Neurobiology of echolocation in bats

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Echolocating bats (sub-order: Microchiroptera) form a highly successful group of animals, comprising approximately 700 species and an estimated 25% of living mammals. Many echolocating bats are nocturnal predators that have evolved a biological sonar system to orient and forage in three-dimensional space. Acoustic signal processing and vocal-motor control are tightly coupled, and successful echolocation depends on the coordination between auditory and motor systems. Indeed, echolocation involves adaptive changes in vocal production patterns, which, in turn, constrain the acoustic information arriving at the bat's ears and the time-scales over which neural computations take place.

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Abbreviations

3-D	three-dimensional
ACC	anterior cingulate cortex
BD	best duration
BF	best frequency
CF	constant frequency
DNLL	dorsal nucleus of the lateral lemniscus
EI	binaural response profile created with excitatory/inhibitory contralateral/ipsilateral inputs
FM	frequency modulated
GABA	γ-amino butyric acid
IC	inferior colliculus
ILD	interaural level difference
PAG	periaqueductal gray
PB	parabrachial nucleus
PLa	paralemniscal tegmentum area
PLS	paradoxical latency shift

Introduction

The echolocating bat's active sensing system supports obstacle avoidance and foraging behavior in complete darkness. It produces ultrasonic vocalizations and uses information contained in the returning echoes to determine the position, size and other features of sonar targets [1]. The timing, frequency content, duration and intensity of sonar signals used by the bat to probe the environment directly influence the information available to its acoustic imaging system. In turn, the bat's auditory representation of the environment guides adaptive motor behaviors, including adjustments of the pinna, head aim, flight path, and the features of subsequent sonar vocalizations [2,3].

Echolocating bats exhibit tremendous diversity in the suborder Microchiroptera, with species displaying adaptations to a broad range of habitats, from the desert to the tropical rain forest [4]. Species-specific signal characteristics are closely linked to the ecological conditions encountered by foraging bats, and several schemes have been proposed to categorize bats according to habitat and sonar signal characteristics [5–9].

Each species of bat has a distinct repertoire of signals that it uses for echolocation, and the features of these sounds determine the acoustic information available to its sonar imaging system. Bat sonar signals fall broadly into two categories, constant frequency (CF) and frequency modulated (FM), see Figure 1a. Species using CF-FM signals for echolocation typically forage in dense foliage, and some of these species adjust the frequency of their sonar vocalizations to compensate for Doppler shifts in returning echoes [10,11]. The CF-FM bat's Doppler shift compensation (DSC) serves to cancel a rise in echo frequency introduced by its own flight velocity and isolates spectral modulations in echoes that come from fluttering insect wings [12]. In some Doppler shift compensating bats, researchers have identified auditory specializations, which give rise to heightened sensitivity and frequency selectivity in the spectral region of the bat's CF signals [13]. By contrast, many FM-bats forage in the open or at the edge of forests, using shorter duration, broadband signals that are well suited for three dimensional (3-D) target localization and for separating figure and ground. FM-bats can discriminate differences in echo delay, the cue for target distance, of less than 60 microseconds [1,14], and they use this delay information to coordinate the timing of sonar vocalizations [15].

As an insectivorous bat flies towards a prey item, the spectral-temporal features of its sonar vocalizations change (Figure 1b). The characteristics of sonar emissions have been used to divide the bat's insect pursuit sequence into different phases: search, approach, and terminal buzz [16]. These phases of insect capture represent distinct modes of action and perception, which provide a valuable system for empirical research on audiomotor feedback control. Moreover, the temporal patterning of the bat's echolocation signals provide explicit data on the timing of vocal–motor

