Front. Biol. 2013, 8(2): 198–215
DOI 10.1007/s11515-012-1212-4

REVIEW

The adaptive value of increasing pulse repetition rate during hunting by echolocating bats

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Abstract **During hunting, bats of suborder *Microchiropetra* emit intense ultrasonic pulses and analyze the weak returning echoes with their highly developed auditory system to extract the information about insects or obstacles. These bats progressively shorten the duration, lower the frequency, decrease the intensity and increase the repetition rate of emitted pulses as they search, approach, and finally intercept insects or negotiate obstacles. This dynamic variation in multiple parameters of emitted pulses predicts that analysis of an echo parameter by the bat would be inevitably affected by other co-varying echo parameters. The progressive increase in the pulse repetition rate throughout the entire course of hunting would presumably enable the bat to extract maximal information from the increasing number of echoes about the rapid changes in the target or obstacle position for successful hunting. However, the increase in pulse repetition rate may make it difficult to produce intense short pulse at high repetition rate at the end of long-held breath. The increase in pulse repetition rate may also make it difficult to produce high frequency pulse due to the inability of the bat laryngeal muscles to reach its full extent of each contraction and relaxation cycle at a high repetition rate. In addition, the increase in pulse repetition rate increases the minimum threshold (i.e. decrease auditory sensitivity) and the response latency of auditory neurons. In spite of these seemingly physiological disadvantages in pulse emission and auditory sensitivity, these bats do progressively increase pulse repetition rate throughout a target approaching sequence. Then, what is the adaptive value of increasing pulse repetition rate during echolocation? What are the underlying mechanisms for obtaining maximal information about the target features during increasing pulse repetition rate? This article reviews the electrophysiological studies of the effect of pulse repetition rate on multiple-parametric selectivity of neurons in the central nucleus of the inferior colliculus of the big brown bat, *Eptesicus fuscus* using single repetitive sound pulses and temporally patterned trains of sound pulses. These studies show that increasing pulse repetition rate improves multiple-parametric selectivity of inferior collicular neurons. Conceivably, this improvement of multiple-parametric selectivity of collicular neurons with increasing pulse repetition rate may serve as the underlying mechanisms for obtaining maximal information about the prey features for successful hunting by bats.**

Keywords bat, echolocation, inferior colliculus, multiple-parametric selectivity, pulse repetition rate

Introduction

During hunting, insectivorous bats such as the big brown bat, *Eptesicus fuscus*, emit ultrasonic pulses and listen to the returning echoes as they search, approach and finally catch the localized insects or avoid obstacles (Griffin, 1958; Simmons et al., 1979; Jen and Kamada, 1982; Surlykke and Moss, 2000). Previous studies have shown that insectivorous bats prepare their auditory system to analyze changing echo parameters for successful orientation and prey capture. They progressively shorten the pulse duration to avoid the overlap between the outgoing sounds and returning echoes and they systematically decrease pulse intensity to compensate for progressively increasing echo intensity so as to ensure the echoes reaching the ear at an optimal level (Novick, 1971; Schnitzler and Henson, 1980; Jen and Kamada, 1982; Kobler et al., 1985; Hartley, 1992a, b; Smotherman and Metzner, 2003; Hiryu et al., 2007). They also contract their middle ear muscles and send inhibitory signals from their vocalization center(s) to suppress the sensitivity of midbrain auditory neurons during pulse emission in order to protect their auditory system from overstimulation by the intense self-emitted pulses but to maintain high sensitivity to weak

Received February 24, 2012; accepted March 12, 2012
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returning echoes (Henson, 1965, 1970; Suga and Schlegel, 1972; Suga and Shimozawa, 1974; Suga and Jen, 1975). Furthermore, they appear to establish a time window after pulse emission during which echoes are processed for echo ranging (Roverud and Grinnell, 1985; Roverud, 1989). This time window for echo ranging is reset with every emitted pulse either by a signal from the vocalization system or by listening to self-emitted pulse. All these studies suggest that the bat auditory system is maximally sensitive to changing pulse parameters of the expected echoes returning within this time window for successful prey capture or obstacle avoidance.

Regarding to variation in pulse repetition rate (PRR), these bats emit pulses with long duration (10–20 ms) at a PRR of about 10–20 pulses per second (pps) during the search phase. As they approach the target, they shorten the pulse duration (4–6 ms) and increase the PRR to about 30–40 pps. When they intercept the localized prey during the terminal phase, they further shorten the pulse duration to 1.5–2 ms and increase the PRR to about 90–150 pps. To analyze the increasing number of returning echoes, they must contain neurons that are able to encode the PRR throughout the entire course of hunting. Many studies have shown that most collicular neurons of the echolocating bats have a best pulse repetition rate to which they discharge maximally (Jen and Schlegel, 1982; Pinheiro et al., 1991; Jen et al., 1993; Condon et al., 1994; Wu et al., 1996). These studies show that the best repetition rate of collicular neurons ranging from 1 to 200 pulses per second (pps) covering the PRR occurring throughout the entire course of hunting.

The progressive increase in PRR during hunting would presumably enable the bat to extract maximal information from the increasing number of echoes about the rapid changes in the target or obstacle position for successful hunting. However, the increase in PRR may make it difficult to produce intense short pulse at high repetition rate at the end of long-held breath. The increase in PRR may also make it difficult to produce high frequency pulse due to the inability of the bat's laryngeal muscles to reach its full extent of each contraction and relaxation cycle at a high pulse repetition rate (Novick and Griffin, 1961; Jen and Suga, 1976; Jen et al., 1978). In addition, the increase in PRR increases the minimum threshold (i.e. decrease auditory sensitivity) and response latency of most collicular neurons of the big brown bat, *Eptesicus fuscus* (Chen and Jen, 1994; Jen and Chen, 1998). This increase in the minimum threshold and response latency reduces the sensitivity of these collicular neurons.

In spite of these seemingly physiological disadvantages in pulse emission and auditory sensitivity, bats do progressively increase PRR throughout a target approaching sequence. Then, what is the adaptive advantage of increasing PRR during echolocation? How does increasing PRR help bats obtain maximal information about the target? What are the underlying mechanisms for obtaining maximal information about the target during increasing PRR? How to neurophysiologically study the effect of increasing PRR on multiple-parametric selectivity of auditory neurons?

In acoustic communication or echolocation, naturally occurring sound pulses of many animal species often are in temporally patterned pulse trains rather than in temporal isolation. Because sequential sound pulses within a temporally patterned pulse train typically vary with time in several parameters including intensity, frequency, duration as well as separation and order of individual sounds (Popper and Fay, 1995; Shannon et al., 1995), the response of auditory neurons to an individual sound pulse is inevitably affected by the preceding and succeeding sounds (i.e. forward and backward masking). For this reason, a neuron's response to a single sound pulse in isolation may not predict well its response to the same sound pulse within a more complex temporal patterned pulse train.

For example, the response size of auditory neurons to a sound pulse is decreased if the sound pulse is presented shortly after or before another one (i.e. forward and backward temporal masking) (Hocherman and Gilat, 1981; Phillips et al., 1989; Calford and Semple, 1995; Brosch and Schreiner, 1997; Litovsky and Yin, 1998). Also, the response size of auditory neurons show larger responses to single pulses presented in temporal isolation than to the same pulse presented in temporally patterned pulse trains (Moriyama et al., 1994). Whereas the response size of auditory neurons progressively decreases with sequentially presented sound pulses (de Ribaupierre et al., 1972; Pinheiro et al., 1991; Hou et al., 1992; Moriyama et al., 1994, 1997; Wu and Jen, 1995a, 1996, 2006a,b; Wu et al., 1996; Lu et al., 1997, 1998; Jen and Zhou, 1999; Zhou and Jen, 2000, 2002b, 2004, 2006; Jen et al., 2001, 2002; Jen and Wu, 2005), some other neurons discharge maximally to pulse trains with a specific frequency of amplitude modulation rate (Condon et al., 1994; Feng et al., 1994).

These neurophysiological findings have been corroborated by behavioral studies which show a human subject or an animal only perceives the leading source when two spatially separated clicks are presented with a brief delay within 5 ms (Wallach et al., 1949; Zurek, 1980; Freyman et al., 1991). When the delay between the two sounds is larger than 8–10 ms range, both the leading and lagging sounds are perceived as individual one (Freyman et al., 1991). However, longer delay of several milliseconds is required for perception of individual sounds when tested with trains of paired sounds or when each leading sound is succeeded by several echoes of various time delays (Yost and Soderquist, 1984; Yost and Guzman, 1996). All these studies indicate that when encountered with temporally patterned sequential sound pulses, the separation of individual sounds (i.e. PRR) is an important temporal attribute that determines an animal's ability in perceiving individual sounds.

For this reason, many studies have examined the selectivity of auditory neurons to pulse parameters in temporally patterned pulse trains of sound pulses. In this review article, electrophysiological data are presented to show that increas-

ing PRR of temporally patterned trains of sound pulses changes the auditory response and improves multiple-parametric selectivity of neurons in the central nucleus of the big brown bat, *Eptesicus fuscus*. These changes in auditory response and selectivity may serve as the neural basis underlying successful prey capture by bats. Because of page limitation, the intent of this review article is to describe the adaptive value of increasing PRR during the bat's biosonar behavior mainly based on the research works that my former coworkers and I have performed. The work of others is described only as it seems pertinent and essential for the discussion of the present topic.

Increasing pulse repetition rate changes the response of collicular neurons

In auditory physiology, a neuron's response is affected not only by sound intensity and frequency but also by the temporal pattern of sound pulses. Two studies showed that the number of impulses of collicular neurons either increased non-monotonically (80%, Fig. 1A a, c) or monotonically (20%, Fig. 1Ab) with increasing pulse intensity (Chen and Jen, 1994; Jen and Chen, 1998). Conversely, the latencies of these neurons decreased to a plateau (72%, Fig. 1B b), hardly changed (7%, Fig. 1B c) with increasing pulse intensity or initially decreased to a minimum before increasing again with further increase in pulse intensity (21%, Fig. 1B a).

