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RESEARCH ARTICLE | *Sensory Processing*

Tuning for rate and duration of frequency-modulated sweeps in the mammalian inferior colliculus

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Morrison JA, Valdizón-Rodríguez R, Goldreich D, Faure PA. Tuning for rate and duration of frequency-modulated sweeps in the mammalian inferior colliculus. *J Neurophysiol* 120: 985–997, 2018. First published May 23, 2018; doi:10.1152/jn.00065.2018.—Responses of auditory duration-tuned neurons (DTNs) are selective for stimulus duration. We used single-unit extracellular recording to investigate how the inferior colliculus (IC) encodes frequency-modulated (FM) sweeps in the big brown bat. It was unclear whether the responses of so-called "FM DTNs" encode signal duration, like classic pure-tone DTNs, or the FM sweep rate. Most FM cells had spiking responses selective for downward FM sweeps. We presented cells with linear FM sweeps whose center frequency (CEF) was set to the best excitatory frequency and whose bandwidth (BW) maximized the spike count. With these baseline parameters, we stimulated cells with linear FM sweeps randomly varied in duration to measure the range of excitatory FM durations and/or sweep rates. To separate FM rate and FM duration tuning, we doubled (and halved) the BW of the baseline FM stimulus while keeping the CEF constant and then recollected each cell's FM duration tuning curve. If the cell was tuned to FM duration, then the best duration (or range of excitatory durations) should remain constant despite changes in signal BW; however, if the cell was tuned to the FM rate, then the best duration should covary with the same FM rate at each BW. A Bayesian model comparison revealed that the majority of neurons were tuned to the FM sweep rate, although a few cells showed tuning for FM duration. We conclude that the dominant parameter for temporal tuning of FM neurons in the IC is FM sweep rate and not FM duration.

NEW & NOTEWORTHY Reports of inferior colliculus neurons with response selectivity to the duration of frequency-modulated (FM) stimuli exist, yet it remains unclear whether such cells are tuned to the FM duration or the FM sweep rate. To disambiguate these hypotheses, we presented neurons with variable-duration FM signals that were systematically manipulated in bandwidth. A Bayesian model comparison revealed that most temporally selective midbrain cells were tuned to the FM sweep rate and not the FM duration.

auditory midbrain; Bayesian modeling; big brown bat (*Eptesicus fuscus*); FM duration tuning; FM sweep rate tuning; temporal processing

INTRODUCTION

Frequency modulation (FM) is a prominent feature of human and nonhuman animal vocalizations, and neural tuning for FM auditory signals is common across mammalian species (bats: Suga 1965; cats: Mendelson and Cynader 1985; rats: Gaese and Ostwald 1995; primates: Liang et al. 2002). Humans show broad usage of FM sounds for communication. For example, in the English language spectral inflection of a sentence changes meaning without altering semantic content: upward inflection in frequency indicates a question, whereas downward inflection indicates a declarative statement. On shorter timescales, such as transitions between phonemes and sometimes within phonemes themselves, there can be upward or downward FM, and such acoustic elements are known as FM sweeps (Doupe and Kuhl 1999; Liberman et al. 1967; Shannon et al. 1995).

The physiology of central auditory neurons selective for FM sweeps in echolocating bats was first described by Suga (1964). Beyond the typical spectral and amplitude response selectivity common to most cells, FM neurons were also selective for the direction of a FM sweep (i.e., upward or downward FM). Directional selectivity was created by neural inhibition evoked at sideband frequencies relative to the cell's frequency-threshold tuning curve (Suga 1965). Neurons were described as having an excitatory frequency response area (eFRA) spanning an excitatory spectral bandwidth (BW). A suprathreshold FM sweep with energy only at frequencies within the eFRA would evoke action potentials regardless of the FM direction (Suga 1965). Flanking one (or either) side of the eFRA is an inhibitory frequency response area (iFRA) spanning an inhibitory spectral BW. A FM sweep starting from within the cell's iFRA would likely not evoke spikes because inhibition would occur before excitation. Suga (1965) hypothesized that neural selectivity for FM directionality arose from different combinations of iFRA thresholds and inhibitory spectral BWs relative to the cell's eFRA and excitatory spectral BW.

Suga's (1964, 1965) work inspired later findings suggesting that selectivity for direction of a FM sweep was created with a mechanism similar to how directional selectivity was created in the tactile (Costanzo and Gardner 1980) and visual (Barlow and Levick 1965; Sillito 1977) sensory systems. Recent studies have shown that FM directional selectivity in the mammalian inferior colliculus (IC) can be created de novo instead of being inherited from FM directional cells in lower brain stem nuclei such as the nucleus of the lateral lemniscus and the superior olivary complex (Gittelman et al. 2009, Pollak et al. 2011). Neural mechanisms underlying the directional selectivity and rate of auditory FM sweeps have been extensively studied

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(e.g., Brimijoin and O'Neill 2005; Gordon and O'Neill 1998; Williams and Fuzessery 2010); however, much less is known about neural selectivity for other types of temporal information in FM sweeps, such as signal duration.

Temporal processing is known to play a vital role in hearing (Capranica 1992), and the existence of duration-tuned neurons (DTNs)—cells selective for the duration of an auditory stimulus—is well documented at and above the level of the auditory midbrain across vertebrates (e.g., frogs: Potter 1965; bats: Casseday et al. 1994; Fuzessery and Hall 1999; Jen and Schlegel 1982; Luo et al. 2008; Mora and Kössl 2004; Pinheiro et al. 1991; rodents: Brand et al. 2000; Pérez-Gonzalez et al. 2006; Wang et al. 2006). Most reports on the physiology of auditory DTNs have tested cells with pure-tone signals (e.g., Aubie et al. 2009, 2012; Casseday et al. 1994; Ehrlich et al. 1997; Faure et al. 2003; Luo et al. 2008; Mora and Kössl 2004; Morrison et al. 2014; Valdizón-Rodríguez and Faure 2017), with fewer studies exploring response selectivity for the duration and/or sweep rate of FM signals (e.g., Fuzessery et al. 2006; Razak and Fuzessery 2006; Trujillo et al. 2011). Investigating duration selectivity with FM signals is of particular interest because there are two temporal parameters to which neurons may respond: signal duration and/or FM sweep rate. Neural tuning for the duration and/or rate of FM would be advantageous for an echolocating bat that emits downward FM sweeps while foraging and uses signal durations and FM sweep rates that change dramatically from the search to the approach and finally to the terminal phase of hunting (e.g., Simmons et al. 1979; Surlykke and Moss 2000).

Neurons with apparent selectivity for the duration of FM sweeps have been reported from both the IC (Ehrlich et al. 1997; Fuzessery et al. 2006) and auditory cortex (Razak and Fuzessery 2006; Trujillo et al. 2011), but in many cases it was unclear whether the responses of these cells were selective to signal duration or the rate of FM (e.g., Ehrlich et al. 1997; Trujillo et al. 2011). Our goal was to disambiguate the temporal selectivity of so-called "FM DTNs" and determine whether their spiking responses are selective for FM signal duration or FM sweep rate.

METHODS

Data were collected from two laboratories—the University of Washington (UW) and McMaster University (MU). Procedures conducted in Seattle were approved by the UW's Animal Care and Use Committee. Procedures conducted in Hamilton were approved by MU's Animal Research Ethics Board and were in accordance with the Canadian Council on Animal Care. Animals in both institutions were housed in an outdoor husbandry facility where the lighting and temperature varied with ambient conditions and water and food were available ad libitum.

Surgical preparation. Electrophysiological recordings were obtained from the IC of 25 awake big brown bats (*Eptesicus fuscus*; 13 from UW: 5 males, 8 females; 11 from MU: 4 males, 7 females). Bats were brought into a temperature- and humidity-controlled room 1–3 days before surgery to allow them to acclimatize. Bats were anesthetized either by a combination of Metofane (methoxyflurane) inhalation (1–5 min) and subcutaneous injection of a neuroleptic cocktail [0.3 ml of 1:1 mixture of 0.025 mg/ml fentanyl citrate + 1.25 mg/ml Inapsine (droperidol); final dose = 19.1 mg/kg assuming a typical bat mass of 20 g] or by isoflurane-oxygen inhalation (mixture 1–5%; flow 1–5 l/min). Anesthetized bats were then placed in a foam-lined restraint molded to the shape of the body to hold the bat firmly yet comfortably while still allowing access to the head. The bat's mouth was placed in a custom bite bar, designed to keep the head stable during surgery, that was fitted with a gas mask for continuous anesthetic inhalation (David Kopf Instruments, model 1900). The hair covering the skull was shaved, and the underlying skin was swabbed with 70–100% ethanol followed by Betadine disinfectant. Local anesthetic (0.2 ml of 5 mg/ml bupivacaine; 50 mg/kg assuming a typical bat mass of 20 g) was injected subcutaneously before a midline incision was made in the scalp. The temporal muscles were reflected, the skull was scraped clean and swabbed with 70–100% ethanol, and after drying a stainless steel post was affixed to the skull to ensure that the position of the bat's head could be precisely replicated between recording sessions. The head post was glued to the dorsal surface of the skull overlying the cortex with cyanoacrylate gel adhesive (Zap Gel, Pacer Technology) or superglue (Henkel Lockite) that was instantly cured with liquid acrylic hardener (Jet Liquid, Lang Dental). One end of a chlorided silver wire attached to the head post was placed under the temporal musculature and served as the reference electrode. The wound was then covered with a piece of Gelfoam coated with Polysporin to prevent infection. After surgery, bats were allowed to recover in a stainless steel holding cage ($25 \times 22 \times 22$ cm, $l \times w \times h$; 1/4-in. mesh) located in a temperature- and humidity-controlled room and were provided food and water ad libitum.

Electrophysiological recording. Neural recordings began 1–2 days after the preparatory surgery and were conducted inside a double-walled sound attenuation booth with electrical shielding (Industrial Acoustics). Each bat was used in one to eight sessions lasting 4–8 h each and conducted on separate days. Recordings were terminated if the bat showed any signs of discomfort. Between sessions, the electrode penetration site was covered with a piece of contact lens and/or Gelfoam covered in topical antibiotic (Neosporin or Polysporin) to prevent infection.

