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MINI-REVIEW

Functional organization of the mammalian auditory midbrain

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Abstract The inferior colliculus (IC) is a critical nexus between the auditory brainstem and the forebrain. Parallel auditory pathways that emerge from the brainstem are integrated in the IC. In this integration, de-novo auditory information processed as local and ascending inputs converge via the complex neural circuit of the IC. However, it is still unclear how information is processed within the neural circuit. The purpose of this review is to give an anatomical and physiological overview of the IC neural circuit. We address the functional organization of the IC where the excitatory and inhibitory synaptic inputs interact to shape the responses of IC neurons to sound.

Keywords Inferior colliculus · Local circuit · GABAergic neuron · Membrane property · Synaptic inputs

Abbreviations

IC	Inferior colliculus
CN	Cochlear nuclei
SOC	Superior olivary complex
NLL	Nucleus of the lateral lemniscus
VCN	Ventral CN
DCN	Dorsal CN
LSO	Lateral superior olive
ILD	Interaural level difference
MSO	Medial superior olive
ICC	Central nucleus of the IC
MGB	Medial geniculate body
LG	Large GABAergic
VGLUT	Vesicular glutamate transporter
R_i	Input resistance
SR	Sustained regular
MNTB	Medial nucleus of the trapezoid body
LNTB	Lateral nucleus of the trapezoid body
DNLL	Dorsal NLL
VNLL	Ventral NLL

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Introduction

The IC is located in the midbrain and is believed to be the first integration center in the auditory pathway. Almost all auditory information is conveyed, integrated, and processed in the IC before being sent to a higher auditory center. Inside the IC neural circuit, auditory information is transformed. The general rules of this transformation have not been fully established, because of incomplete knowledge of the neural circuit in the IC. Here, we discuss the functional organization of the IC to aid our understanding of how the IC processes auditory information. This review focuses on the mammalian auditory system (other clades are discussed elsewhere [1, 2]) We first describe the anatomical and synaptic organization of the IC neural circuitry, then discuss two critical physiological aspects of information processing by the IC neural circuit: the diverse membrane properties of postsynaptic neurons and the convergence of excitatory and inhibitory synaptic inputs.

An overview of the mammalian auditory pathway

Sound is transformed into neural signals in the cochlea, in which the frequency of sound is analyzed (Fig. 1a). Auditory information, for example the spectrum, timing, and location of sound is analyzed in parallel in the lower brainstem nuclei, i.e., cochlear nuclei (CN), superior olivary complex (SOC), and nuclei of the lateral lemniscus (NLL, Fig. 1a). For example, T-stellate neurons in the ventral cochlear nucleus (VCN) can convey sound spectra over a wide range of sound intensity [3]. Fusiform cells in the dorsal cochlear nucleus (DCN) code sound intensity and spectrum in a complex frequency response area and are believed to be the analyzers of spectral cues that are created by the head and pinnae and are necessary for sound location [3]. Neurons in the lateral superior olive (LSO) code interaural level differences (ILD) whereas those in the medial superior olive (MSO) code interaural time difference. Both are necessary for analysis of sound location in space [4]. The dorsal NLL (DNLL) is one of the major sources of GABAergic input to the IC [5]. All of these brainstem structures project to the IC [6]. These projections include both the excitatory and inhibitory inputs to IC (Fig. 1a). These basic patterns of connection from the