When determined with a wide range of PRRs at a given intensity, the latency and minimum threshold of most (80%) collicular neurons increased by 1.5–24 ms and 4–75 dB with increasing PRR (Fig. 2 A1, A2, Fig. 3A1, A2). The increase in response latency was either due to GABAergic inhibition or the increase in the minimum threshold which reduced the effectiveness of the given pulse intensity. On the other hand, the latency and minimum threshold of the remaining (20%) neurons were hardly affected by PRR (Figs. 2B1, B2, Fig.3 B1, B2). What is the adaptive value of this change in auditory sensitivity of collicular neurons with increasing PRR during echolocation?

As described earlier, echolocating bats contract their middle ear muscles during pulse emission to attenuate self-stimulation (Henson, 1965, 1970; Suga and Jen, 1975). They systematically increase PRR and reduce pulse intensity as they approach localized targets to compensate for increasing echo intensity for optimal echo reception (Jen and Kamada, 1982; Kobler et al., 1985; Hartley, 1992a, b; Hiryu et al., 2007). They also perform sonar gain control for optimal echo reception by increasing the threshold for target detection and discrimination (Kick and Simmons, 1984; Hartley, 1992a, b; Simmons et al., 1992).

Throughout the target approach sequence, bats are confronted with two types of changes in echo intensity either due to fluttering of target such as wing beating of insects (target-related echo-intensity change) or shortening of bat-to-target distance (range-related echo-intensity change). To perform sonar gain control for optimal echo reception, bats should reduce sensitivity to range-related increasing echo intensity in order to detect the change of target-related echo intensity. In other words, to detect the change of target-related echo-intensity, auditory sensitivity of collicular neurons should be only affected by the change of echo-intensity due to target structure but not due to shortening of bat-to-target distance. Most collicular neurons (80%) whose minimum threshold increases with PRR so that they become insensitive to range-related increasing echo intensity when bats approach the target (Fig. 3A1, A2). However, they may be sensitive to the change of target-related echo intensity due to fluttering or changes in direction of the target. Therefore, the increase of minimum threshold of these neurons with PRR may serve as the neural substrate underlying the observed threshold increase in target detection or discrimination during the bat's sonar gain control behavior (Kick and Simmons, 1984; Hartley, 1992a, b; Simmons et al., 1992).

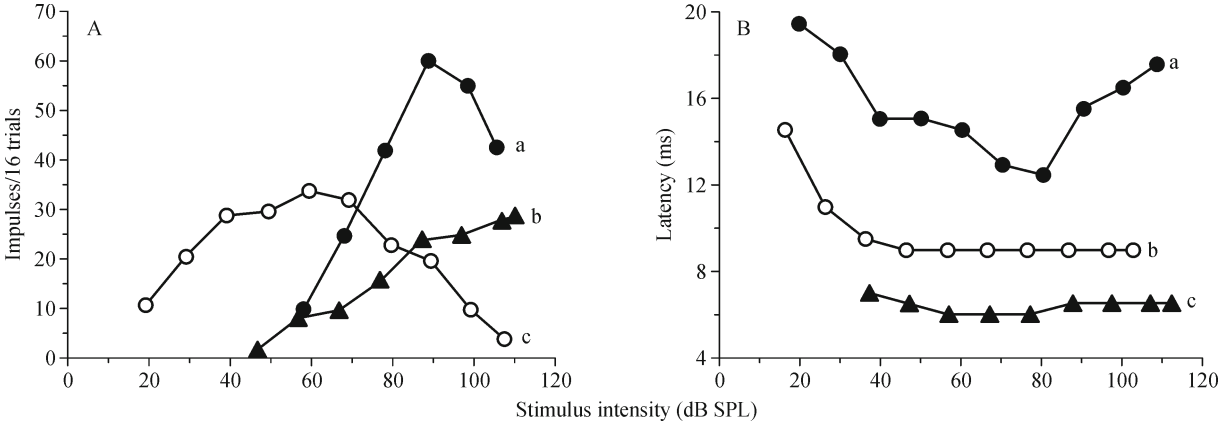


Figure 1 A: Rate-intensity functions of one monotonic (Ab) and two non-monotonic (Aa, Ac) inferior collicular neurons showing variation in the number of impulses with stimulus intensity. B: Latency-intensity functions of three inferior collicular neurons showing variation in latency (ms) with stimulus intensity (Jen and Chen, 1998).

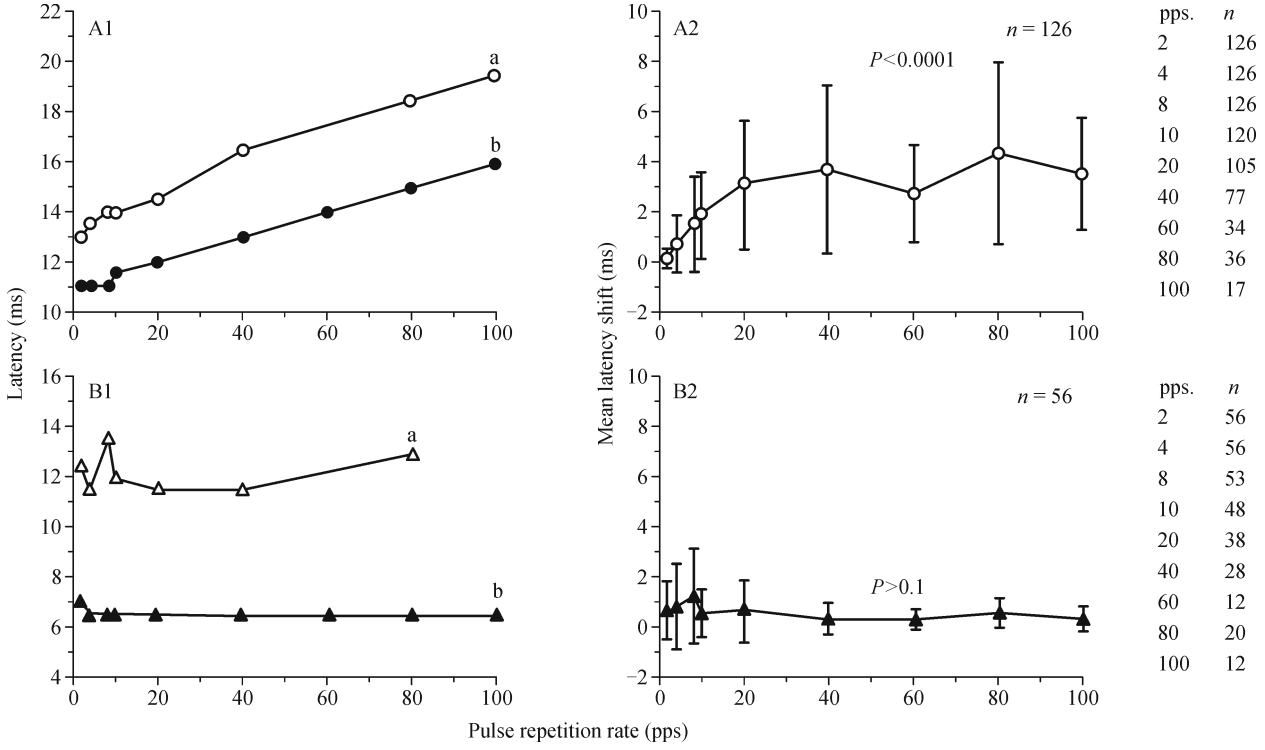


Figure 2 A, B: The latency-pulse repetition rate (PRR) curves of inferior collicular neurons showing the variation of latency with PRR. The latency of one type of collicular neurons increased with PRR (A1a, b) and that of the second type either hardly changed (B1b) or fluctuated within 3 ms (B1a) with PRR. The mean latency shift at each PRR for these two types of collicular neurons are shown in A2 and B2. The vertical bar at each point represents one standard deviation. The number (*n*) of data points averaged at each PRR (pps) is shown at the far right of each panel. *P* significance level from one-way ANOVA (Jen and Chen, 1998).