Before recording, the bat was administered a neuroleptic [0.3 ml; 1:1 (vol/vol) mixture of 0.025 mg/ml fentanyl citrate and 1.25 mg/ml Inapsine; 19.1 mg/kg]. Once sedated, the bat was placed in a foam-lined body restraint that was suspended by springs within a small-animal stereotaxic frame customized for bats (ASI Instruments). The entire apparatus was set atop an air vibration table (TMC Micro-G). The bat's head was immobilized by securing the head post to a stainless steel rod attached to a manual micromanipulator (ASI Instruments) mounted on the stereotaxic frame. A craniotomy was performed with a scalpel blade, and the dura mater over the dorsal portion of the IC was removed with a sharp pin for the insertion of electrodes. In *E. fuscus* the IC can be visually identified as two white ellipses below the translucent skull. Single-unit extracellular recordings were obtained with thin-walled borosilicate glass microelectrodes (outside diameter = 1.2 mm; A-M Systems) filled with either 0.9% or 1.5 M NaCl. Typical electrode resistances ranged between 15 and 30 MΩ, yielding high-quality recordings (signal-to-noise ratio typically ≥2). Single units were identified by the consistency of the spike amplitude/waveform monitored on a digital oscilloscope. Electrodes were positioned orthogonally to the surface of the exposed IC with a manual micromanipulator (ASI Instruments) and advanced into the brain with a stepping hydraulic micropositioner (Kopf model 2650). Electrode depths were referenced to the dorsal surface of the IC; the zero point was marked when the electrode first touched the brain (determined by changes in the recording trace and audio monitoring). Extracellular action potentials were recorded with a neuroprobe amplifier (A-M Systems model 1600) whose 10× output was band-pass filtered and further amplified (500–1,000×) by a Tucker Davis Technologies (TDT) spike preconditioner [TDT PC1; low-pass cutoff frequency (f_c) = 7 kHz; high-pass f_c = 300 Hz]. Spike times were logged onto a computer by passing the TDT PC1 output to a spike discriminator (TDT SD1) and then an event timer (TDT ET1) synchronized to a timing generator (TDT TG6).

Stimulus generation. Sound pulses were digitally synthesized with custom software controlling two signal processing boards (TDT Apos II; sampling rate = 357 kHz) that were optically interfaced to two digital-to-analog converters (D/A) (TDT DA3-2). The output of each D/A was fed through a low-pass antialiasing filter (TDT FT6–2; f_c = 120 kHz) and one (TDT PA5; MU) or two (TDT PA4; UW) programmable attenuators before being mixed in a summer with equal weighting (TDT SM5) and fed through a manual attenuator (Leader LAT-45) before final amplification (Krohn-Hite model 7500). All stimuli were presented monaurally, contralateral to the IC being recorded, with a Brüel & Kjær (B&K) 1/4-in. condenser microphone (type 4939; protective grid on) modified for use as a loudspeaker with a transmitting adaptor (B&K type UA-9020) to correct for nonlinearities in the transfer function (Frederiksen 1977). The diaphragm of the loudspeaker was positioned ~1 mm in front of the external auditory meatus. The output of the speaker, recorded with a B&K type 4138 1/8-in. condenser microphone (90° incidence; grid off) connected to a measuring amplifier (B&K type 2606) and band-pass filter (Krohn-Hite model 3500), was calibrated (B&K type 4231) and expressed in decibels sound pressure level (dB SPL re 20 μPa) equivalent to the peak amplitude of continuous tones of the same frequency (Stapells et al. 1982). The loudspeaker transfer function was flat ± 6 dB from 28 to 118 kHz, and there was at least 30-dB attenuation at the ear opposite the source (Ehrlich et al. 1997). All stimuli had rise/fall times of 0.4 or 0.5 ms shaped with a cosine-squared function and were presented at a rate of 3 Hz.

Single-unit recording. Single neurons were found by stimulating with short-duration (2–10 ms), linear FM downsweeps (6–20 kHz BW). Upon initial isolation of a cell, its acoustic threshold (dB SPL), best center frequency (CEF, kHz), eFRA (kHz), and best duration (BD, ms) were determined. Acoustic threshold was defined as the minimum SPL to evoke spiking in 50% of trials, and once determined all other response parameters were collected at +10 dB above threshold to minimize recruiting neural activity from ipsilateral (i.e., typically inhibitory) auditory pathways and to standardize the level of suprathreshold excitation (and sideband inhibition, if present). The best CEF evoked the highest spike count at +10 dB above threshold and was determined with constant-BW, constant-duration FM sweeps varied in CEF (note: the best CEF is similar to the characteristic frequency and/or best excitatory frequency of an auditory neuron measured with pure tones). The eFRA was defined as the lowest and highest CEFs where spike counts fell to ≤50% of the peak count at the best CEF at +10 dB re threshold. The BD was defined as the duration of the best CEF stimulus evoking the highest spike count at +10 dB re threshold. Acoustic testing was conducted in blocks of trials consisting of 10–20 repetitions per stimulus variable increment. Spectral tuning was measured with BD pulses varied in 0.5- to 1-kHz steps. Temporal tuning was measured with best CEF pulses varied in 0.5- to 1-ms steps. To minimize the effects of spontaneous activity, responses were windowed so that spikes were counted only if they were evoked between stimulus onset and 50 ms after stimulus offset. Data analysis was conducted off-line with automated custom MATLAB and Python scripts.

Sweep direction and rate selectivity. A neuron's directional selectivity and baseline FM sweep BW were determined with best CEF, BD FM pulses that were varied in sweep direction (up vs. down) and BW (1.0- to 4.0-kHz increments) so that cells were presented with FM upsweeps, a CEF pure tone, and FM downsweeps. For each cell we calculated a direction selectivity index (DSI) as

$$\mathrm{DSI} = (D - U)/(D + U)$$

where D and U are the maximum evoked spike counts to downward (D) and upward (U) FM sweeps, respectively (Britt and Starr 1976; O'Neill and Brimijoin 2002). The DSI is not necessarily calculated at the same sweep rate for the D and U directions because a cell's peak response could occur at different BWs (Razak and Fuzessery 2006). The cutoffs defining a cell's baseline FM BW were defined as the lowest and highest frequencies evoking 50% of the peak count (see Morrison et al. 2014; Sayegh et al. 2012). To ensure that we did not include classic pure-tone DTNs, our study excluded cells that responded only to pure tones and/or whose unmanipulated (i.e., baseline) FM BW was <4 kHz at +10 dB re threshold.

In temporally tuned FM cells, spike counts plotted as a function of stimulus duration appear similar to the duration tuning (filter) characteristics of short-pass, band-pass, and long-pass pure-tone DTNs (see Aubie et al. 2009, 2012; Sayegh et al. 2011). Indeed, the temporal selectivity of FM cells can be described as slow pass, band pass, or fast pass when spike counts evoked at each FM duration are plotted as a function of the FM BW traversed per stimulus duration (i.e., the FM sweep rate, kHz/ms; Fuzessery et al. 2006). By definition, the best FM sweep rate evokes maximal spiking. Slow-pass rate-selective neurons, which also exhibit long-pass duration tuning, respond maximally at the best FM sweep rate (or range of sweep rates), with spike counts dropping to ≤50% of the maximum at rates faster than the best rate. Band-pass rate-selective neurons, which also exhibit band-pass duration tuning, respond maximally at the best FM sweep rate (or range of sweep rates), with spike counts dropping to ≤50% of the maximum at sweep rates both slower and faster than the best rate. Fast-pass rate-selective neurons exhibit short-pass duration tuning. Strictly speaking, fast-pass neurons do not have a best FM sweep rate; they respond only when the sweep rate exceeds some minimum rate. But all fast-pass cells have a FM duration (or range of durations) that evokes peak spiking, which we have defined as the FM sweep rate at BD. It is important to note that a fast-pass rate selectivity function can change to band pass when a cell is tested with very short-duration FM signals. Our study used BWs ranging from 2 to 48 kHz (0.5- to 2-kHz increments) over 1 to 80 ms (0.5- to 2.0-ms increments), yielding FM sweep rates that could vary from 0.025 to 48 kHz/ms, depending on the cell.

Data analysis. We used several measures to determine whether so-called FM DTNs were tuned to stimulus duration or the rate of FM. First, a duration tuning function (spike count vs. stimulus duration) was collected for each cell with best CEF and baseline FM BW pulses presented at +10 dB re threshold. This allowed us to define a BD (or range of durations) and calculate the FM sweep rate at BD for every cell. To distinguish between FM duration tuning and FM rate tuning, FM sweeps were varied over the same range of signal durations but with the baseline BW altered—either doubled or halved relative to baseline—while the CEF and SPL were held constant. This allowed us to independently manipulate the FM sweep rate over the same range of signal durations for each cell (Faure et al. 2018). If a neuron was FM duration tuned, then its BD (or range of excitatory signal durations) should not vary with changes in FM BW; however, if a neuron was FM sweep rate tuned, then its BD (or range of excitatory signal durations) should vary linearly with changes in FM BW, with wider BWs evoking spikes primarily at longer FM durations and narrower BWs evoking spikes at shorter FM durations (Fig. 1). Our study necessitated comparing data collected from the same cell across treatments; hence cells were tested with only three BW variants.

Bayesian comparison of FM duration tuning and FM rate tuning. To quantify the evidence for FM rate tuning vs. FM duration tuning, we used a Bayesian analysis (Sivia and Skilling 2006) to compare two hierarchical models (*hypotheses* H_1 and H_2):

H_1: Neurons are FM duration tuned, with best FM durations (μ_i) log-normally distributed around a population mean (M) with standard deviation (S). Independent of the FM BW, the measured FM BD values for *neuron i* are normally distributed around μ_i, with a measurement error (σ) = 2 ms (±1 ms, the duration step size).