Figure 1
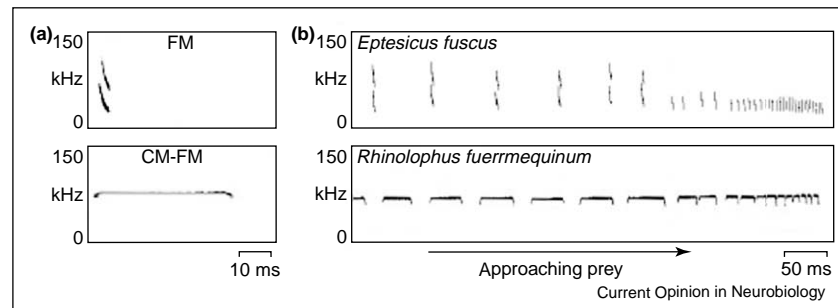
Echolocation signal structures. **(a)** Spectrographic examples of frequency modulated (FM) and constant frequency (CF) signal components used by echolocating bats. **(b)** Spectrographic sequence of signals produced by an FM-bat, *Eptesicus fuscus* and a CF-FM bat, *Rhinolophus ferrumequinum*, while pursuing insect prey. Typical of insectivorous echolocating bats, signal repetition rate increases and the duration decreases as the animal approaches its prey.

commands that feed directly back to the auditory system for spatially guided behavior.

The echolocating bat's adaptive motor behaviors set a context and time-frame within which neuronal responses must operate, and presumably vary, to build representations of the environment. Therefore, it is plausible that the time-scales over which echolocation behaviors operate serve to constrain the time-scales over which neuronal computations take place. The potential dynamic variation in neuronal responses can be mediated at the single cell and network level by processes such as experience-dependent synaptic plasticity. In this review, we focus on the temporal parameters of sonar vocalizations and sound processing as they relate to echolocation behavior in bats.

Auditory processing
The bat's auditory system receives and processes echoes in its environment for the task of spatial orientation, but it is essentially a standard mammalian auditory system. Many of the same cues used by other species to localize sound and to process complex patterns of acoustic information are exploited by the bat for spatial orientation and perception by sonar. Binaural cues for sound localization are used to estimate the azimuthal position of a sonar target. The bat's external ear produces changes in the spectrum of incoming echoes, which creates patterns of interference that are used by the bat to estimate target elevation [17]. The bat estimates the third spatial dimension, target range, from the time delay between the outgoing vocalization and the returning echo [14], and FM-bats show extraordinary spatial selectivity along the range axis [18,19].

Major nuclei comprising the primary auditory pathway and important feedforward and feedback excitatory and inhibitory connections are shown schematically in Figure 2. (For a detailed exposition of commonalties

and differences in auditory pathways and function in bat species see Fay and Popper [20].) Recent research findings demonstrate that feedback connections can lead to time-dependent modifications in the functional processing of auditory stimuli [21]. This in turn has important consequences for the processing of sequences or combinations of naturally occurring or artificially generated stimuli.

Many neuronal mechanisms operate in the range of 10s to 100s of milliseconds, and act in creating response types presumably important in processing echolocation information. Mechanisms range from the dependence on the complement of ion currents [22] to the distribution of inhibitory inputs [23], both of which can be shaped through experience. In addition, mechanisms exist that affect neural integration time, such as active conductances, membrane oscillations [24•] and post-inhibitory rebound [25], which can modify network-level interactions.

Neural selectivity to temporal parameters of auditory stimuli has been studied extensively in echolocating bats. These include selectivity to sound duration, to delay between pulse-echo sound pairs, and to temporal rates of sound sequences, all parameters that vary in the vocal signals produced by foraging bats.

One attribute of echolocation calls is signal duration, a characteristic that changes markedly as bats approach a prey item (Figure 1b). Temporal filtering for sound duration has been reported at different levels of the auditory pathway and in several bat species [26,27] and other mammals (mouse: [28]). The underlying mechanism for duration-tuned response profiles has been investigated using neuropharmocological [29,30] and intracellular recording methods [26]. The response type appears to be first created at the inferior colliculus (IC), and is a consequence of the timing between excitatory and inhibitory converging inputs. More recently by