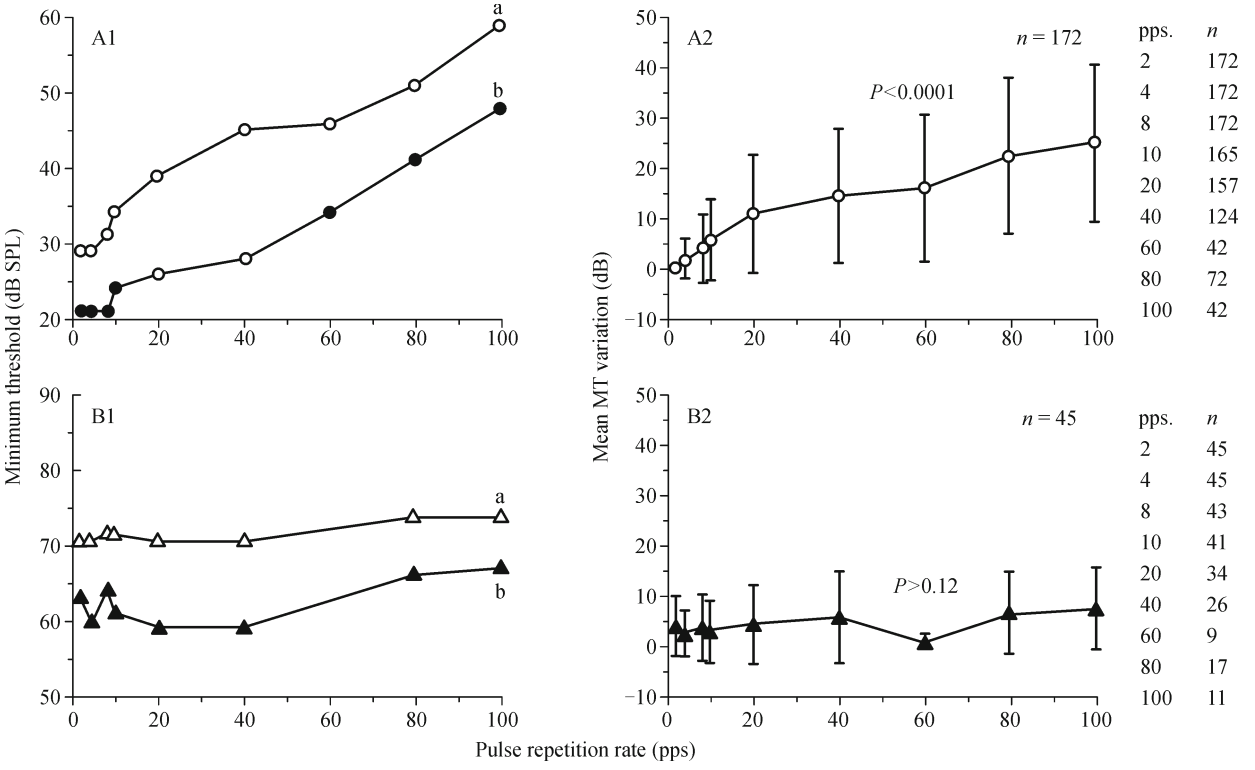


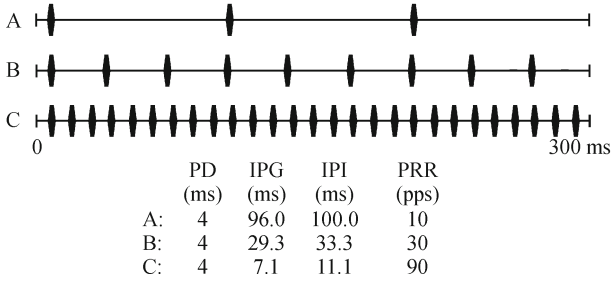
Figure 3 A, B: The minimum threshold-PRR curves of inferior collicular neurons showing the variation of minimum threshold with PRR. The minimum threshold of one type of collicular neurons increased with PRR (A1a, b) and that of the second type fluctuated within 5 dB (B1a, b) with PRR. The mean minimum threshold variation at each PRR for these two types of neurons is shown in A2 and B2. (see Fig. 1 for legends, from Jen and Chen, 1998).

On the other hand, to perform echo intensity compensation for optimal echo reception, bats have to be sensitive to range-related increasing echo intensity associated with increasing PRR. In theory, the increasing echo intensity can be accurately reflected by the increasing number of impulses if the neuron's minimum threshold or sensitivity is not changed by increasing PRR (i.e., as the bat approaches the target) and the change in echo intensity is within the neuron's response range of the intensity-rate function (i.e. Figure 1 A). For this reason, the collicular neurons (20%) whose minimum threshold is hardly affected by pulse repetition (Fig. 3B1, B2) would be able to reflect the increase in range-related echo intensity by proportionally increasing the number of impulses as bats approach the target. Therefore, bats certainly can utilize the response of these collicular neurons to extract the change of range-related echo intensity throughout the course of hunting for optimal echo reception.

Temporally patterned trains of sound pulses and the role of GABAergic inhibition

Three 300 ms temporally patterned trains of sound pulses are used for studying the effect of PRR on multiple-parametric selectivity of collicular neuron (Fig. 4). These pulse trains contain 4 ms best frequency pulses (which elicits maximal number of impulses from the neuron) with 0.5 ms rise-decay times and are delivered at PRR of 10, 30 and 90 pps by setting the inter-pulse interval (IPI) within pulse trains at 100, 33.3 and 11.1 ms (i.e., the number of pulses is 3, 9 and 27 within each pulse train). These three PRRs are comparable to the PRRs occurring during the search, approach and terminal phases of hunting by *Eptesicus fuscus* (Griffin, 1958; Simmons et al., 1979; Jen and Kamada, 1982).

Because gamma aminobutyric acid (GABA) is one of the major inhibitory transmitters in the inferior colliculus (Roberts and Ribak, 1987a, b; Fubara et al., 1996), the role of GABAergic inhibition in shaping the multiple-parametric selectivity of collicular neurons with increasing PRR of temporally patterned pulse trains is studied by means of application of GABA or bicuculline, an antagonist for $GABA_A$ receptors (Cooper et al., 1982; Bormann, 1988, 2000). The $GABA_A$ receptor allows chloride ions flowing into neurons via chloride channels resulting in hyperpolarization in the neurons (Bormann, 1988; Perkins and Wong, 1997). Conversely, bicuculline blocks several forms of GABA-mediated inhibition (Bormann, 1988, 2000; Rabow et al., 1995).



	PD (ms)	IPG (ms)	IPI (ms)	PRR (pps)
A:	4	96.0	100.0	10
B:	4	29.3	33.3	30
C:	4	7.1	11.1	90

Figure 4 Three 300 ms temporally patterned trains of sound pulses at different PRRs used to study the multiple-parametric selectivity of inferior collicular neurons. The number of pulses is shown within each pulse train. The pulse duration (PD) inter-pulse gap (IPG), inter-pulse interval (IPI) and pulse repetition rate (PRR) are shown at the bottom of the three pulse trains.

The response of collicualr neurons varies with sequentially presented sound pulses within temporally patterned trains

To determine the role of GABAeric inhibition in shaping the variation of response of collicular neurons with sequentially presented sound pulses within temporally patterned trains, the discharge pattern and the number of impulses of collicular neurons in response to the 300 ms pulse train with a PRR of 30 pps (i.e. Figure 4B) was studied before and during bicuculline or GABA application (Jen and Wu, 2005). These collicular neurons discharged maximally in number of impulses to the first pulse and the number of impulses progressively decreased with sequentially presented sound pulses (Fig. 5Aa, 6Aa). Bicuculline application produced varying degree of increase in the number of impulses of the collicular neuron in response to all sound pulses (Fig. 5Ab, Bicuculline). Conversely, GABA application produced varying degree of decrease in the number of impulses of the collicular neuron in response to all sound pulses (Fig. 6Ab, G, A, B,A).

As shown in Fig. 5B, the average number of impulses of 56 collicular neurons in response to the first pulse significantly decreased with sequentially presented sound pulses (Fig. 5B, unfilled circles, One-way ANOVA, $P < 0.0001$). Bicuculline application increased the number of impulses of these collicular neurons and the increase became progressively larger with sequentially presented sound pulses (Fig. 5B, filled circles, C, One-way ANOVA, $P < 0.0001$). As a result, the trend of significant decrease in the response size with sequentially presented sound pulses was abolished during bicuculline application (Fig. 5B, filled circles, One-way ANOVA, $P > 0.05$).

Conversely, GABA application significantly decreased the number of impulses of 54 collicular neurons and the decrease became progressively smaller with sequentially presented sound pulses (Fig. 6C, One-way ANOVA, $P < 0.0001$). As a result, the trend of significant decrease in the number of impulses in response to sequentially presented sound pulses was also abolished (Fig. 6B, filled circles, One-way ANOVA, $P > 0.05$).

The result of both drug application indicate that increasing strength of GABAergic inhibition contributes to decreasing auditory sensitivity of collicular neurons to sequentially

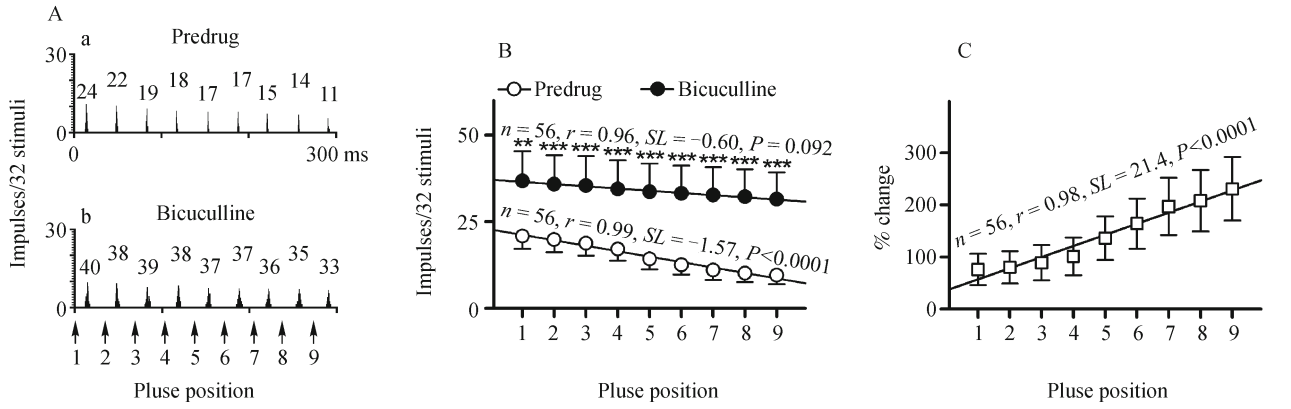


Figure 5 A: Peri-stimulus-time (PST) histograms showing the discharge pattern of a collicular obtained with 300 ms pulse trains containing 9 sound pulses of 4 ms before (Aa) and during (Ab) bicuculline application. The position of sequentially presented pulses is shown at the bottom and the neuron's number of impulses in response to 32 presentations of each pulse is shown within each PST histogram. B: The average number of impulses discharged to sequentially presented sound pulses before (unfilled circles) and during (filled circles) bicuculline application. Bicuculline application produced significant increase in the number of impulses in response to each sound pulse (filled circles vs. unfilled circles, paired t-test, $***P < 0.001$ and $**P < 0.01$). Note that the average number of impulses significantly decreased with sequentially presented sound pulses only before (unfilled circles) but not during (filled circles) bicuculline application (one-way ANOVA, $P < 0.0001$ vs. > 0.05). C: The average percent increase in the number of impulses in response to each sound pulse during bicuculline application. Note that the percent change progressively increased with sequentially presented sound pulses (one-way ANOVA, $P < 0.0001$). The *n*, *r*, *SL* and *P* represent the number of collicular neurons studied, correlation coefficient, slope and significance level for each linear regression line (Jen and Wu, 2005).