H_2: Neurons are FM sweep rate tuned, with best FM sweep rates (r_i) log-normally distributed around a population mean (M) with standard deviation (S). The measured BD values for *neuron i* are normally distributed around BW/r_i, with a measurement error (σ) = 2 ms (±1 ms, the duration step size).

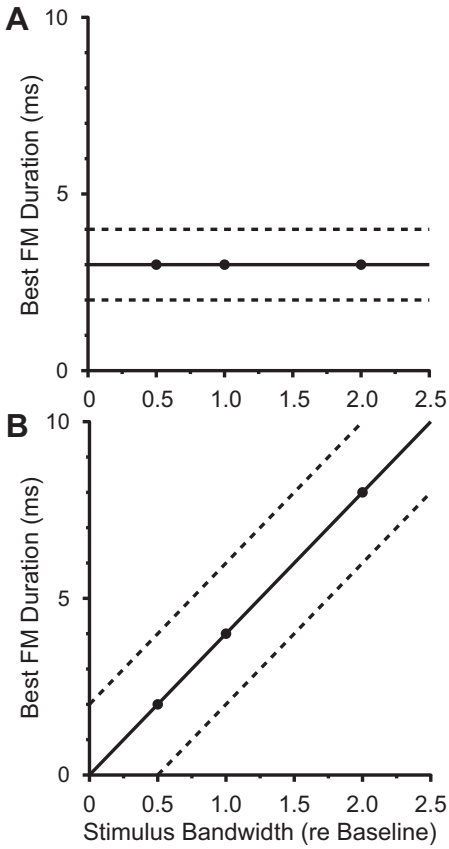

Fig. 1. Visual representation of theoretical hypotheses H_1 and H_2. *A*: in H_1, the cell is assumed to be frequency-modulated (FM) duration tuned so each of its measured best durations remains constant when tested with FM signals that are halved (0.5) or doubled (2.0) in spectral bandwidth (BW) relative to an initial baseline BW (1.0). Thus the cell's best durations should all fall on a horizontal line (solid line) with an intercept representing best duration, μ, within some standard deviation, σ (dashed lines), that represents the measurement error. *B*: in H_2, the cell is assumed to be FM rate tuned with a best FM sweep rate, r, so its measured best durations should increase linearly with the spectral BW such that best duration equals BW/r within some standard deviation, σ.

We computed a Bayes factor (BF) from our data set (D). The BF is the ratio of the marginal likelihoods of our two models and is computed as

$$\mathrm{BF} = P(\mathrm{D}|H_2)/P(\mathrm{D}|H_1)$$

where the numerator is the probability of observing the data set given H_2 and the denominator is the probability of observing the data set given H_1. When the BF is >1 the data favor H_2; otherwise the data favor H_1 (i.e., BF < 1). Within each model, we set step-function priors over hyperparameters M and S. For H_1, the prior over M was uniform from 0 to 3 ln(ms) and the prior over S was uniform from 0.1 to 2 ln(ms). For H_2, the prior over M was uniform from −1 to 2 ln(kHz/ms) and the prior over S was uniform from 0.1 to 2 ln(kHz/ms). We defined data point $d_{i,k}$ = best FM sweep duration obtained from *neuron i* at sweep BW *k*; $\mathrm{BW}_{i,k}$ = FM sweep BW associated with $d_{i,k}$; D_i = the set of all data from *neuron i* (i.e., $\{d_{i,k}\}$); $\mathrm{D}_{<i}$ = the set of all data from all neurons before *neuron i* (i.e., D_1, D_2, ..., D_{i-1}); and D = entire data set of all neurons: (i.e., $\{\mathrm{D}_i\}$). We discretized M, S, μ, and r and computed the marginal likelihoods for each model.

The marginal likelihood for *model* H_1 was computed as

$$p(\mathrm{D}|H_1) = \prod_{i=1}^{35} p(\mathrm{D}_i|\mathrm{D}_{<i},H_1) = \prod_{i=1}^{35}\left[\sum_{\mu_i} p(\mathrm{D}_i|\mu_i,H_1)p(\mu_i|\mathrm{D}_{<i},H_1)\right]$$

where

$$p(\mathrm{D}_i|\mu_i,H_1) = \prod_{k=1}^{3}\frac{1}{\sqrt{2\pi}\sigma}\exp\left[-\frac{(d_{i,k}-\mu_i)^2}{2\sigma^2}\right]$$

and

$$p(\mu_i|\mathrm{D}_{<i},H_1) = \sum_{\mathrm{M,S}} p(\mu_i|\mathrm{M,S},H_1)p(\mathrm{M,S}|\mathrm{D}_{<i},H_1) = \sum_{\mathrm{M,S}}\frac{\mathrm{d}\mu}{\mu_i\sqrt{2\pi}\mathrm{S}}\exp\left[-\frac{(\ln\mu_i-\mathrm{M})^2}{2\mathrm{S}^2}\right]p(\mathrm{M,S}|\mathrm{D}_{<i},H_1)$$

The posterior over (M,S) was updated iteratively with Bayes' rule:

$$p(\mathrm{M,S}|\mathrm{D}_i,\mathrm{D}_{<i},H_1) = \frac{p(\mathrm{D}_i|\mathrm{M,S},H_1)p(\mathrm{M,S}|\mathrm{D}_{<i},H_1)}{\sum_{\mathrm{M,S}} p(\mathrm{D}_i|\mathrm{M,S},H_1)p(\mathrm{M,S}|\mathrm{D}_{<i},H_1)}$$

where

$$p(\mathrm{D}_i|\mathrm{M,S},H_1) = \sum_{\mu_i} p(\mathrm{D}_i|\mu_i,H_1)p(\mu_i|\mathrm{M,S},H_1)$$

The marginal likelihood for *model* H_2 was computed in a similar fashion:

$$p(\mathrm{D}|H_2) = \prod_{i=1}^{35} p(\mathrm{D}_i|\mathrm{D}_{<i},H_2) = \prod_{i=1}^{35}\left[\sum_{r_i} p(\mathrm{D}_i|r_i,H_2)p(r_i|\mathrm{D}_{<i},H_2)\right]$$

$$p(\mathrm{D}_i|r_i,H_2) = \prod_{k=1}^{3}\frac{1}{\sqrt{2\pi}\sigma}\exp\left\{-\frac{\left[d_{i,k}-(\mathrm{BW}_{i,k}/\mathrm{r}_i)\right]^2}{2\sigma^2}\right\}$$

$$p(r_i|\mathrm{D}_{<i},H_2) = \sum_{\mathrm{M,S}} p(\mathrm{r}_i|\mathrm{M,S},H_2)p(\mathrm{M,S}|\mathrm{D}_{<i},H_2) = \sum_{\mathrm{M,S}}\frac{\mathrm{dr}}{\mathrm{r}_i\sqrt{2\pi}\mathrm{S}} \times \exp\left[-\frac{(\ln\mathrm{r}_i-\mathrm{M})^2}{2\mathrm{S}^2}\right]p(\mathrm{M,S}|\mathrm{D}_{<i},H_2)$$

$$p(\mathrm{M,S}|\mathrm{D}_i,\mathrm{D}_{<i},H_2) = \frac{p(\mathrm{D}_i|\mathrm{M,S},H_2)p(\mathrm{M,S}|\mathrm{D}_{<i},H_2)}{\sum_{\mathrm{M,S}} p(\mathrm{D}_i|\mathrm{M,S},H_2)p(\mathrm{M,S}|\mathrm{D}_{<i},H_2)}$$

$$p(\mathrm{D}_i|\mathrm{M,S},H_2) = \sum_{\mathrm{r}_i} p(\mathrm{D}_i|\mathrm{r}_i,H_2)p(\mathrm{r}_i|\mathrm{M,S},H_2)$$

Additional statistical analysis. Conventional statistical tests were calculated with IBM SPSS Statistics version 20. Independent-samples *t*-tests were used to compare FM rate tuning response classes. Pearson's correlation coefficient (R) was used to report the strength of association between two variables, and the coefficient of determination (R^2) was used to report the proportion of the variance in the dependent variable that is predicted from the independent variable.

RESULTS

Organization and response properties. We recorded responses from 46 temporally selective FM neurons from the IC of *E. fuscus*. All neurons responded to FM signals and had their best CEF within the spectral range of the fundamental acoustic element of the bat's echolocation call (20–70 kHz). Tonotopic organization is a well-known property of mammalian auditory systems, in which neurons along a spatial gradient within a brain nucleus are organized by characteristic frequency or best excitatory frequency. This finding has been repeatedly demonstrated in the central auditory system of bats (Casseday and Covey 1992; Haplea et al. 1994; Jen and Wu 2006; Grothe et al. 2001; Morrison et al. 2014). Our results confirm that FM neurons with duration selectivity were also tonotopically organized in the IC, with CEFs showing a strong positive relation to electrode depth (Fig. 2; $R^2 = 0.6572$, $P < 0.001$). Visual inspection of the data reveals that a high proportion of units had CEFs clustered within the spectral range from 25 to 40

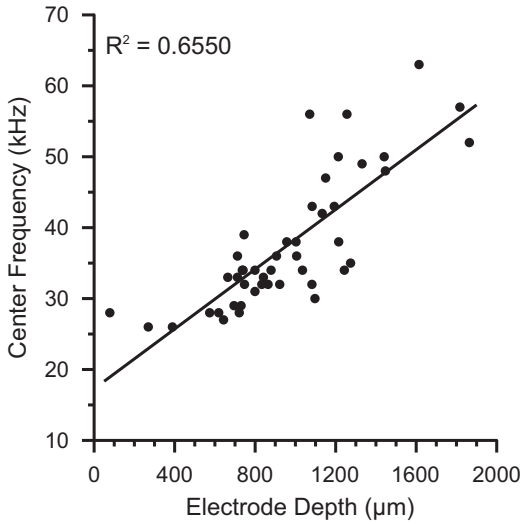

Fig. 2. Tonotopic organization of so-called frequency-modulated (FM) duration-tuned neurons in the inferior colliculus of *E. fuscus*. Note the cluster of data points between 500 and 1,300 μm with center frequencies between 25 and 40 kHz. This spectral range encompasses the frequency band of the fundamental acoustic element of the bat's FM echolocation calls, which sweep down in frequency from 50 to 20 kHz. $n = 46$ neurons.

kHz, and this BW largely overlaps the frequencies of the fundamental acoustic element of the downward FM sweeps of the echolocation calls of *E. fuscus* (Casseday and Covey 1992; Simmons et al. 1979, Surlykke and Moss 2000).