Figure 2
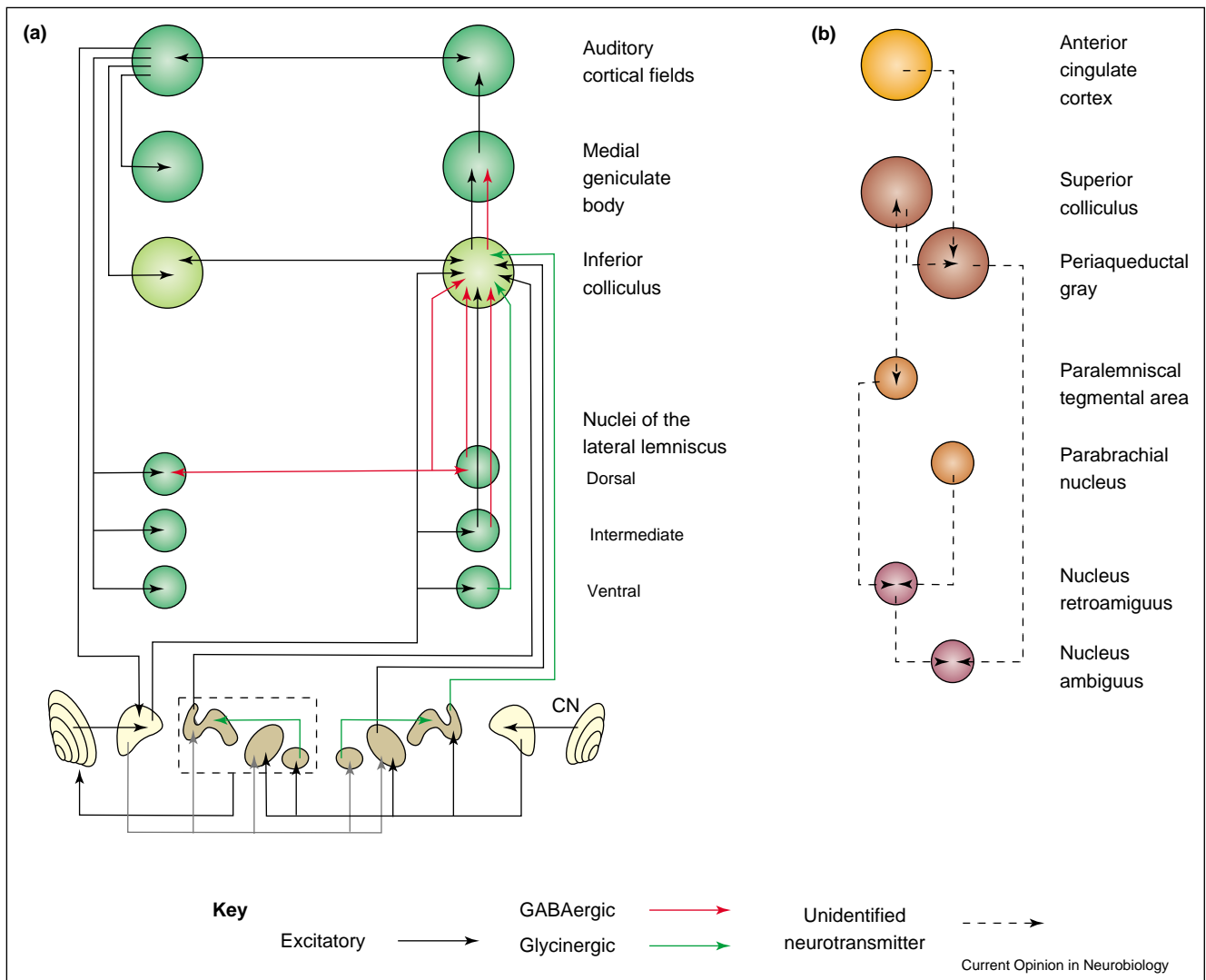
Major connections of the **(a)** ascending auditory system, and descending auditory corticofugal projections. The dashed box demarcates nuclei of the superior olivary complex (SOC) that includes the lateral superior olive, the medial; superior olive and the medial nucleus of the trapezoid body. **(b)** Selected projections of vocal production circuitry from cited works. Excitatory projections are shown with black lines, inhibitory GABAergic projections are shown with red lines, inhibitory glycinergic projections are shown with green lines, and connections with as yet unidentified neurotransmitters are shown with dashed black lines. Abbreviations: CN, cochlear nucleus.