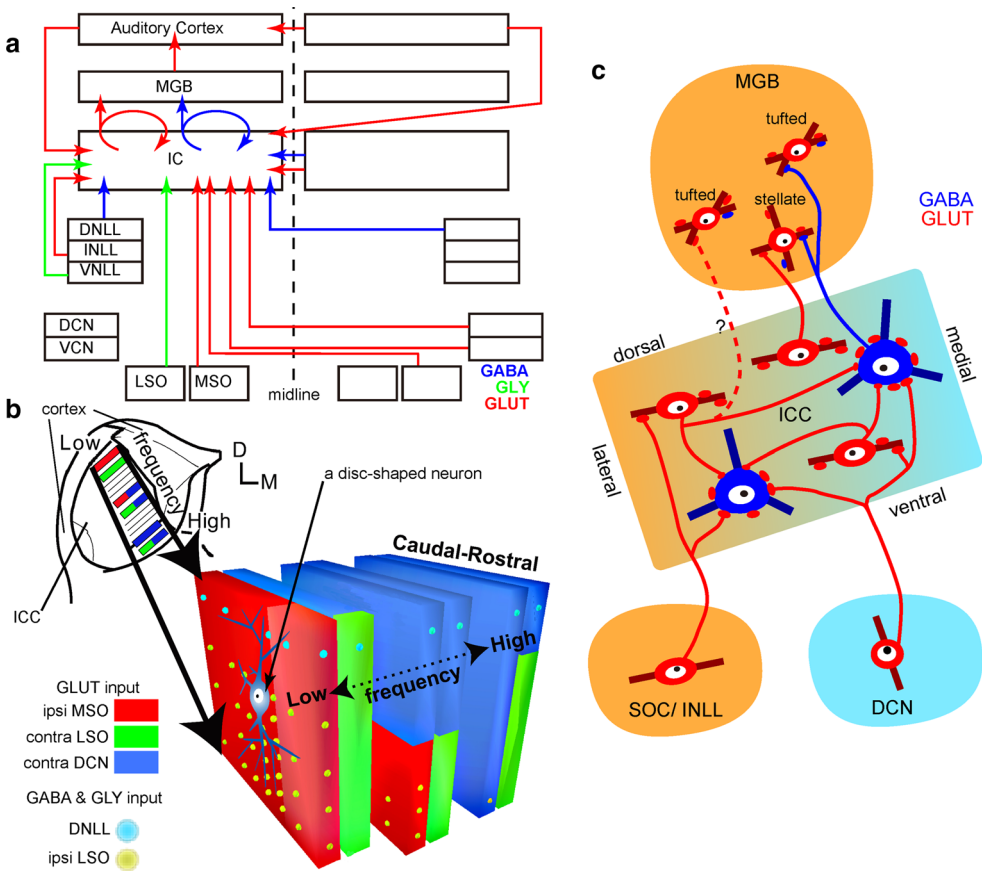

Fig. 1 The neural circuit of the inferior colliculus. **a** Schematic diagram of main inputs to the IC of mammals. *Red*, *blue*, and *green arrows* indicate glutamatergic, GABAergic, and glycinergic projection. *DNLL* dorsal nucleus of the NLL, *INLL* intermediate nucleus of the NLL, *VNLL* ventral nucleus of the NLL. **b** A model of synaptic organization of the ICC. Each functional module is denoted by a *different shade* and represents a different excitatory brainstem input (*red*, ipsilateral MSO; *blue*, contralateral DCN; *green*, contralateral LSO). Inhibitory inputs (ipsilateral LSO, *yellow spheres*; DNLL, *blue spheres*) terminate in particular domains and avoid others. The distribution of some modules is highly related to the tonotopic map (stacked laminae inside the ICC), because some inputs are absent at the ends of the frequency ranges. Within each lamina, disc-shaped neurons (shown in a *red lamina*) extend their dendrites. Adapted, with permission, from Ref. [6]. **c** Schematic diagram of neural circuitry in which LG neurons (*blue cells*) are involved. Inside the ICC, more ventral and medial domains receive dense ascending inputs from the DCN whereas the more lateral domain receives dense inputs from the SOC and NLL. LG neurons receive glutamatergic (*red*) inputs from local and ascending sources. Because local excitatory neurons innervate LG neurons located in different synaptic domains and those located in the same domain, an LG neuron may mix information from multiple synaptic domains. LG neurons may control specific local circuitry in the thalamus, because LG neurons innervate stellate neurons and a subpopulation of tufted neurons in the MGB (color figure online)

lower auditory nuclei to the IC are well-preserved among the mammalian clade [7].

Functional structure of the IC

The IC is subdivided into the central nucleus (ICC) and a surrounding cortex (Fig. 1b). Most of the ascending fibers from the lower auditory brainstem nuclei terminate in the ICC (Fig. 1a) [6]. The IC cortex receives inputs mainly from the ICC [8] and descending fibers from the cerebral cortex [9, 10], which suggests the IC cortex is involved in attention to sound. Interestingly, some neurons in the IC cortex can detect changes in the auditory scene [11]. In addition to the auditory inputs, the lateral cortex of the IC receives visual [12, 13] and somatosensory information [14], which suggests it may also be involved in multimodal integration.