Acoustic thresholds of FM neurons with duration selectivity were also spatially organized (Fig. 3*A*). There was a positive correlation between acoustic threshold and CEF ($R = 0.3565$, $P < 0.001$, $n = 46$). This relationship was more variable than that for tonotopy, with the greatest variation occurring within the frequency band from 25 to 40 kHz. One possibility is that this correlation may be influenced by outer and middle ear filter function gains because the distribution of thresholds is similar to the shape of the behavioral audiogram of *E. fuscus* (Koay et al. 1997).

Other spectral and temporal auditory response properties showed evidence of a spatial organization. There was a modest linear relation between the baseline FM sweep rate and the neuronal CEF (Fig. 3*B*; $R = 0.5649$, $P < 0.001$, $n = 43$), demonstrating that neurons with higher CEFs responded to faster sweep rates. The baseline FM BW was also positively related to the neuronal CEF (Fig. 3*C*; $R = 0.4618$, $P = 0.001$, $n = 42$), revealing that cells tuned to higher CEFs responded to a wider range of frequency excursions, suggesting selectivity for faster rates of FM. Importantly, across the population of cells tested, our initial measure of a cell's eFRA (determined with constant-BW, constant-duration FM sweeps varied in CEF) was positively related to the final baseline FM BW that was later used and systematically altered in our BW manipulation experiment (Fig. 3*D*; $R = 0.6051$, $P << 0.001$, $n = 40$).

We presented neurons with linear FM sweeps that were randomly varied in duration so that the rate of FM also varied while keeping the CEF and BW constant. The majority of cells tested showed band-pass selectivity for FM sweep rate (34/46, 73.9%), with the remaining cells showing fast-pass selectivity (12/46, 26.1%). None of the FM cells we recorded exhibited slow-pass selectivity for FM sweep rates, likely because our sample of temporally selective FM neurons did not include cells with long-pass duration tuning. Cells with band-pass and fast-pass FM rate selectivity differed in several respects. Fast-pass FM neurons were found at deeper electrode depths ($t = 3.866$, $P < 0.001$) and thus were tuned to significantly higher CEFs ($t = 4.510$, $P < 0.001$) compared with FM cells with band-pass rate selectivity (Fig. 4*A*). Fast-pass FM neurons responded to a wider range of CEFs ($t = 2.434$, $P = 0.019$) and were tuned to shorter BDs for FM signals ($t = 2.604$, $P = 0.013$). Importantly, there was a bimodal distribution of rate selectivity, with fast-pass cells exhibiting selectivity for higher FM sweep rates compared with band-pass cells ($t = 5.728$, $P < 0.001$; Fig. 4*B*).

Directional selectivity. We tested neurons for selectivity to the direction of FM sweeps by varying both the sign (FM up vs. FM down) and BW of constant-duration FM signals around the best CEF so that cells were presented with FM upsweeps (positive BWs), a CEF pure tone (BW = 0 kHz), and FM downsweeps (negative BWs). We then computed a DSI in 45 of 46 cells (97.8%; 1 band-pass rate-selective cell was not formally tested). The DSI value can range between −1 and +1, with positive values indicating selectivity for FM downsweeps and negative values indicating selectivity for FM upsweeps. For example, a DSI = 0.6 indicates that a neuron's maximum spiking response to FM downsweeps was four times larger than to FM upsweeps, and a DSI = 0.33 indicates the response to FM down was twice that to FM up.

Two examples of responses of neurons tested for directional selectivity to FM are shown in Fig. 5. The first neuron had a DSI = 1.0 and responded exclusively to FM downsweeps (Fig. 5*A*). This cell did not respond to a CEF pure tone or to FM upsweeps at any BW tested. Peak spiking (2.8 ± 0.5 spikes/stimulus) was evoked by −12- and −16-kHz frequency excursions, and these BWs also yielded the shortest first spike latencies (FSLs; 14.01 ± 0.15 ms and 14.01 ± 0.12 ms, respectively); spikes evoked by larger downward BW excursions were both reduced and delayed. The second neuron had a DSI = 0.30 and exhibited modest selectivity for FM downsweeps (Fig. 5*B*). The cell's responses to CEF pure tones (0.8 ± 0.9 spikes/stimulus) and to FM upsweeps covering an identical range of frequency excursions were both reduced and delayed compared with FM downsweeps. Peak spiking (2.6 ± 1.2 spikes per stimulus) was evoked by −8.0-kHz BW at a short FSL (15.07 ± 0.74 ms). Interestingly, the FSLs evoked at −10 kHz (14.92 ± 0.75 ms) and −12 kHz (14.97 ± 0.84 ms) were slightly shorter even though the spike counts at these BWs were weaker (1.7 ± 0.8 and 1.1 ± 0.7 spikes/stimulus, respectively) compared with −8.0 kHz.

The distribution of DSI values revealed that most IC neurons (42/45, 93.3%) showed a clear directional preference for FM downsweeps (Fig. 5*C*). Indeed, 13 of 45 cells (28.9%) had responses that were exclusive (DSI = 0) and 19 of 45 cells (42.2%) had responses that were nearly exclusive (DSI ≥ 0.85) to downward FM. Only 3 of 45 (0.07%) cells had a DSI < 0 indicating a preference for FM upsweeps, and all were weakly selective (i.e., $-0.3 \leq \text{DSI} < 0$), with none showing exclusive spiking to FM up. Across the population, a CEF pure tone evoked spiking in 15 of 45 cells (33.3%); however, in 5 of these neurons the response was weak (i.e., ≤0.2 spikes/stimulus). Most neurons with fast-pass FM rate selectivity responded to pure tones (8/12, 66.60%), whereas the majority of

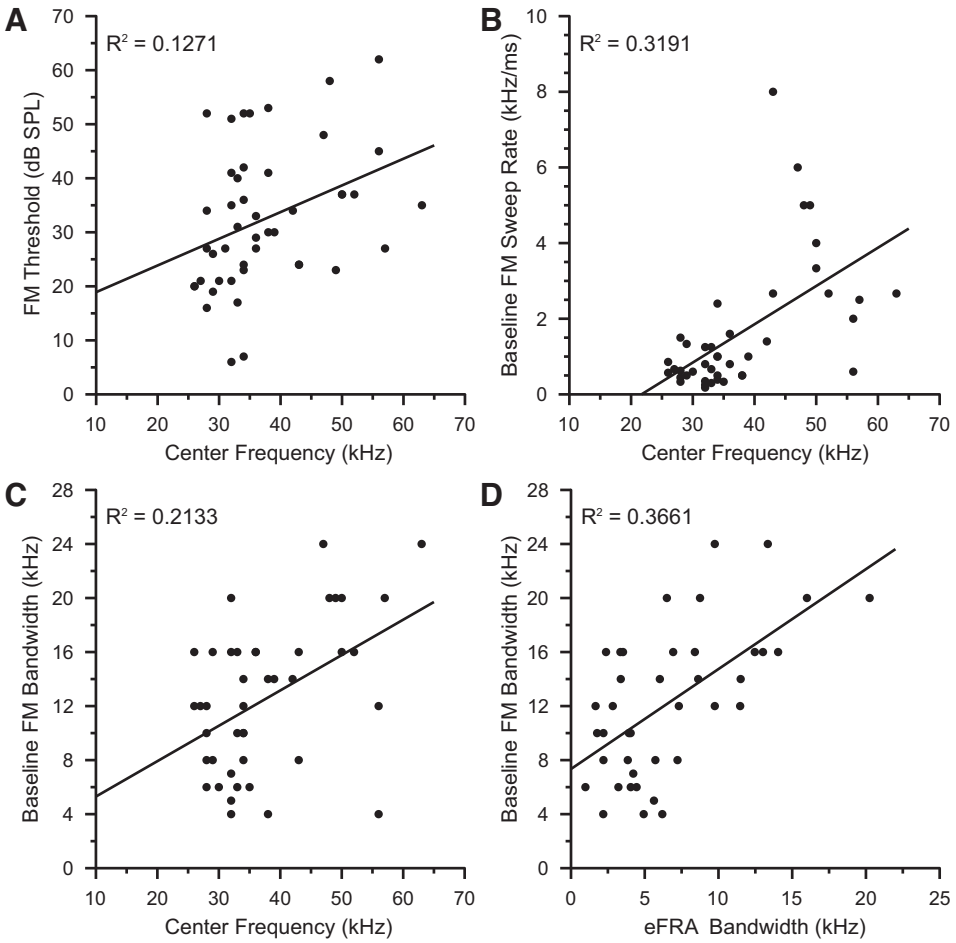

Fig. 3. Organization of response characteristics of temporally tuned frequency-modulated (FM) cells in the inferior colliculus. *A*: there was a positive correlation between neuronal acoustic thresholds and center frequencies (CEFs). There was also a wider range of threshold variability within the CEF range between 25 and 50 kHz, which corresponds to the frequencies in the fundamental acoustic element of the FM echolocation calls of *E. fuscus*. *B*: there was a positive correlation between best FM sweep rate and neuronal CEF. At higher CEFs, there was also greater variability in best FM sweep rates. *C*: there was a positive correlation between best FM sweep bandwidth (BW) and neuronal CEF, indicating that cells tuned to higher frequencies also had larger FM BWs. *D*: there was a positive correlation between the baseline FM BW that was altered in the BW manipulation experiment and our initial estimate of a cell's excitatory frequency response area (eFRA). See text for sample sizes.

cells with band-pass FM rate selectivity did not (only 7/33, 21.2%). The distribution of DSI values differed significantly between fast-pass ($n = 12$) and band-pass ($n = 33$) rate-selective neurons (Fig. 5*C*). Cells with a DSI ≥ 0.6 were classified as downward FM specialists. Most neurons (27/33, 81.8%) with band-pass FM rate selectivity were classified as downward FM specialists, whereas most fast-pass rate selective cells were not (only 4/12; 33.3%).