employing a two tone stimulus paradigm that used a probe tone at the neuron's best frequency (BF) and best duration (BD), and a masking (competing) tone with a nonexcitatory (NE) duration the latency, duration, and decay of the afferent input inhibition was delineated [31•]. By manipulating the onset, overlap, and offset of the probe and masking tone, the time course of inhibition has been shown to shape BD, the duration tuning characteristics, and first spike latency.

The distance between the bat and sonar target may be represented by the activity profile in a population of neurons that respond selectively to two sounds, which

simulate sonar cry and echo, separated by a limited and biologically relevant range of temporal delays [32,33]. These 'delay-tuned' neurons are present in the midbrain [34–36], thalamus and cortex [37,38]. Delay-tuned neurons, which are likely to be established at the level of the midbrain [39,40], are sensitive to additional stimulus dimensions, for example, the absolute amplitude, the spectral content, and the temporal rate at which a series of stimulus pairs are presented. Thus, these neurons may not only encode target distance but also might potentially encode other stimulus dimensions [41]. A recent study explored this by using two overlapping echoes, temporally offset to simulate sonar reflections

Figure 3
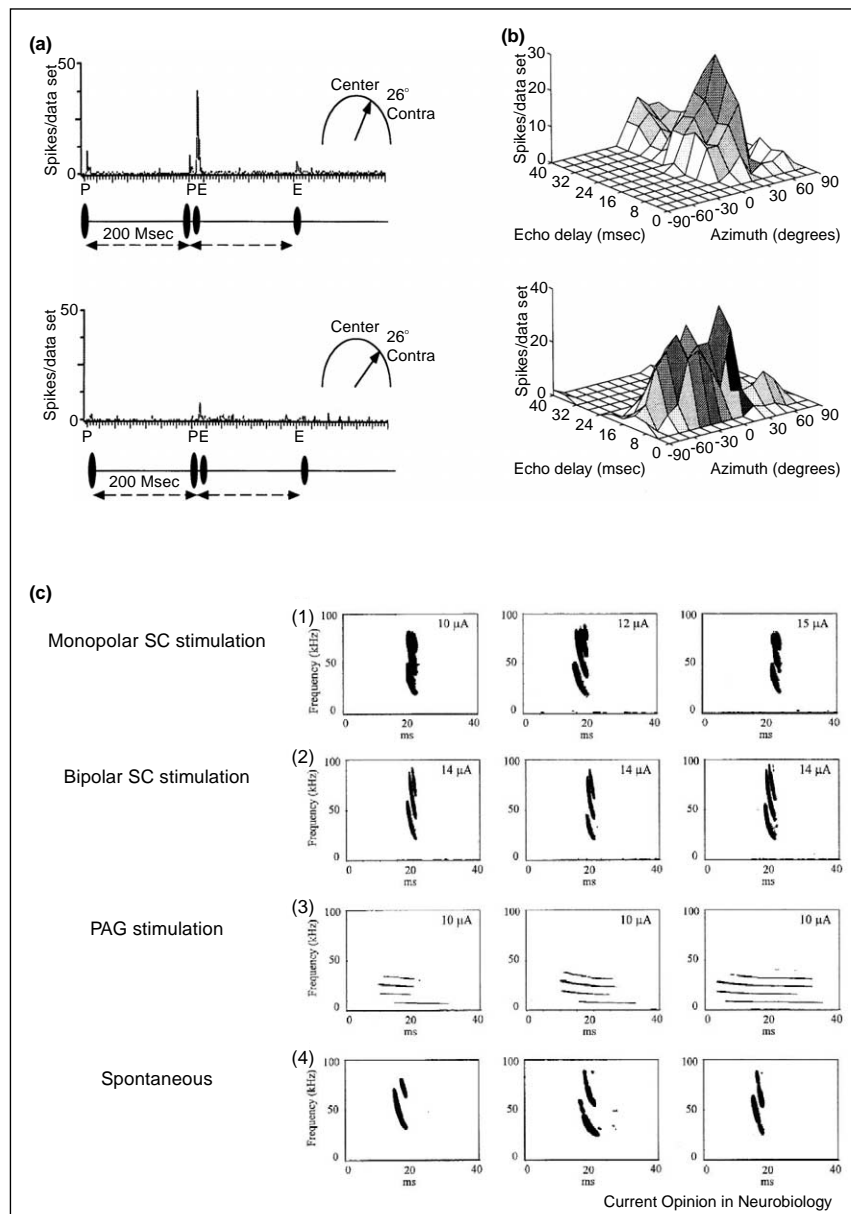
(a) Neural recordings from the bat superior colliculus. Echo delay tuned neuron in the bat SC shows a facilitated response to a pulse-echo pair separated by 12 msec. The response is vigorous at an azimuth of 26 deg contralateral to the recording site but falls off at 39 deg. Abbreviations: E, echo; P, pulse; PE pulse and echo. (b) Spatial response profiles of two SC neurons that show selectivity to azimuth and delay. (Adapted from [36].) (c) Sonar vocalizations elicited by electrical stimulation of the SC (1 and 2) and communication calls elicited by stimulation of the PAG (3). Stimulation current levels are shown in the upper right corner of each example. Spontaneous vocalizations recorded from flying bats (4). Abbreviations: PAG, periaqueductal gray; SC, superior colliculus (Adapted from [66]).