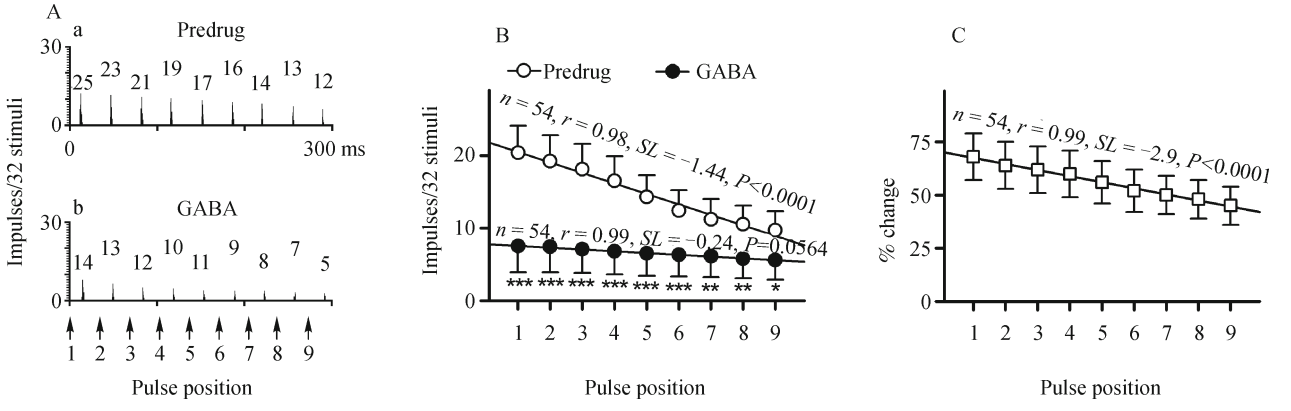


Figure 6 A: PST histograms showing the discharge pattern of a collicular neuron obtained with 300 ms pulse trains before (Aa) and during (Ab) GABA application. B: The average number of impulses discharged to sequentially presented sound pulses before (unfilled circles) and during (filled circles) GABA application. GABA application significant decreased the number of impulses elicited by each sound pulse (filled circles vs. unfilled circles, paired t-test, $***P < 0.001$, $**P < 0.01$ and $*P < 0.05$). Note that the average number of impulses significantly decreased with sequentially presented sound pulses only before (unfilled circles) but not during (filled circles) GABA application (one-way ANOVA, $P < 0.0001$ vs. > 0.05). C: The average percent decrease in the number of impulses elicited by each sound pulse during GABA application. Note that the percent change in the number of impulses progressively decreased with sequentially presented sound pulses (one-way ANOVA, $P < 0.0001$ (Fig. 5 for legends, from Jen and Wu, 2005).

presented sound pulses. What may be the neural mechanisms underlying these findings? During synaptic transmission, excitatory and inhibitory signals that arrive repetitively at a postsynaptic neuron will produce temporal facilitation of opposite postsynaptic potentials (IPSP vs. EPSP). However, at higher repetition rates, temporal depression will occur due to depletion of neurotransmitters resulting in decreasing postsynaptic potentials (Zucker, 1989; Wu and Betz, 1998). A previous study on the rat pyramidal neurons showed that excitatory synaptic currents displayed stronger depression than inhibitory synaptic currents in response to sustained activation at high stimulus repetition rates (Galarreta and Hestrin 1998). This study indicates that the time course of temporal facilitation and depression may differ between the two opposing postsynaptic potentials. In this study, the PRR of the temporally patterned train of sound pulses is 30 pps (Fig. 4B). It is conceivable that at a stimulation rate of 30 pps, the release of GABA was facilitated at a faster rate than the

release of excitatory transmitters. Alternatively, the release of GABA was depressed at a slower rate than the release of excitatory transmitters. In either case, the relative ratio of GABAergic inhibition over excitation would become progressively larger with sequentially presented sound pulses. For this reason, the effect of bicuculline application on the response size of collicular neurons became progressively effective with sequentially presented sound pulses while the opposite effect was observed during GABA application (Figs. 5, 6 B, C).

While GABAergic inhibition contributes significantly in shaping the response size of collicular neurons to sound pulses in rapid sequences, it also shapes the mutiple-parametric (direction, intensity, frequency and duration) selectivity of collicular neurons with PRR. The studies of the role of GABAergic inhibition in shaping mutiple-parametric selectivity of collicular neurons determined with temporally patterned pulse trains with varied PPR are reviewed in the following.

Multiple-parametric selectivity of collicular neurons determined with increasing PRR of temporally patterned trains of sound pulses

Directional selectivity

Echo localization is essential for the survival of insectivorous bats that emit ultrasonic sounds and listen to the returning echoes to extract information about insects and obstacles. Behavioral studies have shown that *Eptesicus fuscus* have a horizontal target resolution of $\pm 1.5°$ and a vertical resolution of $\pm 5°$ (Lawrence and Simmons, 1982, 1983; Masters et al., 1985). To determine the neural basis of this remarkable acoustic behavior, many studies have examined the directional selectivity of neurons in different level of the bat's auditory pathway (the cochlea nucleus, Suga, 1964; superior olivary complex, Jen, 1980; Harnischfeger et al., 1985; the nucleus of lateral lemniscus, Shimozawa et al., 1974; the inferior colliculus, Grinnell, 1963; Grinnell and Grinnell, 1965; Schlegel, 1977; Schnitzler and Grinnell, 1977; Jen and Sun, 1984; Fuzessery and Pollak, 1985; Jen et al., 1987; Sun and Jen, 1987; Schlegel et al., 1988; Jen and Wu, 1993; Wu and Jen 1995b, 1996; Grothe et al., 1996; Jen and Zhang, 2000; the auditory cortex, Jen et al., 1989). By means of temporally isolated repetitive sounds delivered from different angles, these studies showed that most auditory neurons discharged maximally or displayed the lowest threshold to sounds delivered from an angle or a range of angles (the best angle) within the frontal auditory space. These studies also showed that the slope of directional selectivity curves (drawn by plotting the number of impulses against the azimuthal angle) of most neurons sharpened with increasing pulse frequency (Shimozawa et al., 1974; Schlegel, 1977; Fuzessery and Pollak, 1985; Jen et al., 1987; Schlegel et al., 1988; Jen and Wu, 1993). The shape of directional selectivity curve and the best angle of most neurons also varied with pulse intensity (Schlegel et al., 1988; Grothe et al., 1996). These observations suggest that echo directional selectivity of auditory neurons could be affected by other co-varying echo parameters during hunting.

When stimulated with biologically relevant temporally patterned pulse trains at different PRR (i.e. Figure 4), the directional sensitivity of collicular neurons changed in three ways. One, the sharpness of directional selectivity curves of collicular neurons increased with PRR (Fig. 7 filled circles vs unfilled circles vs. filled triangles). Two, the directional selectivity of collicular neurons changed from non-directional to directional (Fig. 7 D, filled circles vs unfilled circles and filled triangles). Three, the best angle of the directional selectivity curves of some neurons shifted almost exclusively toward the midline (Fig. 7 B, E, F). This improvement of the directional selectivity of collicular neurons with increasing PRR of temporally patterned pulse trains is mainly due to greater strength of GABAergic inhibition at higher than at lower PRRs.

To compare the role of PRR and GABAerdic inhibition in shaping the directional selectivity of collicular neurons, the sharpness of directional selectivity curves of collicular neurons is expressed with a normalized angular range (nAR) which is obtained by dividing the maximal number of impulses by half of the angular range at 50% below the maximum. The larger the nAR is, the sharper the directional selectivity of a neuron is. As shown in Fig. 8, the nAR progressively increases with increasing PRR before bicuculline application (values indicated with filled circles). Bicuculline application either completely changes the directional selectivity curves of collicular neurons from directional to non-directional (Fig. 8 A) or produces more pronounced broadening of directional selectivity curves and larger decrease in the nAR at higher than at lower PRR of pulse trains (Fig. 8B, shown by % change in nAR).

All in all, these data show that increasing PRR of pulse trains not only improves directional selectivity of most collicular neurons but also shifts the best angle of some neurons toward the midline. These data suggest that increasing PRR of emitted pulses during hunting would increase selectivity of bats to echo direction and facilitate interception of insects within the frontal gaze.

Frequency and intensity selectivity

In sound analysis, frequency and intensity are two fundamental parameters of a sound stimulus. They are the basis of perception of pitch and loudness. For this reason, many studies have determined the frequency and intensity selectivity of auditory neurons in different animals (Popper and Fay 1995). These studies determine how a change in frequency or intensity of repetitive sound pulses may affect the responses