FM duration vs. FM rate tuning. To determine whether the responses of FM cells were selective to stimulus duration or the rate of FM, we presented cells with variable-duration FM signals at three standardized BWs—the baseline BW, one-half the baseline BW, and double the baseline BW—so that the rate of FM covaried. Figure 6 shows dot raster displays of two cells tested with this paradigm. Responses from the first cell reveal tuning to FM duration because the BD was 2 ms in each BW treatment, evoking spike counts of 2.2 ± 1.0 (1/2BW), 3.1 ± 0.9 (baseline BW), and 2.0 ± 0.5 ($2 \times$ BW) spikes per stimulus (Fig. 6*A*). The FSLs at this BD were also fairly constant at 8.30 ± 0.55 (1/2BW), 7.73 ± 0.32 (baseline BW), and 8.15 ± 0.40 ms ($2 \times$ BW). In this cell spikes always occurred after signal offset, and FSLs were always longer than the BD. Responses from the second cell show neural tuning to the FM sweep rate because the BD (and range of temporal selectivity) increased linearly from 5.0 (1/2 BW) to 10.0 (baseline BW) to 20 ms ($2 \times$ BW) across the BW treatments (Fig. 6*B*). The FSLs at BD also increased from 9.53 ± 0.16 (1/2 BW) to 12.01 ± 0.14 (baseline BW) to 17.03 ± 0.21 ms ($2 \times$ BW). Note that spikes occurred during the ongoing portion of the stimulus when the cell was tested with the baseline (Fig. 6*B*, *center*) and double BW (Fig. 6*B*, *right*) stimuli.

Figure 7 shows spike count functions of two neurons evoked in response to baseline BW, one-half baseline BW, and double baseline BW FM signals. The data are plotted as a function of FM duration and FM sweep rate. When plotted as a function of stimulus duration, the peak spike counts of *cell MU74.12* were similar across the standardized BW treatments (Fig. 7*A*). Note how the peaks of each function converged on the same BD of 2 ms (dot rasters for this cell are shown in Fig. 6*A*). When the same data were plotted as a function of the FM sweep rate (sweep rate = BW/duration), the spike count functions at each standardized BW separated, revealing three distinct peaks occurring at different sweep rates (Fig. 7*B*). Because the duration curves of this cell were tolerant to changes in signal BW, these data demonstrate selectivity to FM duration and not FM sweep rate.

In contrast, both the BD and shape of the duration functions of a second cell clearly differed when its spike counts in response to variable-duration FM signals at three standardized BWs were plotted as a function of FM duration (Fig. 7*C*). When the same data were plotted as a function of the FM sweep rate, the spike count functions collapsed and showed the same pattern of excitation at each BW (Fig. 7*D*). Moreover, the maximum spike counts were nearly identical, converging onto the same sweep rate of ~1 kHz/ms. Because the FM sweep rate tuning curves of this cell were tolerant to changes in signal

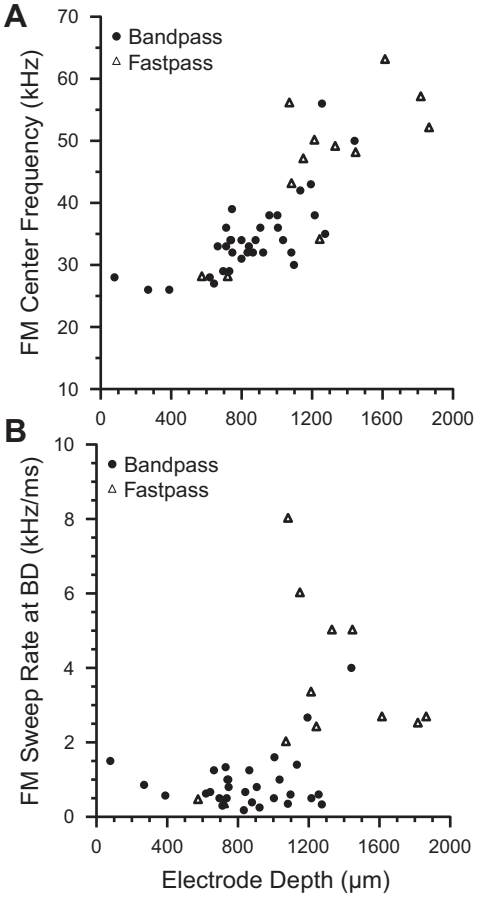

Fig. 4. Neuronal center frequencies (CEFs) and frequency-modulated (FM) sweep rate response selectivity of temporally tuned FM cells. *A*: fast-pass cells were tuned to higher CEFs and were found at deeper electrode depths in the inferior colliculus (IC) than band-pass FM rate selective cells. *B*: fast-pass cells also showed significantly higher absolute best FM sweep rates compared with band-pass FM rate-selective cells. From these plots it is evident that there is a shift from band-pass FM rate tuning to fast-pass FM rate tuning in the IC at electrode depths below ~1,200 μm. $n = 46$ neurons. BD, best duration.

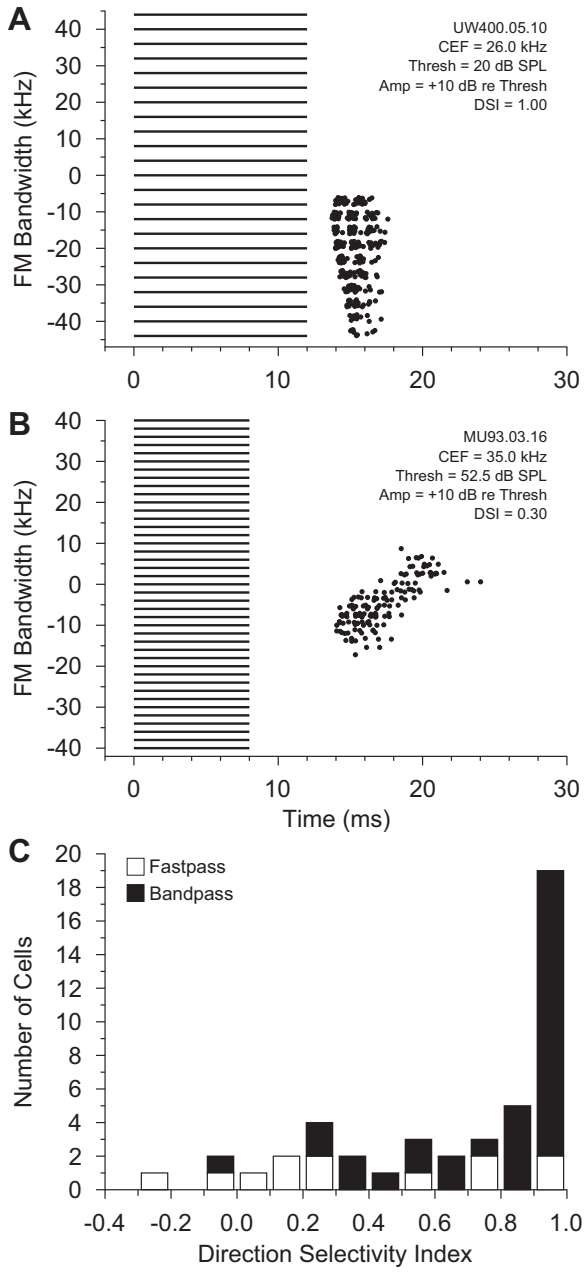

Fig. 5. Directional selectivity of inferior colliculus neurons for frequency-modulated (FM) sweeps. *A* and *B*: dot raster displays of 2 band-pass rate-selective neurons responding to constant-duration signals that were varied in bandwidth (BW) around the center frequency (CEF); positive BWs represent upward FM sweeps, BW = 0 represents a CEF pure tone, and negative BWs represent downward FM sweeps. *A*: example neuron with a direction selectivity index (DSI) = 1.00 that responded exclusively to FM downsweeps (BW step size = 4.0 kHz). The peak spike count occurred at 2 BWs, −6.0 and −8.0 kHz, with both yielding the shortest first spike latencies (FSLs). *B*: example neuron with a DSI = 0.30 that preferred FM downsweeps (BW step size = 2.0 kHz). This cell also responded, albeit more weakly, to FM upsweeps and a CEF pure tone. The peak spike count occurred at a BW of −4.0 kHz, which also yielded close to the shortest FSL. *C*: distribution of DSI values of 45 FM neurons showing fast-pass ($n = 12$) or band-pass ($n = 33$) rate selectivity. Negative DSI values indicate a response preference for FM upsweeps (see METHODS for DSI calculation). Most neurons preferred FM downsweeps.

BW, these data demonstrate neural selectivity to FM sweep rate but not FM duration. As revealed in the next analysis, most of the FM cells that we recorded from showed this response pattern.

Bayesian comparison of FM duration and FM rate tuning. We used a Bayesian model to determine how well the spiking responses of FM neurons matched theoretical models of FM duration and FM sweep rate tuning. For neurons that are tuned to FM duration, and assuming the FM BW falls within the cell's eFRA, then the BD of the cell should be unaffected by changes to the FM sweep BW (H_1; Fig. 1*A*). For neurons that are tuned to the FM sweep rate, the BD should increase as the FM BW broadens. Hence, a sweep rate tuning model predicts a linear increase in BD with increasing FM BW (H_2; Fig. 1*B*).

