

Spectral and temporal integration in the auditory cortex of awake primates and its implications for coding of species-specific communication sounds

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I will discuss recent work in my laboratory in a vocal primate model, the common marmoset. The long-term objective of our studies is to understand how biologically important vocal communication sounds are represented by the auditory cortex. We have examined some fundamental issues in cortical coding of complex sounds across neural populations in the auditory cortex of awake marmosets and attempted to relate spectral and temporal integration mechanisms to cortical representation of species-specific vocalizations.

1) Temporal integration:

Both humans and animals are capable of perceiving time-varying features of complex sounds in a wide range of time scales from sub-millisecond to tens and hundreds of milliseconds. Yet it has long been noticed that discharges of auditory cortical neurons do not faithfully follow rapidly changing stimulus components. A number of previous studies have showed that cortical neurons can only be synchronized to temporal variations at a rate far less than 100 Hz, compared with a limit of greater than 1 kHz at the auditory nerve. The functional significance of this apparently “slow” response rate at the auditory cortex is unclear. The lack of synchronized cortical responses to rapidly changing stimulus components has been puzzling. It has been suspected that the much reduced discharge synchronization may be partially caused by anesthetics that have long been known to alter temporal response properties of the auditory cortex (Goldstein *et al.* 1959).

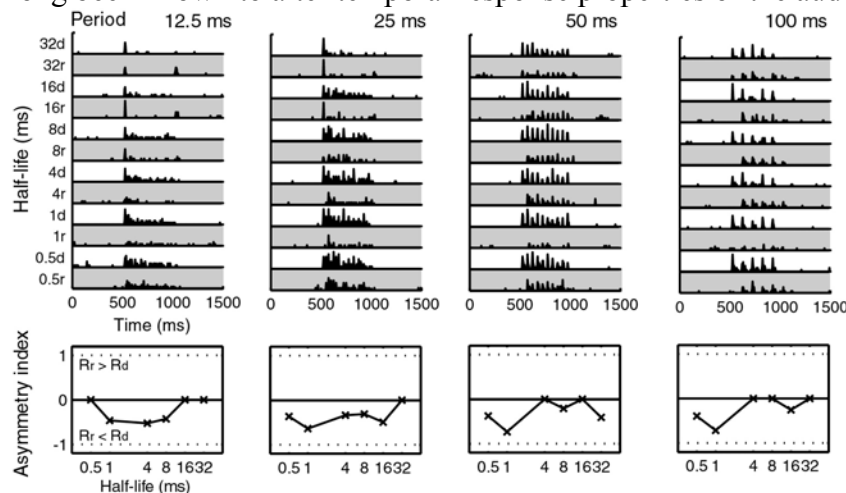


Figure 1. Selectivity of A1 neurons for temporal asymmetry introduced using a set of ramped (r, shaded) and damped (d) sinusoids with half-life ranging from 0.5 to 32 ms (y-axis). The stimuli consisted of sequences of ramped or damped sinusoids (onset at 500 ms, duration 1000 ms). The effect of stimulus period on response selectivity was also tested. Stimulus periods tested were (from left to right columns): 12.5, 25, 50 and 100 ms. The neuron shown responded overall more strongly to damped sinusoids. Asymmetry index was calculated as $(R_r - R_d) / (R_r + R_d)$, where $R_r + R_d$ are mean firing rates to ramped and damped stimuli, respectively. (Modified from Lu *et al.* 2001)

changes of the inter-click interval with monotonically changing discharge rate when inter-click intervals were short. This population of neurons can therefore *implicitly* represent rapidly changing temporal intervals by their mean firing rates. On the basis of these two populations of neurons, the auditory cortex can represent a wide range of time intervals in sequential, repetitive stimuli. While response characteristics of the stimulus-synchronized population observed in A1 of awake marmosets is qualitatively similar to that observed in anesthetized cats (Lu and Wang 2000), the large number of neurons with non-synchronized and sustained discharges have not been observed in anesthetized animals. We further found that neurons in both populations were sensitive to temporal asymmetry within a brief time window (~25 msec) in their mean

Using narrow- and wide-band click trains, we have identified two populations of neurons (*synchronized* and *non-synchronized*) in the primary auditory cortex (A1) that appear to encode sequential stimuli in very different manners (Lu *et al.* 1999, Wang *et al.* 2001). Neurons in the synchronized population showed stimulus-following discharges at long inter-click intervals but little responses at short inter-click intervals. This population of neurons can thus represent slowly changing temporal events *explicitly* using a *temporal* code.