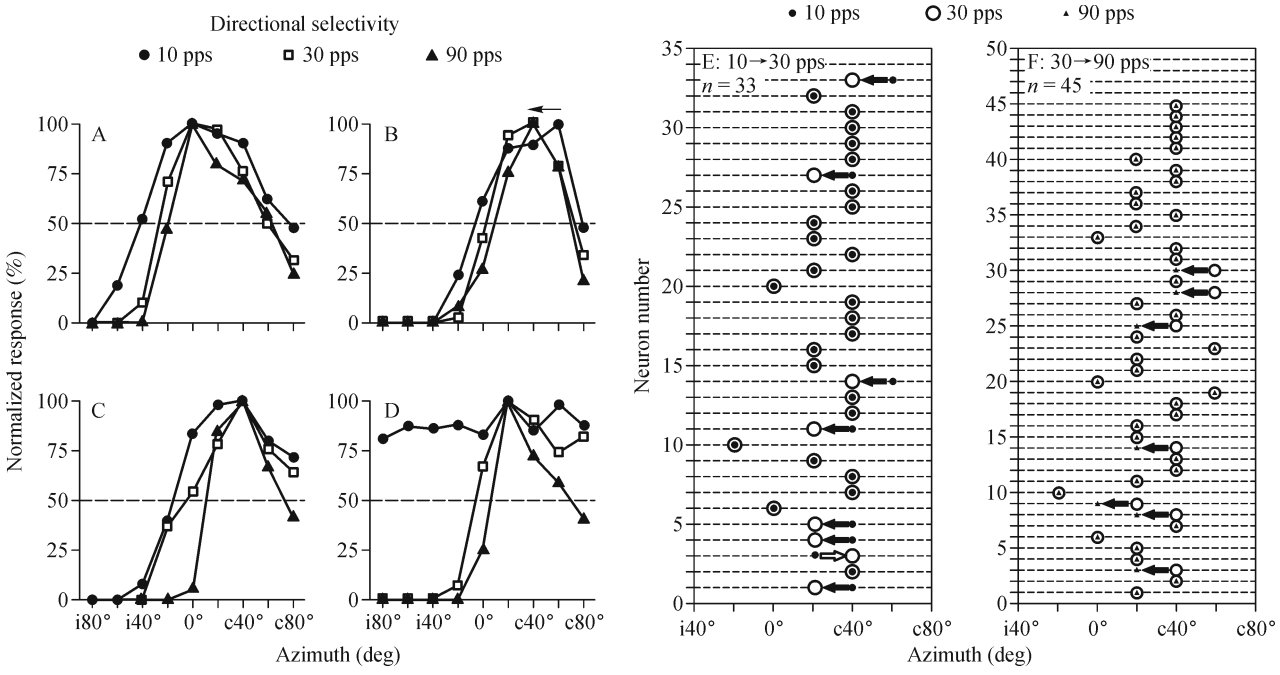


Figure 7 A–D: Directional selectivity curves of four collicular neurons plotted with the number of impulses obtained with three temporally patterned pulse trains of different PRRs (i.e. Fig. 4). Each horizontal dashed line indicates the 50% maximal response. Directional selectivity curves of two neurons (A,B) were not affected by the PRR while that of other two neurons (C,D) changed from one type to another. Note that the best azimuth of one neuron moved toward the midline as the PRR of the pulse train increased from 10 pps to 30 pps (B arrow). E, F: Distribution of the best azimuth of individual collicular neurons determined with pulse trains of different PRRs. The best azimuths of most collicular neurons were not affected by PRR of the pulse train (shown as filled circles within unfilled circles, or filled triangles within unfilled circles). However, best azimuths of 16%–21% neurons shifted with increasing PRR of the pulse train (filled and unfilled arrows). The best azimuth of all but one neuron shifted toward the midline with increasing PRR of the pulse trains (filled arrows in A, B) (from Zhou and Jen, 2002).

of auditory neurons such as the number of impulses, latency, response probability or threshold.

In the frequency domain, the frequency selectivity of a collicular neuron is studied by measuring its threshold frequency tuning curve (FTC) in which the threshold to each responsive frequency is determined. The sharpness of each threshold FTC is expressed by Qn (Q_{10}, Q_{20}, Q_{30}) values which are obtained by dividing the best frequency (the sound frequency that elicits the maximal number of impulses or the lowest threshold from a neuron) by the bandwidth at 10 dB, 20 dB and 30 dB above the minimum threshold. A neuron whose threshold FTC has large Qn values has large frequency selectivity. A neuron's frequency selectivity is also studied by measuring its iso-intensity FTC in which the number of impulses to a pulse train delivered at a given intensity (e.g. 20–30 dB above its minimum threshold) at several responsive frequencies is recorded. The sharpness of each iso-intensity FTC is expressed by the bandwidth at 90%, 75% and 50% of the maximal number of impulses. A neuron whose iso-intensity FTC has narrow bandwidth has sharp frequency selectivity.

The effect of PRR on the frequency selectivity of collicular neurons has been studied using three biologically relevant temporally patterned trains of sound pulses (Jen et al., 2001, 2002). These studies show that the sharpness of the threshold FTC of all collicular neurons greatly improves (as evident by increasing Qn values) with increasing PRR (Fig. 9A-1,B-1,C-1). Sharpening of the threshold FTC with increasing PRR is primarily mediated through different strength of GABAergic inhibition with PRR because application of bicuculline broadens the threshold FTC at a greater degree at higher PRR than at lower PRR (Fig. 9A-2,B-2,C-2). This is evident by a greater change in Qn values at high than at low PRR during bicuculline application. In the same token, the sharpness of iso-intensity FTC of all collicular neurons greatly improves (as evident by decreasing bandwidth values) with increasing PRR of temporally patterned trains of sound pulses (Fig. 9D-1,E-1,F-1). Application of bicuculline broadens the iso-intensity FTC at a greater degree at higher than at lower PRR. This is evident by a greater change in bandwidth values at high than at low PRR (Fig. 9D-2,E-2,F-2). All these observations indicate that the improvement of the sharpness of threshold FTC and iso-intensity FTC of collicular neurons with increasing PRR is due to PRR-dependent GABAergic inhibition which is stronger at high than at low PRR. Because bats rely on the sharpness of frequency tuning of auditory neurons for analysis of target features, improvement of frequency selectivity of collicular neurons with increasing

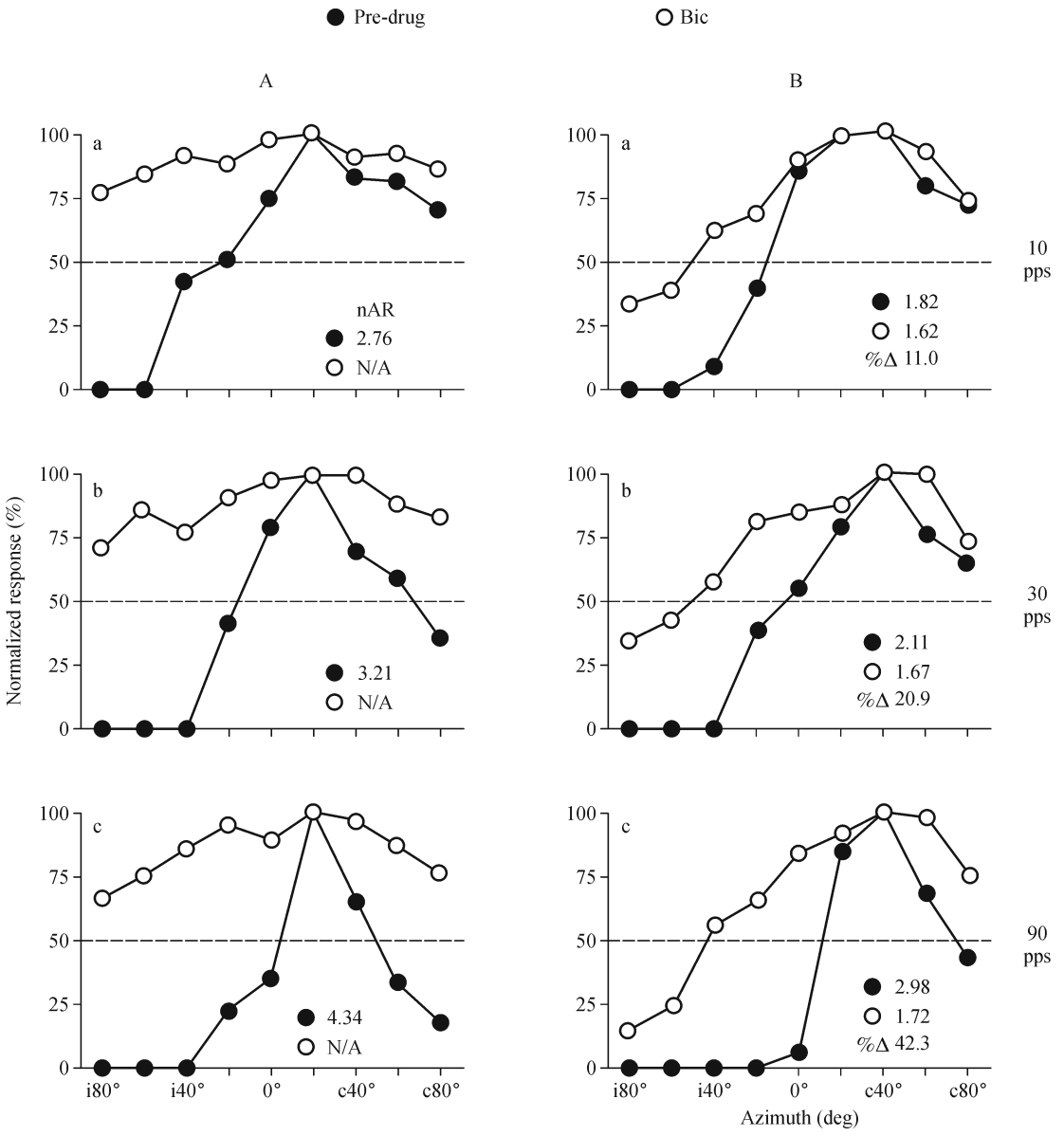


Figure 8 A, B: Directional sensitivity curves of two collicular neurons plotted with three temporally patterned pulse trains of different PRRs before and during bicuculline application. The nAR determined before and during bicuculline application and the percentage change (%△) of nAR are shown within each plot. Note that the directional selectivity curve of neuron A changed from directional to non-directional during bicuculline application so that the nAR is not available during drug application (see text for details, from Zhou and Jen, 2002).

PRR would enable the bat to perform fine discrimination of target features.