Example data from two cells illustrating FM duration tuning (H_1) and from two cells illustrating FM rate tuning (H_2) are shown in Fig. 8. For the cells in Fig. 8, *A* and *B*, a hypothesis of FM duration tuning (H_1) was better supported by the data than a hypothesis of FM rate tuning (H_2) because each cell's measured BD either remained constant (e.g., *MU74.12*) or nearly constant (e.g., *MU74.16*) as the FM sweep BW increased. The data points from each cell were better estimated

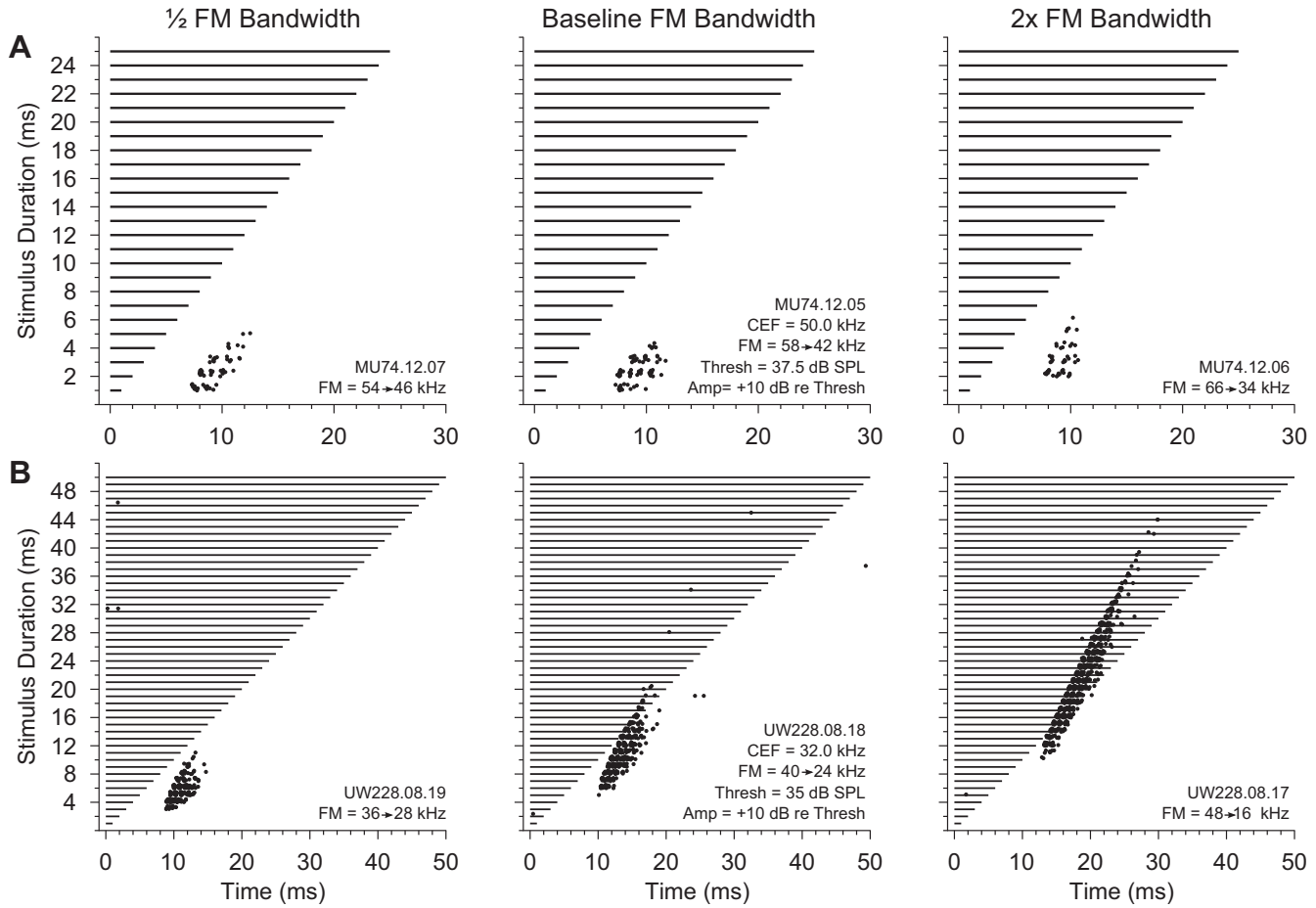

Fig. 6. Testing for neuronal selectivity to stimulus duration and/or rate of frequency modulation (FM). Dot raster displays of spiking from 2 temporally selective inferior colliculus neurons presented with variable-duration, downward FM sweeps of constant center frequency (CEF) at +10 dB above threshold at 3 standardized bandwidths (BWs): one-half the baseline BW (*left*), the baseline BW (*center*), and twice the baseline BW (*right*). Cell ID, CEF, and FM stimulus details are shown. *A*: responses from a band-pass rate-selective neuron tuned to FM duration. The best duration (BD) was constant (2 ms) and the first spike latency (FSL) at BD remained nearly constant (~8 ms) across BW treatments, with spikes occurring after signal offset and at a FSL longer than the BD. n = 10 trials per stimulus. *B*: responses from a band-pass rate-selective neuron tuned to FM sweep rate. Both the BD and FSL at BD increased with signal BW. Note the spiking that occurs during the ongoing portion of the stimulus when the cell was tested with baseline and wideband FM. n = 15 trials per stimulus.

by a horizontal line with a slope of 0 than by a line with a positive slope and an origin at 0 (the duration tuning and rate tuning curves for *MU74.12* are shown in Fig. 7, *A* and *B*). The fits demonstrate that the likelihood of obtaining these results was much higher given a FM duration tuning hypothesis (H_1) than given a FM rate tuning hypothesis (H_2).

Conversely, for the cells shown in Fig. 8, *C* and *D*, a hypothesis of FM rate tuning (H_2) was better supported than a hypothesis of FM duration tuning (H_1) because in both neurons the measured BD increased as a function of the FM sweep BW in a roughly linear manner. For both cells, the three data points were better estimated by a linear function with an origin at 0 than by a horizontal line with a nonzero intercept (the duration tuning and rate tuning curves for *MU68.04* are shown in Fig. 7, *C* and *D*). The fits demonstrate that the likelihood of obtaining these results was much higher given a FM rate tuning hypothesis (H_2) than a FM duration tuning hypothesis (H_1).

We conducted a Bayesian analysis to quantitatively determine whether the BW manipulation data supported a FM duration tuning (H_1) or a FM rate tuning (H_2) hypothesis. We calculated the marginal likelihood of obtaining the data set given either hypothetical model. The ratio of marginal likelihoods was the BF expressing the degree of support for H_2 relative to H_1. When we evaluated the spiking responses of the entire population of FM units it was evident that in most cells the BD for FM signals increased with increasing FM BW (Fig. 9*A*), whereas only a few neurons displayed increasing best FM sweep rates with changes in signal BW (Fig. 9*B*). Our Bayesian model comparison considered that all neurons were either FM duration tuned (H_1) or FM rate tuned (H_2). Given only these possibilities, the calculated BF of 7×10^{122} provided overwhelming support for the FM rate tuning model (i.e., H_2).

We further explored our models to determine whether the responses of a subset of neurons were tuned to the duration of FM stimuli. We did this by calculating a BF for each neuron individually and disregarded the data from other cells in the computation. The median individual neuronal BF was 63 (n = 35). In total, 27 neurons had a BF $>$ 1, and 8 neurons had a BF $<$ 1. Thus when cells were considered individually, a clear majority (77%) were classified as FM rate tuned, with a minority as FM duration tuned.

In some neurons the calculated BF was close to 1, indicating that one model was only slightly favored over the other. To remove the influence of cells with weak support for a model,

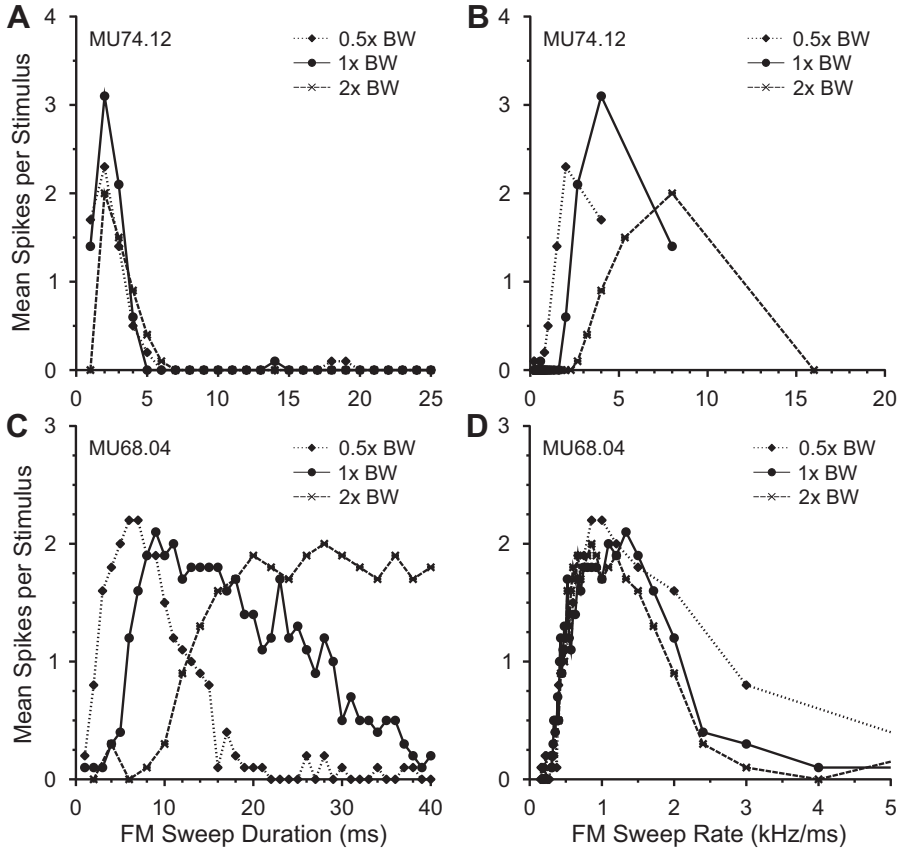

Fig. 7. Spike count functions from 2 temporally selective frequency-modulated (FM) cells as a function of FM sweep duration (*A* and *C*) or FM sweep rate (*B* and *D*). Each plot shows the mean spikes per stimulus at +10 dB above threshold in response to FM pulses randomly varied in duration and presented in 3 blocks of trials where the sweep bandwidth (BW) was set to be the baseline BW (1 × BW), one-half the baseline BW (0.5 × BW), or double the baseline BW (2 × BW). The best duration stimulus is the FM duration evoking the maximum spike count, and the best sweep rate stimulus is the FM sweep rate evoking the maximum spike count at each BW. *A* and *C*: spike counts as a function of stimulus duration. *B* and *D*: spike counts as a function of FM sweep rate (FM rate = BW/duration). *A* and *B*: responses from *cell MU74.12* (n = 15 trials/stimulus) were duration tuned and tolerant to changes in FM BW because spike counts collected at each BW converged when plotted as a function of stimulus duration but not when plotted as a function of the FM sweep rate. *C* and *D*: in contrast, responses from *cell MU68.04* (n = 10 trials/stimulus) were not FM duration tuned because the spike counts collected at each BW did not converge when plotted as a function of FM duration but did converge when plotted as a function of FM sweep rate.