from closely spaced surfaces [42]. The authors showed evidence for enhanced responses when pairs of partially overlapping echoes were presented after a simulated sonar cry, suggesting a response profile sensitive to both the temporal and spectral structure of stimuli.

Echolocating bats use sonar returns to localize objects in azimuth, elevation and distance, leading to the prediction that auditory neurons show spatial selectivity in 3-D space. A population of auditory neurons in the intermediate and deep superior colliculus (SC) of the bat, *Eptesicus fuscus*, show 3-D spatial response profiles ([36]; Figure 3a). In this population of 3-D neurons, echo delay-tuning is tagged to the azimuth and elevation of a sound source. The representation of 3-D target location in the SC of the bat would be important for the coordination of sensory

and motor signals that drive its acoustic orientation, as changes in the bat's echolocation behavior are closely tied to position [15].

The principal cue bats and other mammals use to localize the direction of high frequency sound is interaural level difference (ILD). Neurons that are excited by stimulation of one ear and inhibited by stimulation of the other ear (binaural response profile created with excitatory/inhibitory contralateral/ipsilateral inputs [EI]) are thought to encode ILD. This response type serves as the putative mechanism for spatial localization among bats; the timing of convergent excitatory and inhibitory inputs onto these neurons being crucial in shaping their response patterns. Timing is also important when one considers the duration over which the excitation or inhibition lasts, as this can significantly affect the response of an ILD neuron to subsequent sounds. This last point has recently been investigated [43•] by combining extracellular recordings with iontophoretic application of antagonists, and/or presentation of a pair of binaural sounds. The persistent inhibition initiated at the dorsal nucleus of the lateral lemniscus (DNLL) prevents the DNLL from responding for a period of time. As many IC cells receive inhibitory input from DNLL, they are temporarily transformed from strongly inhibited EI neurons to weakly inhibited EI, or even monaural, cells when DNLL activity is shut down. Two clear implications arise, both related to the temporal aspects of neural processing of multiple sounds. The first is that EI response properties can change over time, on the basis of the temporal pattern of binaural stimulation showing a state dependent response. This is a consequence of timing and persistence of inhibition in this network of neurons, and suggests that codes for spatial localization that are formed on the basis of EI neuronal responses change with multiple stimuli. The second implication is a consequence of the loss of the EI property. When IC inhibitory input is reduced, the EI cells lose their ILD specificity, and respond to sounds from a larger in region in space.

