and across (B-D) layers, Bicellular data had higher the best temporal modulation frequencies (bTMFs). (E-H) For best spectral modulation frequency (bSMF), the Bicellular data was higher in granular and infragranular layers.

Figure 9.

Estimating nonlinear input/output functions (nonlinearities). (A) The stimulus is processed by the STRF, resulting in a set of projection values. (B) The projection values for all stimuli are estimated. (D) Projection values for stimuli preceding a spike are separated into a separate distribution. (C,E) The standard deviation of the distribution for all stimuli is used to normalize both distributions, and the resulting distributions are in units of SD. (F) The distributions in (C,E) are then binned, and the ratio between the two binned distributions is proportional to the nonlinearity (red curve, denoted by $F(x)$).

Figure 10.

Bicellular nonlinearity example for one pair of neurons. (A,C,E) STRFs of the neurons of one pair, and corresponding Bicellular STRF. (B,D,F) Nonlinearities for the three STRFs. Parametric curve fits are shown in gray. Vertical line indicates the threshold (theta) of the nonlinearity obtained from the curve fit. The transition (sigma) parameter indicates the smoothness of the nonlinearity near the threshold.

Figure 11.

Pairwise nonlinearity parameter comparison. (A) Nonlinearity threshold comparison for neurons in a pair. Each point represents one pair of neurons, and is grouped according to significant (Sync) and non-significant (UnSync) functional connectivity. (B) Distribution of nonlinearity threshold differences across the population of pairs and across cortical layers. Thresholds were most similar between pairs of neurons in granular layers, and more variable in infragranular layers. (C) Nonlinearity transition comparison for each pair of neurons. (D) Distribution of threshold differences for pairs of neurons. Supragranular and granular layers had pairs with more similar transitions, while infragranular layers had pairs with less similar nonlinearity transitions. P_D, S_D, G_D , and I_D represent Population (P), Supragranular (S), Granular (G), and Infragranular (I) pairwise data differences, while P_R, S_R, G_R , and I_R represent pairwise differences from random pairwise sampling.

Figure 12.

Bicellular nonlinearity analysis. Threshold and transition parameters of nonlinearities for pairs of neurons and for corresponding Bicellular STRFs. Values were obtained from nonlinearity curve fits (see Fig. 10). For each pair of neurons, the Bicellular (BC) value was compared to the values for each neuron in the pair. Matched (M) data for a pair was the value for the neuron in the pair that was most similar to the BC value. The Non-Matched (NM) data was the value for the neuron in the pair that was least similar to the BC value. Left column: Threshold of the nonlinearities. Right column: Transition of the nonlinearities. (A,B) Population distributions. (C-H) Laminar distributions. Insets show population means $\pm$ standard error of the mean. Bicellular data have higher thresholds and less noisy transitions than single neuron nonlinearities.

Figure 13.

Summary of Bicellular parameter analyses. For each layer, mean population values derived from Bicellular STRFs are compared to the mean of the values for matched data (error bars indicate SE). For each pair of neurons, the matched data is the value for the neuron in the pair that is most similar to the Bicellular value. (A) Best temporal modulation: Bicellular values were significantly higher in Supra- and Granular layers. (B) Best spectral modulation: Only Infragranular layers showed differences between Bicellular values and the values of the pair of neurons. (C) Nonlinearity threshold: Bicellular nonlinearities had higher thresholds in all layers. (D) Nonlinearity transition: Bicellular nonlinearities had lower transition values in all layers, indicating that Bicellular nonlinearities have more rectified nonlinearities. (E) STRF information: Bicellular spikes conveyed more information in all layers.