we used a more stringent criterion and determined the numbers of neurons with BF $>$ 10 and BF $<$ 0.1. The goal of increasing our classification criterion was not to increase the proportion of units classified as FM rate tuned or as FM duration tuned; rather, it was to increase the confidence with which cells could be classified by excluding cells whose BFs provided less confident categorization and support for a model. With this more conservative classification, 18 neurons had a BF $>$ 10, 3 neurons had a BF $<$ 0.1, and 14 neurons were excluded from the analysis (i.e., 0.1 $<$ BF $<$ 10). Thus 86% of cells were classified with high confidence as FM rate tuned, and only 14% were classified with high confidence as FM duration tuned. Finally, using an even more stringent criterion, we found that 17 neurons had a BF $>$ 100 and none had a BF $<$ 0.01 (18 cells were excluded from the analysis). According to this even more conservative criterion, 100% of cells that were classified with very high confidence were FM rate tuned. In summary, as more stringent criteria were applied our analyses discovered that most FM neurons in the IC of *E. fuscus* could be classified with high or very high confidence as being FM rate tuned, with fewer cells being classified with high confidence as being FM duration tuned.

DISCUSSION

The auditory midbrain contains a population of neurons with patterns of spiking in response to variable-duration FM sweeps that appear to be similar to the pattern of spiking of classic DTNs in response to variable-duration pure tones. This is the first study to test cells with FM sweeps that were systematically manipulated to encompass both BW increases and decreases in determining whether the temporally selective responses of FM neurons were tuned to the duration or rate of FM. Our results confirm that FM sweep rate selectivity was the dominant parameter of temporal tuning for FM cells in the IC of *E. fuscus*. Although most neurons had spiking responses that could be initially classified as tuned to either FM duration or FM sweep rate, it became clear that the overwhelming majority of cells in the IC did not maintain their duration selectivity at altered stimulus BWs. Instead, the responses were selective to the direction and rate of FM, with most cells showing a clear directional preference for FM downsweeps, although we acknowledge that our choice of search stimuli—short duration, downward FM signals—may have biased against finding cells with selectivity to longer durations and FM upsweeps. This main finding was further supported by our Bayesian modeling results, which classified the majority of FM selective neurons as tuned to the FM sweep rate. The IC has several populations of neurons performing different computational tasks, and the Bayesian approach employed in our study is also valid to test for other types of more complex response selectivity.

Cellular organization in the inferior colliculus. Like other types of central auditory neurons, cells responsive to the rate of FM were tonotopically organized. (Fig. 2). Interestingly, >75% of the cells we tested had best CEFs between 25 and 45 kHz—a spectral band important for target ranging and corresponding to the fundamental acoustic element of the FM echolocation calls of *E. fuscus* (Simmons et al. 1979; Surlykke and Moss 2000). To confirm the generality of our findings, future studies employing a similar methodology should record from FM neurons with CEFs closer to the tonotopic boundaries

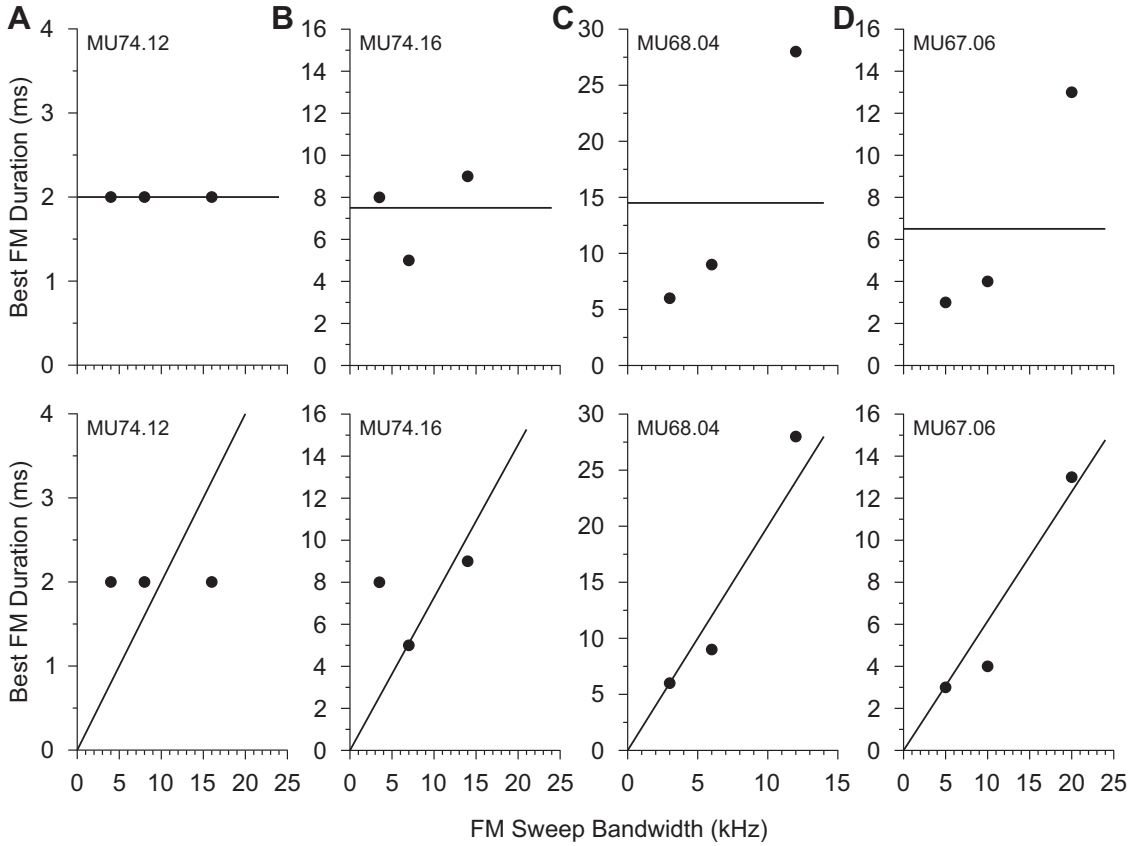

Fig. 8. Bayesian estimation of best duration (BD) as a function of stimulus bandwidth (BW) under 2 models of temporal tuning in 4 frequency modulation (FM)-selective neurons. Each plot shows the BD measured at +10 dB (re threshold) in response to variable-duration FM sweeps presented at 3 standardized BWs (see Fig. 6): one-half the baseline BW (0.5 × BW), the baseline BW (1 × BW), and double the baseline BW (2 × BW). The BD values (●) are plotted against the expected neuronal selectivity (solid line) under 2 theoretical models of temporal tuning (see Fig. 1). *Top*: a duration model (H_1) predicts no change in BD with increasing FM BW, so measured BD values are expected to fit a horizontal line (i.e., slope = 0) with a *y*-intercept that represents the neuronal BD. *Bottom*: a FM rate tuning model (H_2) predicts a linear increase in BD with increasing FM BW, so measured BD values are expected to fit a line with a positive slope, with the *y*-intercept constrained to 0. Each line is a "constrained regression" that depicts the data under a given temporal tuning hypothesis. *A* and *B*: for example *cells MU74.12* and *MU74.16*, visual inspection of the data suggests a FM duration tuning hypothesis. In support of this conclusion, the Bayes factors (BFs) calculated for these neurons were BF = 0.553 and BF = 0.067, respectively. *C* and *D*: for example *cells MU68.04* and *MU67.06*, visual inspection of the data suggests a FM rate tuning hypothesis. In support of this conclusion, the BFs calculated for these neurons were BF = 1.302×10^{14} and BF = 890, respectively.

of the IC and/or in other species. We observed several population-level organizational patterns that suggest that FM cells may play an important role in processing echolocation signals. Acoustic thresholds, response selectivity for FM sweep rates, and best FM BWs all increased with increasing CEFs (Fig. 3). In the context of echolocation, FM cells with lower CEFs would respond best to the long-duration, narrowband biosonar pulses that *E. fuscus* emit while searching for prey. Cells tuned to higher CEFs would respond best to the short-duration, broadband FM pulses that bats emit while closing on prey (Surlykke and Moss 2000).

The organization of temporal response parameters in the population of FM cells we tested also suggests of a role in echolocation. For example, temporal tuning for FM sweep rates changed abruptly in the IC below a depth of ~1,200 μm (Fig. 4*B*), and the spatial organization of fast-pass and band-pass cells suggests that the IC contains two functionally distinct groups of temporally selective FM neurons. Fast-pass cells were tuned to higher CEFs than band-pass cells (Fig. 4). Fast-pass cells were also selective for faster sweep rates. Although this latter result may seem obvious, it is important to remember that the term "fast pass" describes the shape of a cell's FM filter characteristic and is not directly related to specific FM sweep rates. For example, the FM filter function of a fast-pass cell could peak at a very low FM sweep rate, but the cell could still be responsive to a broader range of FM sweep rates than a band-pass cell whose response selectivity peaks at an absolutely higher FM sweep rate.