Recently, there has been a growing interest in the processing of acoustic communication signals in the central nervous system (CNS) of echolocating bats. Interestingly, auditory regions traditionally studied in the context of biosonar processing appear to play a role in communication signal processing. Researchers find that neural responses to communication signals depend on the temporal–spectral characteristics of sounds, similar to findings for biosonar signals. These results suggest that the processing of sounds used for orientation and communication occurs through overlapping auditory networks [44–46].

Corticofugal modulation

Time-dependent changes in basic auditory neuronal receptive field parameters have been demonstrated [47] and recently expanded on in a series of elegant experiments. The research not only suggests the involvement of the amygdala and cholinergic basal forebrain in auditory plasticity [48] but also strongly supports a role for corticofugal (descending projections from the cortex) modulation in adjusting neuronal receptive field properties based on the salience of an auditory stimulus. The effects have been observed at the level of auditory cortical fields (ACF), medial geniculate body (MGB), IC [49,50], and the cochlea [51]. Using repetitive acoustic stimulation, fear conditioning, focal electrical microstimulation of the primary auditory cortex (AI) or IC, or electrical microstimulation combined with auditory stimulation, frequency response areas of auditory neurons in bats can be shifted in an experience-dependent manner. Neurons with temporal combination-selectivity are also influenced (delay-tuned: [52,53]; duration-tuned: [54]) at both cortical and subcortical levels. The observed changes arise over the course of minutes and can last from a few seconds to hours [55]. Protocols that involve associative learning (e.g. electrical foot stimulation, paired with a conditioning tone stimulus) demonstrate changes in the receptive fields of AI neurons, which can last up to 26 h [56]. The time-course and underlying mechanism of this long-term change in best frequency (as evaluated using N-methyl D-aspartate [NMDA] agonists and blockers) suggests the involvement of experience-dependent transcriptionally mediated processes in order to maintain long-term changes in a neuron's best frequency response area [57–59]. The experience-dependent plasticity is observed in both FM [56,60] and CF-FM emitting bat species [53,61]. Work with similar protocols suggests that these corticofugal modulations are likely to generalize to other mammals [62]. The implication, in our view, is that central and peripheral auditory processing in bats can be rapidly modulated to adjust the analysis of auditory signals in the context of changing vocal patterns and corresponding echoes. The rapid experience-dependent plasticity clearly demonstrates that the inputs to neurons putatively involved in processing echolocation information can be dynamically modulated, which permits a shift in their classical receptive field arrangement. Although these experiments do not employ echolocation behavior, they do involve processing in neuronal populations sensitive to sonar calls, and provide evidence for the potential range of plasticity possible when the bat is actively engaged in echolocation.

Motor production

The behavioral context within which bats echolocate plays a central role in shaping the parameters of sonar vocalizations. Sonar vocalizations produced by bats during insect pursuit show considerable variation in duration, bandwidth, spectral content, and temporal patterning (Figure 1). The species-specific variations in call design, relative motion of the bat with respect to its target, changes in call structure and temporal patterning all influence the information available to the bat's auditory system.

Using electrical and chemical microstimulation techniques, several brainstem regions involved in sonar vocal production have been studied. Experiments have focused on midbrain regions, identifying cytoarchitectural regions that elicit vocalizations and their interconnections. In the midbrain the paralemniscal tegmentum area (PLa), periaqueductal gray (PAG), reticular formation, parabrachial nucleus (PB), SC, and their direct or indirect projections to brainstem nucleus retroambiguus (RA) and nucleus ambiguus (NA) have been elucidated [63–65,66•].