Encoding of pulse intensity by collicular neurons is studied by measuring its rate-intensity function with the total number of impulses elicited by the intensity of each pulse train delivered at the miminum threshold and at 10-dB increments above its minimum threshold (Fig. 1A, Chen and Jen, 1994; Jen and Chen, 1998; Jen and Schlegel, 1982; Pinheiro et al.,1991; Wu and Jen, 1991). When measured with three biologically relevant pulse trains, the rate-intensity function of all collicular neurons varies with three pulse trains at different pulse repetition rates (Fig. 10). The intensity selectivity of these neurons is studied by calculating the dynamic range and slope of the rate-intensity function. The dynamic range is defined as the intensity range from 10% below the maximal to 10% above the minimal number of impulses. The dynamic range represents the intensity range within which a neuron's response monotonically increases with pulse intensity. Thus, a large dynamic range represents a wide intensity response range. The slope of the rate-intensity function is obtained by dividing the percent change in the number of impulses within the dynamic range by the dynamic

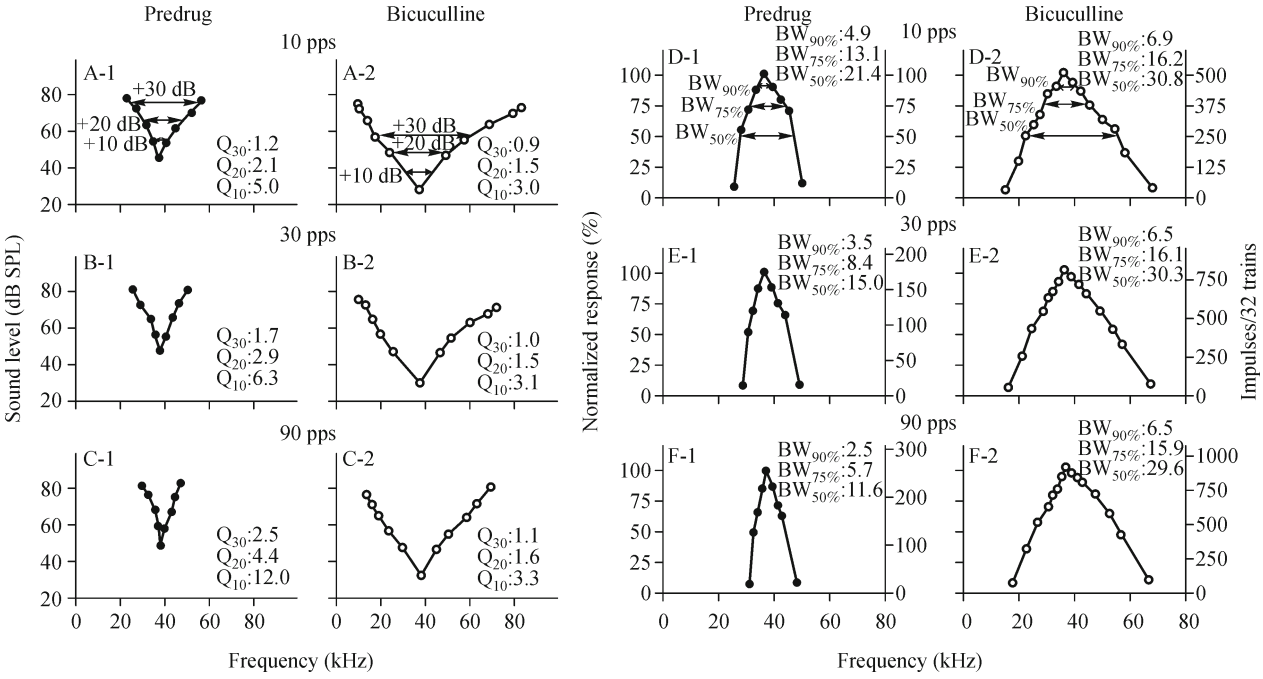


Figure 9 A, B, C: The threshold-frequency tuning curve (FTC) of a collicular neuron measured with three temporally patterned pulse trains of different PRRs before (A-1, B-1, C-1) and during (A-2,B-2,C-2) bicuculline application. The sharpness of each FTC was expressed by Q_n values. D, E, F: Isolevel-FTC of a collicular neuron measured with three pulse trainsat three PRRs before (D-1, E-1,F-1) and during (D-2, E-2, F-2) bicuculline application. The sharpness of each FTC was expressed by the bandwidths at 90, 75 and 50% of maximal response (from Jen et al., 2002).

range. A large (steep) slope represents a high sensitivity to variation in pulse intensity.

The intensity selectivity of collicular neurons varies with PRR in two different ways. The intensity selectivity of one group of collicular neurons increases with the PRR from 10 to 30 pps but decreases at the PRR of 90 pps (Fig. 10 A-1, A-2, A-3). The dynamic range of rate-intensity function of these neurons decreases at 30 pps but increases again at 90 pps. Conversely, the slope of the rate–intensity function of these neurons increases at 30 pps but decreases at 90 pps. These collicular neurons apparently are most sensitive to minor change in echo intensity within a smaller range of lower intensity during the approaching phase of hunting. However, during the terminal phase of hunting, these neurons become sensitive to high intensity due to extended dynamic range. Conceivably, these neurons could help bats detect any sudden intense pulses such as those emitted by other bats during the terminal phase of hunting.

On the other hand, the intensity selectivity of another group of collicular neurons progressively increases with increasing PRR by systematically decreasing the dynamic range but increasing the slope of rate-intensity function (Fig. 10 B-1, B-2, B-3). As such, the intensity selectivity of these neurons becomes sharper in detection of minor change in intensity within a smaller range of lower intensity. Conceivably, this group of neurons may help bats not only to detect minor change in echo intensity but also may serve as an additional mechanism to ensure optimal echo intensity level during echo-intensity compensation by the bats (Jen and Kamada 1982; Kobler et al. 1985; Hartley 1992a, b).

The fact that PRR affects the intensity sensitivity of auditory neurons has been shown in previous studies. Two studies show that increasing PRR changes the monotonic rate-intensity function of some collicualr neurons into non-monotonic rate-intensity function as well as modulate the best intensity and slope of their rate-intensity functions (Phillips et al. 1989; Pinheiro et al. 1991). Two other studies show that increasing PRR improves the slope but decreases the dynamic range of rate-intensity function of collicular neurons (Galazyuk et al. 2000; Smalling et al. 2001).

Duration selectivity

Sound duration is an important feature that contributes to the distinct spectral and temporal attributes of individual biological sounds. Previous studies of selectivity of auditory neurons to sound duration has been conducted in many animals including frogs (Narins and Capranica, 1980; Feng et al., 1990; Gooler and Feng, 1992), bats (Jen and Schlegel, 1982; Pinheiro et al., 1991; Casseday et al., 1994, 2000; Ehrlich et al., 1997; Galazyuk and Feng, 1997; Fuzessery and Hall, 1999; Jen and Feng, 1999; Jen and Zhou, 1999; Faure et al., 2003; Jen and Wu, 2005; Zhou and Jen, 2001, 2002a, 2006; Wu and Jen, 2006a,b, 2008), cats (He et al., 1997), chinchillas (Chen, 1998), mice (Brand et al., 2000) and rats (Pérez-Gonzalez et al., 2006). The sound duration to which

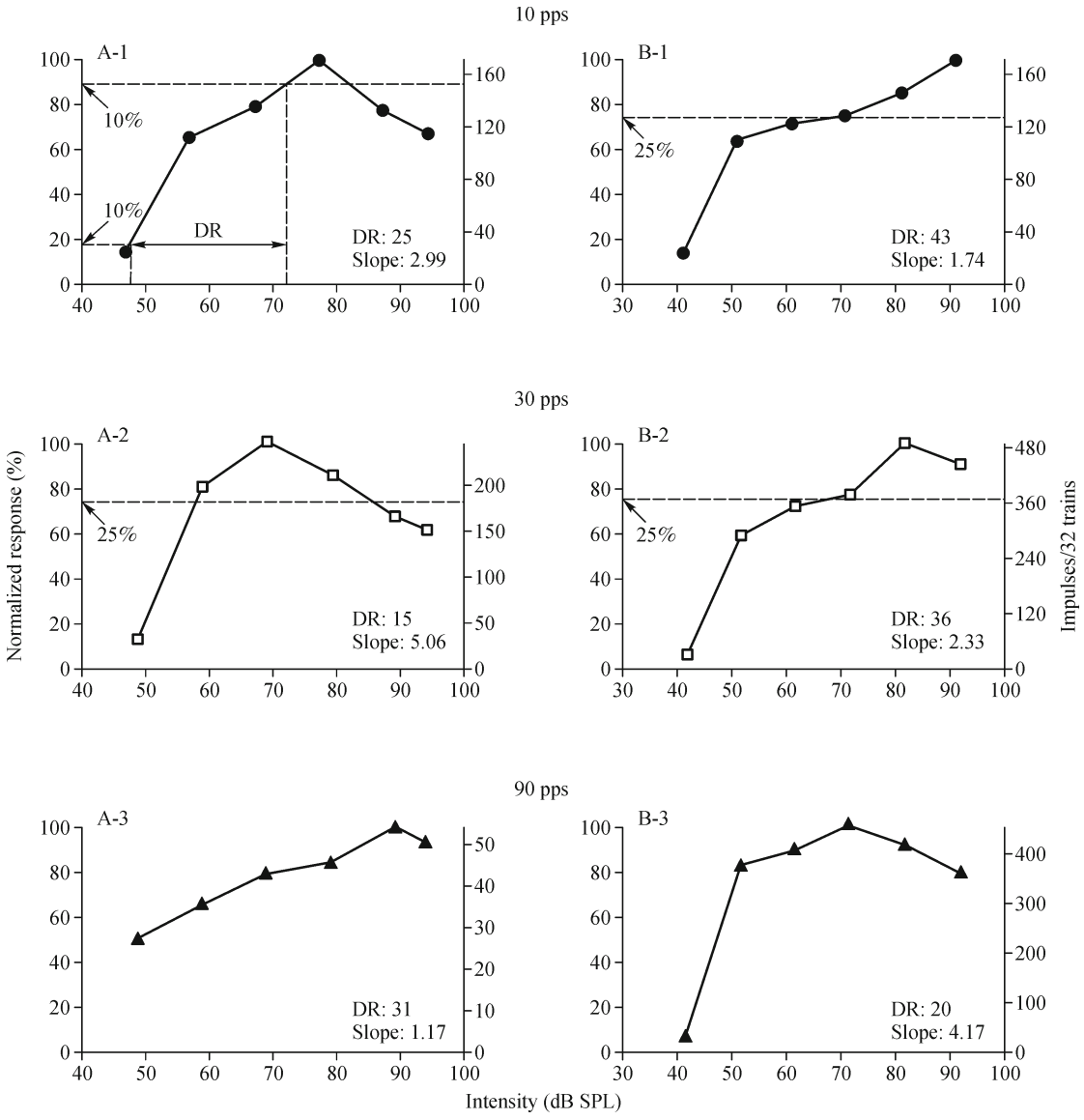


Figure 10 Rate-intensity functions of two collicular neurons determined with three temporally patterned pulse trains of different PRRs. The dynamic range (DR) of each rate-intensity function was the intensity range corresponding to the number of impulses that was 10% below the maximum and 10% above the minimum (A1, indicated by dotted lines). The slope (%/dB) of the rate-intensity function was obtained by dividing the percent change in the number of impulses within the DR by the DR (from Jen et al., 2001).

these neurons are tuned corresponds closely to the behaviorally relevant sounds in these animal species. Presumably, these duration-tuned neurons not only play an important role for bat echolocation but also for sound recognition particularly in human speech and animal communication (Popper and Fay, 1995; Shannon et al., 1995; Covey and Casseday, 1999).