Our findings suggest that the IC of *E. fuscus* contains two subgroups of rate-selective neurons that may be specialized for different roles in the processing of FM sweeps. Band-pass cells could function as narrow auditory filters for the detection and identification of specific FM sweep rates, while fast-pass cells could function as broad auditory filters for the detection of FM signals that meet or exceed some minimum FM sweep rate. In terms of echolocation by *E. fuscus*, band-pass cells could be specialized for the detection of echoes of calls emitted during the search phase of foraging. Search-phase calls start at ~50 kHz and sweep downward to ~20 kHz over 10–20 ms (Surlykke and Moss 2000); thus they have relatively slow FM sweep rates varying between ~1 and 3 kHz/ms. In our data set, all but one band-pass cell was tuned to FM sweep rates <3 kHz/ms (Fig. 4*B*). During the search phase of echolocation, tuning for slow FM sweep rates may help bats discriminate

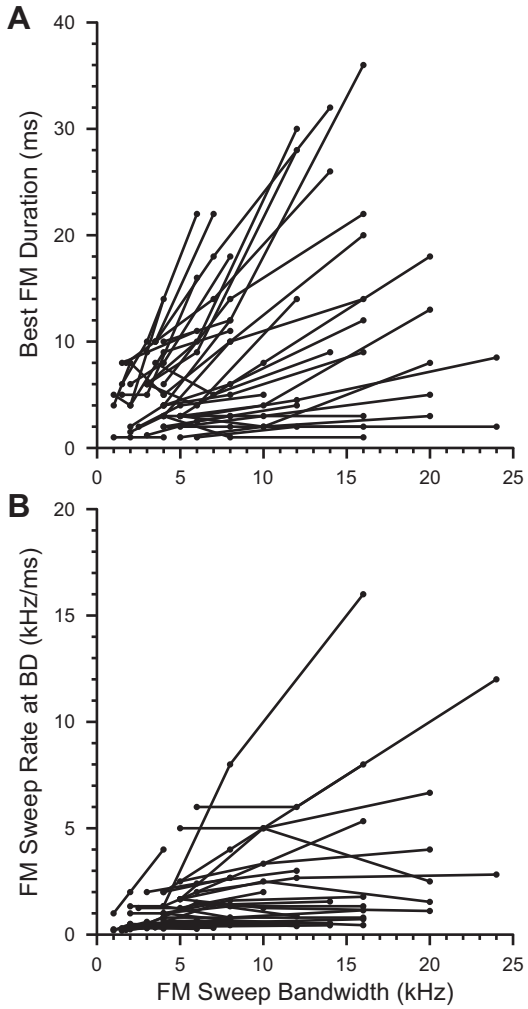

Fig. 9. Midbrain frequency-modulated (FM) best duration (BD) tuning and FM sweep rate tuning in response to FM signals systematically varied in bandwidth (BW). *A*: individual neuronal BDs (i.e., the FM signal duration that evoked maximal spiking) measured at 3 standardized BWs. In almost every case, the cell's BD increased as the FM BW increased, demonstrating that FM duration was not tolerant to changes in signal BW. *B*: individual neuronal best FM sweep rates (i.e., the FM signal sweep rate that evoked maximal spiking) measured at 3 BWs. In most cells, the best FM sweep rate remained constant as the FM BW increased, demonstrating that FM sweep rate tuning was tolerant to changes in signal BW.

echoes of their own calls from those emitted by other bats hunting nearby. Because bats decrease pulse duration and increase signal BW from the search to the approach phase of hunting, FM sweep rates tend to systematically increase (Simmons et al. 1979; Surlykke and Moss 2000). Calls emitted from nearby bats in different phases of hunting are likely to have slightly different FM sweep rates compared with the echoes expected by a bat, and band-pass cells with narrow selectivity for the rate of FM may assist in discriminating such subtle differences between signals.

Fast-pass cells may be specialized for detecting approach-phase and terminal-phase echolocation signals. Increasing FM sweep rates during the approach phase of hunting makes these signals less similar to the search-phase calls emitted by nearby bats. Fast-pass cells were broadly tuned, with spectral BWs spanning the range of frequencies emitted by *E. fuscus* during the approach and terminal phases of aerial hunting. The BWs of approach-phase echolocation calls vary between ~20 and 40 kHz over durations from ~3 to 10 ms, encompassing FM sweep rates that range between ~2 and 13 kHz/ms. Terminal buzz-phase calls have BWs varying between ~15 and 30 kHz over durations from ~0.5 and 3 ms, resulting in FM sweep rates ranging between ~5 and ≥60 kHz/ms (Surlykke and Moss 2000). In the terminal phase, the bat has already acquired (i.e., detected) its target, so the goal is to hone in and capture the prey. As the bat closes, it receives echoes with increasingly faster FM sweep rates that arrive at shorter time delays (Simmons et al. 1979). In combination with delay-tuned neurons from the IC whose responses are selective to specific pulse-echo intervals (Dear and Suga 1995), fast-pass cells may also help to process echoes received during the terminal feeding buzz phase of echolocation.

We did not find other patterns of spatial organization for the temporal response parameters of FM cells in the IC. A previous report suggested that FM cells in the IC may be organized along the anterior-posterior plane (Ehrlich et al. 1997), and if this is true then our dorsal-ventral spatial measurements were orthogonal to this cellular organization. Future studies using more detailed spatial measurements in three dimensions are needed to explore this possibility.

Tuning for FM sweep rate or FM duration? Our work was inspired by an earlier study in the IC of *E. fuscus* that reported that some DTNs were tuned to the duration of FM sweeps (Ehrlich et al. 1997). We sought to answer whether these so-called "FM DTNs" were tuned to stimulus duration in the same manner as classic pure-tone DTNs or if they were tuned to the FM sweep rate and thus could be considered an entirely different class of temporally tuned neuron. We used a Bayesian comparison to assess whether our data were better represented by a model assuming FM duration tuning or FM rate tuning. We performed the analysis on each cell individually and on the entire neural population. We found that some cells had responses selective to the duration of FM sweeps; however, across the population as a whole, the responses of most temporally selective FM cells were better described by a FM rate tuning model. Furthermore, every neuron in our sample that could be classified as a FM DTN also responded to pure tones; hence the possibility exists that these cells were simply classic pure-tone DTNs with permissive (broad) frequency tuning that were not excluded by our criteria. We conclude that previous studies on the responses of "FM DTNs" were likely reporting from cells that were tuned to the FM sweep rate.

That FM neurons were better described as rate tuned than duration tuned was not surprising as FM rate tuning has been reported in both the mammalian IC (Ehrlich et al. 1997; Poon et al. 1991) and auditory cortex (Heil et al. 1992; Mendelson et al. 1993; Ricketts et al. 1998). In particular, FM rate tuning has been extensively studied in the auditory pathway of the pallid bat (*Antrozous pallidus*) (Fuzessery 1994), a species with echolocation behavior somewhat similar to *E. fuscus*. Our study reports on a population of FM neurons that are also found in the IC of *A. pallidus*, but in *E. fuscus* there appears to be an emphasis on cells with a directional preference for downward FM sweeps. Almost half (~42%)of the cells that we recorded from responded exclusively or nearly exclusively to downward FM, and the majority (69%) were classified as downward FM specialists. In contrast, only 13% of cells reported by Fuzessery (1994) were classified as downward FM specialists. Further-

more, only 33% of FM cells in *E. fuscus* were also duration tuned for pure tones, compared with 50–60% of FM cells showing duration selectivity in *A. pallidus*. This difference may reflect differences in the echolocation behavior between the two species. Big brown bats consume small flying insects and rely on echolocation for both orientation and prey detection (Masters et al. 1985; Simmons et al. 1979). In contrast, pallid bats use echolocation for orientation and hunting, but they can also use passive hearing to detect and localize faint prey-generated sounds of orthopteran and coleopteran insects (Fuzessery et al. 1993; Lenhart et al. 2010). Higher central auditory centers of *A. pallidus* appear to separate auditory processing into two distinct streams to analyze both types of sounds (i.e., FM sweeps and broadband noise bursts; Razak et al. 2007), and this may explain why the auditory midbrain of *A. pallidus* shows less specialization for downward FM sweeps compared with *E. fuscus*.

Our study was designed to determine the temporal tuning characteristics of FM cells in the IC of *E. fuscus*; the results demonstrate that an overwhelming majority of so-called FM DTNs were better described as FM rate-tuned neurons. We conclude that sweep rate tuning is the dominant parameter for temporal selectivity of FM cells in the IC of *E. fuscus*. Several mechanisms have been proposed to explain temporal tuning in FM neurons (for a review, see Covey and Casseday 1999), including duration tuning (Fuzessery et al. 2006), asymmetric facilitation (Barlow and Levick 1965; Fuzessery et al. 2006, 2011; Gittelman et al. 2009; Sillito 1977), and delayed high-frequency inhibition (Brimijoin and O'Neill 2005; Fuzessery et al. 2006, 2011; Gordon and O'Neill 1998). It is important to note that mechanisms that create temporal selectivity for FM sweeps are not mutually exclusive, as different mechanisms have been observed within the same neuronal population (e.g., Fuzessery et al. 2006). Although we did not record the necessary data to make conclusions about such underlying neural mechanisms, future electrophysiology studies on FM neurons should use two-tone stimulation and/or neuropharmacological agents to help elucidate the neural mechanisms that create FM rate tuning in the auditory midbrain.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

P.A.F. conceived and designed research; J.A.M., R.V.-R., and P.A.F. performed experiments; J.A.M., R.V.-R., D.G., and P.A.F. analyzed data; J.A.M., R.V.-R., D.G., and P.A.F. interpreted results of experiments; J.A.M. and R.V.-R. prepared figures; J.A.M., R.V.-R., D.G., and P.A.F. drafted manuscript; J.A.M., R.V.-R., D.G., and P.A.F. edited and revised manuscript; J.A.M., R.V.-R., D.G., and P.A.F. approved final version of manuscript.

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