The second population of neurons did not exhibit stimulus-synchronized discharges at both long and short inter-click intervals. They responded, however, to

firing rates (Lu *et al.* 2001), suggesting a rate-based coding mechanism within presumably the integration window of a neuron. Figure 1 shows responses of an A1 neuron to sequences of exponentially ramped and damped sinusoids. As the period of each sinusoid was shortened, stimulus-synchronized discharges became weaker and eventually turned into non-synchronized firing. The overall preference for the damped stimuli was maintained throughout.

Another important observation we have made in our experiments with time-varying stimuli is that many neurons in the auditory cortex displayed selectivity for specific temporal modulation frequencies by their mean firing rates or stimulus-synchronized discharges (Liang *et al.* 1999, Wang *et al.* 2001), regardless of how the modulation was introduced (in the amplitude or frequency domain, with tone or noise carriers).

The preferred modulation frequency measured by mean firing rate was higher than that measured by stimulus-synchronized firing in many neurons. The selectivity for a particular temporal modulation frequency was often observed in the mean firing rate in the absence of stimulus-synchronized discharges, which represents a temporal-to-rate transformation. A representative example is shown in Fig.2. This neuron showed a preferred temporal modulation frequency of 64 Hz when tested by sinusoidal amplitude- and frequency-modulated sounds (sAM and sFM) and amplitude-modulated broadband noises (nAM). These findings suggest an inherent temporal selectivity in cortical neurons that is applicable to a wide range of time-varying stimuli.

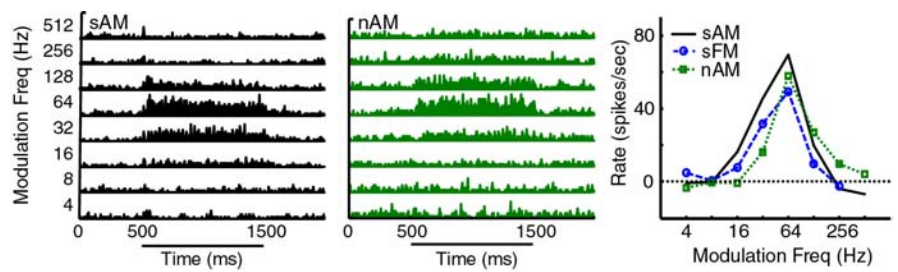


Figure 2. A representative example of single-unit responses in A1 to various temporally modulated stimuli. *Left:* PSTH of responses to sAM stimuli (onset at 500 ms, duration of 1000 ms). *Middle:* PSTH of responses to amplitude-modulated broad-band noises (nAM). *Right:* Modulation transfer functions based on discharge rate. The stimulus parameters (d - modulation depth) are: CF 4.7 kHz, 70 dB SPL, $d_{(sAM)}$ 75%, $d_{(sFM)}$ 512 Hz; $d_{(nAM)}$ 75%. The carrier frequencies for sAM and sFM stimuli were set at the unit's CF.

2) Spectral integration:

Like the primary visual cortex, neurons in A1 are linked through a network of long-range horizontal connections. Such anatomical structures suggest spectral integration over a large part of the acoustic spectrum. We found that single neurons in A1 are influenced by spectral inputs outside the classical receptive field (i.e., CF-centered excitatory area with flanking inhibitory areas), as far as 1-3 octaves away from CF (Kadia and Wang 2001). In a sub-population of A1 neurons, these distant spectral inputs were manifested in the form of multi-peaked tuning (often harmonically related) as revealed by single tones. Facilitation can be demonstrated by simultaneously stimulating a multi-peaked neuron with harmonically related CF and off-CF tones. The majority of A1 neurons exhibited well-known single-peaked tuning characteristics. However, when tested by simultaneous presentations of two tones, both facilitation and inhibition can be introduced by distant, off-CF tones. In contrast to neurons with multi-peaked tuning, the distant inhibition rather than facilitation showed a harmonic structure (with respect to the CF) in the single-peaked neurons. These findings indicate that A1 neurons integrate spectral inputs from a broad range of frequencies, far beyond the region surrounded the CF. The facilitation observed in A1 neurons may serve as a basis for processing contextual information in acoustic scenes. The harmonically related distant inhibitions may function to eliminate unwanted harmonic byproducts commonly produced by non-linear mechanisms in acoustic generators in order to segregate a target signal from other concurrent sounds. Our recent experiments further showed that an A1 neuron's responsiveness can be constrained by the temporal relationship between multiple spectral components. By temporally co-modulating spectral components placed both inside and outside the excitatory receptive field of a neuron, the neuron's responsiveness can be significantly altered (Barbour and Wang 2000). We have investigated these problems using two-tone paradigms and random spectrum stimuli, both of which are temporally modulated. These findings indicate that while the auditory cortex is tonotopically organized globally, local integration of widespread spectral components is an important part of the information processing circuit.

3) Representation of species-specific vocalizations:

There are two central issues in our understanding of cortical coding of species-specific vocalizations: *a)* neural encoding of statistical structure of communication sounds and *b)* the role of behavioral relevance in shaping cortical representations (Wang 2000). While individual examples of vocalizations have been widely used as stimulus tokens, cortical responses to these stimuli alone may not be sufficient to reveal the underlying coding schemes. This is because animal vocalizations, like human speech sounds, have both

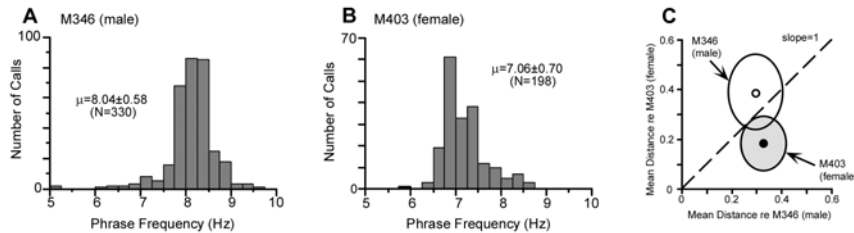


Figure 3 A, B. Distribution of phrase frequency of twitter calls from a male (A) and a female (B) marmoset. Both marmosets lived in the same colony and engaged in frequent vocal exchanges. C. The results of a multi-dimensional clustering analysis of twitter calls of the pair of marmoset monkeys in A and B. Four parameters were calculated for each twitter call sample and used in the analysis (number of phrases, phrase frequency, spectral-peak frequency of the first phrase and the second phrase). Two ellipsoids are drawn using the mean and standard deviation of a distance measure d_i (see definition below). The open circle marks the mean distances of calls made by the male monkey (abscissa) with respect to its own group mean and the female monkey's group mean (ordinate); the open ellipsoid (male monkey) outlines the standard deviations along both axes. The filled circle and shaded ellipsoid are calculations for calls from the female monkey.

$$d_j(n) = \sqrt{\sum_{k=1}^4 (P_{jk}(n) - \bar{m}_{jk})^2} \quad n = 1, 2, \dots, N_j; \quad \bar{m}_{jk} = \frac{\sum_{n=1}^{N_j} P_{jk}(n)}{N_j}$$

where i, j are animal designation (1: M346, 2: M403); N_i is number of call samples from i th animal ($N_1=330, N_2=198$); $P_{jk}(n)$ is k th parameter in the n th call of the i th animal, and \bar{m}_{jk} is mean value of the k th parameter of call samples from i th animal. (Modified from Wang 2000)

with distinct acoustic structures and that vocalizations produced by individual monkeys form separable clusters in a multi-dimensional space (See the example in Fig.3). The statistical structures of marmoset vocalizations are correlated to spectral and temporal characteristics of neurons in the auditory cortex in many ways. For example, the distribution of preferred temporal modulation frequencies of A1 neurons matches well with the distribution of modulation frequencies in some most frequently used call types of the marmoset.

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