These studies show that the duration tuning curves of auditory neurons behave as band-, short-, long- and all-pass filters to pulse duration by plotting the number of impulses against the pulse duration (Fig. 11). Whereas neurons with band-, short- and long-pass duration tuning curves discharge maximally to a specific duration or a range of duration (the best duration, BD), neurons with all-pass duration tuning curves are not selective to any sound duration. The sharpness of duration selectivity of collicular neurons is expressed with a normalized duration-width (nDW) which is obtained by dividing the maximal number of impulses by the width of a duration tuning curve at 75% of the maximum (Fig. 11, DW indicated by a double-head arrow). A neuron with a large nDW has a narrow duration tuning curve and sharp duration selectivity.

The responses of two representative collicular neurons to three biologically relevant temporally patterned trains of sound pulses are shown in Figs. 12 and 13. Both neurons adapt to sequentially presented pulses in different degree at each pulse train (Figs.12, 13A, B, C). When the duration tuning curve is plotted with the average number of impulses

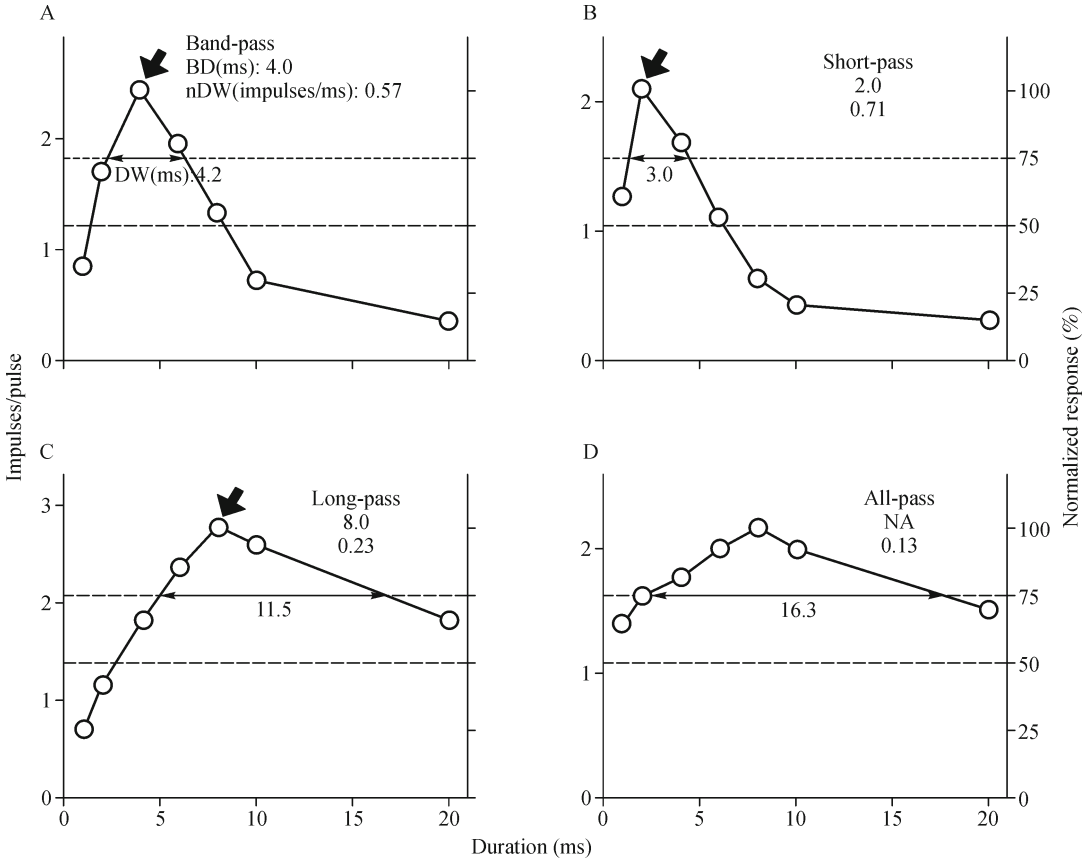


Figure 11 Duration tuning curves of four collicular neurons. Left and right ordinates represent the number of impulses per 32 presentations of pulse trains and normalized response. The abscissa represents pulse duration (ms). Duration tuning properties of these neurons are (A) band-pass, (B) short-pass, (C) long-pass and (D) all-pass. Each horizontal dashed line indicates the 50% maximal response. Duration selectivity of each curve is expressed with a best duration (BD) and a normalized duration width (nDW). The BD (ms) of the band-, short- and long-pass duration tuning curves is indicated with an arrow. An nDW (impulses/ ms) is obtained by dividing the maximum by the duration width (DW indicated with a double arrow-headed bar) of a duration tuning curve at 75% maximum (from Wu and Jen, 2006).

per pulse against pulse duration, one neuron always has a band-pass duration tuning curve regardless of PRR (Fig. 12 Da, Ea, Fa). The duration tuning curve of the other neuron changes from all-pass to short-pass and finally to band-pass with increasing PRR (Fig. 13 Da, Ea, Fa). Each neuron's duration selectivity progressively increased with PRR as evident by decreasing best duration and increasing nDW (Figs. 12, 13).

The role of GABAergic inhibition in shaping the improvement of duration selectivity of collicular neurons with PRR is studied by measuring the duration tuning curve before and during bicuculline or GABA application. Bicuculline application produces a greater increase in the neuron's number of impulses for non-BD durations than for the BD resulting in more pronounced broadening of duration tuning curves and significantly increase in the BD and decrease in the nDW of collicular neurons at high than at low PRR (Fig. 12, Db,Eb,Fb). Conversely, GABA application produces more pronounced narrowing of duration tuning curves and significantly larger decrease in the BD and increase in the nDW of collicualr neurons at low than at high PRR (Fig. 13 Db, Eb, Fb). In both cases, significant improvement of duration selectivity with PRR is abolished during drug applications.

The opposite effect of bicuculline and GABA application on duration tuning curves of collicular neuron clearly supports the role of GABAergic inhibition in shaping the duration selectivity of IC neurons as reported earlier (Casseday et al. 1994, 2000; Jen and Feng, 1999; Jen and Wu, 2005; Wu and Jen, 2006a, b). Sharpening of duration tuning curve by GABAergic inhibition is a result of varying degree of inhibition with pulse duration. This is evident by the observation that the increase in the number of impulses during bicuculline application is greater for non-BD durations than for the BD (Fig. 12). Conversely, the decrease in the number of impulses during GABA application is greater for non-BD durations than for the BD (Fig. 13). All these observations indicate that GABAergic inhibition shapes the improvement of duration selectivity of collicular neurons by increasing the sharpness of duration tuning curves and

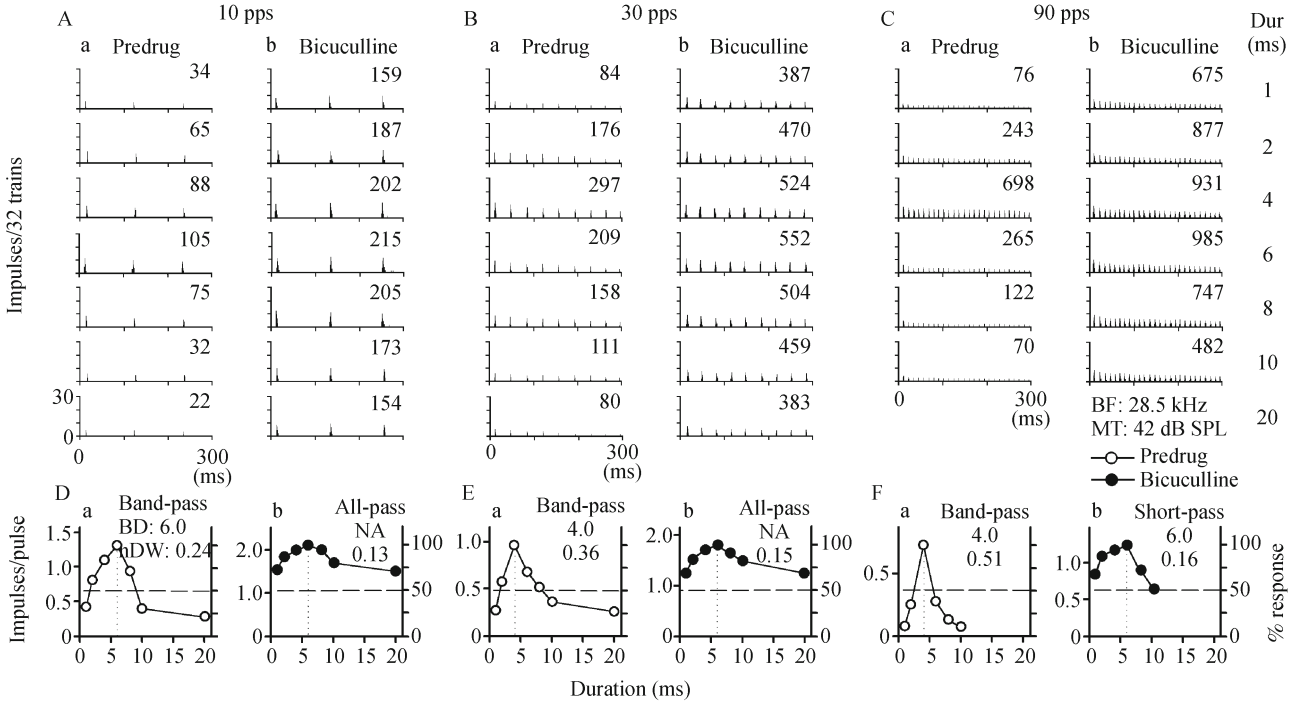


Figure 12 A, B, C: Peri-stimulus-time (PST) histograms showing the discharge patterns of a collicular neuron obtained with three temporally patterned pulse trains containing pulses of different durations (shown at far right) before (predrug) and during bicuculline application. D,E,F: The neuron's duration tuning curves plotted with the total number of impulses (shown at the right of each histogram) before (unfilled circles) and during (filled circles) bicuculline application. The type, BD (ms) and nDW (impulses/ms) of the duration tuning curve are shown within each plot. NA indicates that a BD is not available (from Wu and Jen, 2006).

shortening the best duration.