Researchers have proposed that sonar vocal production has evolved from vocal communication pathways [67]. Recent work [68•] has identified dual pathways for the production of sonar and communication calls at the midbrain level in the neotropical FM bat, *Phyllostomus discolor*. One pathway, encompassing medial loci in the ventral PAG, elicits classes of communication calls following chemical stimulation using dialysis of non-lesion concentrations of kainic acid. A second pathway involves a locus in the lateral PAG and the PLa, both eliciting sonar vocalizations when electrically and chemically stimulated. This experiment is the first to show a dual role for the PAG, a region considered to be mandatory in the vocal production pathway for communication calls [69].

Experiments that investigate audio–vocal interactions in the midbrain PLa show that the PLa can contribute to timing aspects of sonar vocalizations; however, lesions of the PLa do not eliminate the ability to produce sonar vocalization [70], which suggests that it is not a mandatory component of sonar vocal circuitry. Recent experiments studied the role of the PB in sonar vocalizations in the CF-FM bat, *Rhinolophus ferrumequinum* [71]. Using iontophoretic application of γ-amino butyric acid (GABA)ergic and L-glutamate agonists and antagonists, the authors demonstrated that the PB plays a role in the control of call frequency. Application of muscimol ($GABA_A$ agonist) or CNQX (6-cyano-7-nitroquinoxaline-2,3-dione; a glutamatergic anatagonist) lowered the call frequency emitted at rest and during DSC behavior. Conversely, excitation induced by application of α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) or by blocking inhibition using BMI (bicuculline methiodide, a $GABA_A$ antagonist) increased sonar call frequencies.

The PB study of the horseshoe bat is the first to demonstrate midbrain control over production of sound frequency [71]. Stimulation experiments in other midbrain sites have only reported influences on the timing and number of sonar vocalizations but not specifically the spectral content. Site-dependent spectral characteristics of electrically elicited vocalizations have been reported for the anterior cingulate cortex (ACC) in another CF-FM bat species, *Pteronotus parnellii* [72]. Electrical microstimulation of the ACC elicited sonar vocalizations in rostral ACC, whereas microstimulation of more caudal ACC regions elicited communication sounds. In the case of PB microstimulation [71], control of the amount of excitation and inhibition more crucially impacts the frequency in the emitted CF component of the sonar vocalization.

Adaptive behaviors to dynamic stimuli require the integration of sensory information with motor programs to guide appropriate responses, and a wealth of data suggests that the midbrain SC plays a role in sensorimotor integration. In individual species, the functional organization of the SC reflects the importance of a particular sensory modality to an animal's goal-directed orienting responses. In bats, control of vocal signals is an integral part of its acoustic orienting system. It is, therefore, not surprising that microstimulation of the bat SC elicits head and pinna movements, along with the production of sonar vocalizations (Figure 3b; [66•,73]). Consistent with this result, premotor bursts are recorded from the bat SC before each sonar vocalization [74].

Combined, these studies suggest that a complex circuit of interconnected nuclei serve to control the timing and spectro-temporal parameters of sonar vocalizations. Most of these regions receive projections from auditory nuclei, and they may have evolved from areas involved in the production of communication calls [67,72].

Conclusions
As the echolocating bat orients in the environment and pursues insect prey, its sound production patterns adapt to changing acoustic information [2,3,15]. These adaptive vocal production patterns provide a window to the information sought and collected by the active sonar system for acoustic imaging under different task conditions. Researchers have taken advantage of the signals recorded from echolocating bats engaged in behavioral tasks to employ biologically relevant stimuli for studies of auditory information processing in the brain. The dynamic patterning of the bat's sonar vocalizations establishes a time scale for studying echo processing, both at the level of individual sounds and across sequences of sounds. Researchers have also begun to study pre-motor areas that are involved in sonar production. A complete understanding of the neurobiology of bat echolocation, however, requires detailed CNS studies of the bat actively engaging in vocal–motor behaviors that result in sonar echo returns.

Acknowledgements

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- • of special interest
- •• of outstanding interest

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