As described earlier, bats shorten pulse duration throughout a target approaching sequence to avoid pulse-echo overlap (Griffin, 1958; Simmons et al., 1979; Jen and Kamada, 1982; Surlykke and Moss, 2000). The progressive improvement of duration selectivity of collicular neurons with PRR undoubtedly would facilitate recognition of progressively decreasing echo duration by bats during the final phase of hunting.

GABAergic inhibition underlies improvement of multiple-parametirc selectivity of collicular neurons with PRR

In auditory physiology, the processing of auditory signals has traditionally been explained by excitatory and inhibitory interactions of divergent and convergent projections within the auditory system (Suga, 1997; Suga et al., 1998; Lu and Jen, 2002) The inhibitory inputs to the inferior colliculus are glycinergic, which originates extrinsically, and GABAergic, which originates extrinsically and intrinsically (Oliver and Roberts and Ribak, 1987a, b; Shneiderman, 1991; Oliver et al., 1994; Fubara et al., 1996).

By means of application of bicuculline, many studies have shown that the interplay of excitation and GABAergic inhibition shapes the discharge pattern, response latency, frequency tuning, duration selectivity, binaural signal processing, recovery cycle, and selectivity for frequency modulation and increases sensitivity of neurons to sound motion cues (Faingold et al., 1991; Vater et al., 1992; Yang et al., 1992; Park and Pollak, 1993, 1994; Casseday et al., 1994, 2000; Klug et al., 1995; Fuzessery and Hall, 1996; Le Beau et al., 1996, 2001; Lu et al., 1997, 1998; Koch and Grothe, 1998; Jen and Feng, 1999; Zhang et al., 1999; Jen and Zhang, 2000; Lu and Jen, 2001; Jen et al., 2001, 2002, 2003; McAlpine and Palmer, 2002; Zhou and Jen 2003; Jen and Wu, 2005; Wu and Jen, 2006a,b). In addition to these findings, the data presented in this review have shown that GABAergic inhibition contribute significantly to the improvement of mutiple-parametric (direction, intensity, frequency and duration) selectivity of collicular neurons with PRR. As such, there is a decrease in response size to sequentially presented sound pulses within a pulse train and an improvement of the sharpness of directional sensitivity curve (i.e. decreasing azimuth range, AR), frequency tuning curves (i.e. increasing Qn values), rate-intensity function (i.e. decreasing DR and increasing slope) and duration tuning curves (i.e. shortening

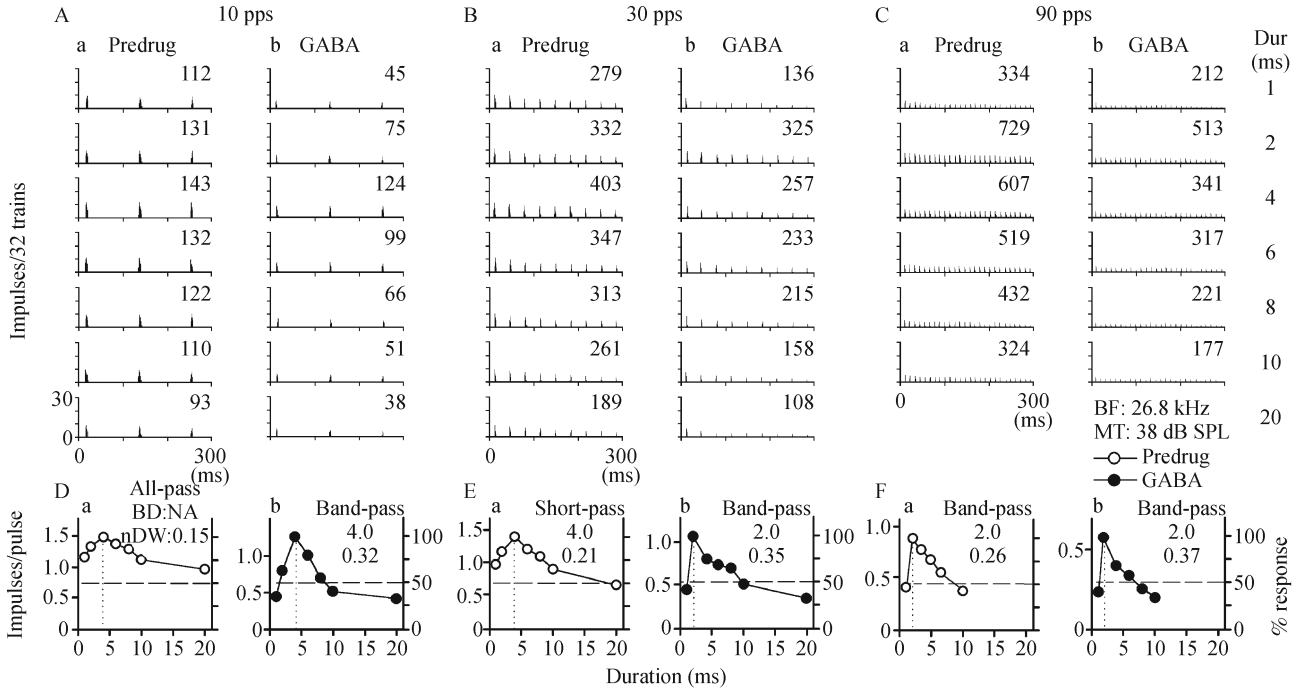


Figure 13 A, B, C: Peri-stimulus-time (PST) histograms showing the discharge patterns of a collicular neuron obtained with three temporally patterned pulse trains containing pulses of different durations (shown at far right) before (predrug) and during bicuculline application. D,E,F: The neuron's duration tuning curves obtained before (unfilled circles) and during (filled circles) GABA application (Fig. 12 for legends, from Wu and Jen, 2006).

of BD and increasing nDW) of collicular neurons with increasing PRR (Figs. 5–13). This improvement of multiple-parametric selectivity of collicular neurons with PRR is a result of increasing strength of GABAergic inhibition with PRR This PRR-dependent GABAergic inhibition is conceivably due to the fact that GABAergic inhibition is either facilitated at a faster rate or depresses at a slower rate than excitation with increasing PRR.

Because the inferior colliculus also receives glycinergic inputs from the superior olivary complex and ventral complex of the lateral lemniscus (Glendenning et al., 1992; Malmierca et al., 1998; Saint Marie et al., 1989) and glycinergic inhibition has been shown to contribute temporal response properties, frequency tuning and binaural processing of collicular neurons (Le Vater et al., 1992; Klug et al., 1995; Beau et al., 1996, 2001; Koch and Grothe, 1998; Lu and Jen, 2001), glycinergic inhibition may conceivably also contributes to improvement of multiple-parametric selectivity of collicular neurons with increasing PRR. Future works need to be conducted to confirm this contention.

Adaptive value of increasing PRR during hunting

As described earlier, echolocating bats progressively increase the PRR throughout the entire sequence of hunting presumably to extract maximal information from the increasing number of echoes about the rapid changes in the target features. All studies reviewed in this article show that increasing PRR improves multiple-parametric selectivity of collicular neurons. It is possible that this improvement of multiple-parametric selectivity of collicular neurons may serve as the underlying mechanisms for obtaining maximal information about the target features during hunting.

Previous studies have shown that the auditory system of bats is fundamentally similar to that of other mammals and the interplay of inhibition and excitation that shapes many response properties of collicular neuron is similar across many mammalian species (Casseday and Covey, 1995; Covey and Casseday, 1995, 1999; Klug et al., 1995; Fuzessery and Hall, 1996; LeBeau et al., 1996, 2001; Koch and Grothe, 1998; Jen and Feng, 1999; Jen and Zhou, 1999; Jen and Zhang, 2000; Jen et al., 2001, 2002; Lu and Jen, 2001). Therefore, the findings reviewed here are likely also applicable to other mammalian species as well. Conceivably, increasing strength of GABAergic inhibition with sequentially presented sound pulses shown in this review might also be the neural mechanism underlying the psychophysical phenomena of temporal masking as well as facilitation of speech processing in humans.

Acknowledgements

The research works described in this review article have been supported by the National Science Foundation and National Institute of Health of USA, Human Frontier Science Program of International Brain Research Organization, the Research Board, Research Council, College of Arts and Sciences, and Division of Biologic Sciences of University of Missouri-Columbia, USA. I particularly like to express my sincere thanks to my former coworkers in participation of all the studies described in this review. They are Drs, Qi-Cai Chen, Rui-Ben Feng, Tsutomu Kamada, Erika Hou, Ruihong Luan, Toshio Moriyama, Danial Pinheiro, Peter Schlegel, Xinde Sun, Haibing Teng, Min Wu, Chung Hsin Wu, Ji Ping Zhang and Xiaoming Zhou.

Compliance with ethics guidelines

Philip H.-S. Jen declares that he has no conflict of interest. This article does not contain any studies with human or animal subjects performed by the author.

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