The ICC has a characteristic anatomical organization characterized by fibrodendritic laminae that contain functional zones in different parts of the same layer [15–18]. Disc-shaped neurons have oriented dendrites that form fibrodendritic laminae with flattened plexuses of afferent axons [15] (Fig. 1b). These laminae are the basis of the tonotopic organization of the ICC, and the neurons in the same lamina share a similar best frequency [17, 19]. Although the fibrodendritic laminae that receive inputs share similar frequency tuning, the distribution of afferent inputs from the lower brainstem auditory nuclei is not homogeneous within a lamina. For example, DCN axons terminate in the more dorsomedial parts of the ICC laminae [20] whereas LSO axons terminate on the ventrolateral parts [21] (Figs. 1b, c). This distribution of ascending inputs on the laminae organizes ICC layers into synaptic domains, each of which receives a specific combination of ascending inputs from different brainstem nuclei [6, 18, 22] (Fig. 1b). Thus, in the same lamina, neurons that receive a different combination of afferent inputs will, accordingly, have a substantial differences in their responses to sound [18, 19, 23]. Fibrodendritic laminae and synaptic domains overlap each other and subdivide the ICC into local functional zones (Fig. 1b). In contrast to the ICC, the IC cortex is organized in several layers each of which has distinct input and output connections. The functional organization of the IC cortex is less well known than that of the ICC, but a recent imaging study showed that layer 1 of the dorsal IC cortex has region-specific frequency selectivity [24]. Layer 2 of the IC lateral cortex contains a periodic module composed of small GABAergic neurons (the GABA module, [25]) that have distinct intrinsic membrane properties [26] in GAD67-GFP knock-in mice [27].

Synaptic organization of local circuit in the IC

A unique feature of the IC is that it sends both excitatory and inhibitory projections [28, 29] to the medial geniculate body (MGB, Fig. 1a). IC neurons are either glutamatergic or GABAergic [26, 30], although many kinds of neuromodulator are also expressed in the IC [31–34]. Tectothalamic GABAergic neurons have large somata and a distinctive synaptic structure [29]. Large GABAergic (LG) neurons are covered by numerous axosomatic and axodendritic excitatory terminals. LG neurons are found in a variety of mammalian species (rats, mice, rabbits, bats, and monkeys; unpublished data), suggesting the IC GABAergic neural circuitry is widely preserved among mammals. Calyx-like or endbulb-like synapses have not been found in the IC, and LG neurons have been shown to receive converging inputs from multiple axons from different sources [35–38]. The excitatory axosomatic terminals on LG neurons are positive for vesicular glutamate transporter (VGLUT) 2 but not for VGLUT1 [29], and originate from neurons which express VGLUT2 in the brainstem (DCN, SOC, NLL) and in the IC itself [37, 38]. For example, a single IC excitatory neuron can form an axonal plexus parallel to and within a fibrodendritic lamina and make axosomatic contacts with 10–30 LG neurons within the plexus over a distance of several hundreds of microns. Therefore, the fibrodendritic lamina is the field of convergence for local and ascending axonal inputs. Along a single fibrodendritic lamina, the density of terminals from each ascending source is not homogenous but separated into separate synaptic domains as described above (Fig. 1b). The local excitatory neurons may affect the LG neurons located in neighboring synaptic domains as well as in its own. This suggests that an LG neuron mixes ascending auditory information that it receives directly from ascending fibers with information received by neurons in the neighboring domains (Fig. 1c).

Diverse physiological properties of IC neurons

Previous whole-cell recording studies in the IC in vitro and in vivo showed there were neurons with distinctive firing properties (modeled discharge patterns are shown in Fig. 2a). They were classified into 6–8 types on the basis of the responses to depolarizing and hyperpolarizing currents (Fig. 2a) in mice, rats, and bats [26, 39–41]. It has been suggested that different expression patterns of potassium and calcium channels create these different firing types [26, 39]. IC neurons are also diverse in their input resistances (R_i, Table 1). In-vivo recordings from mature animals revealed that R_i ranged from 30 to 450 MΩ (bat, ICC) [41]

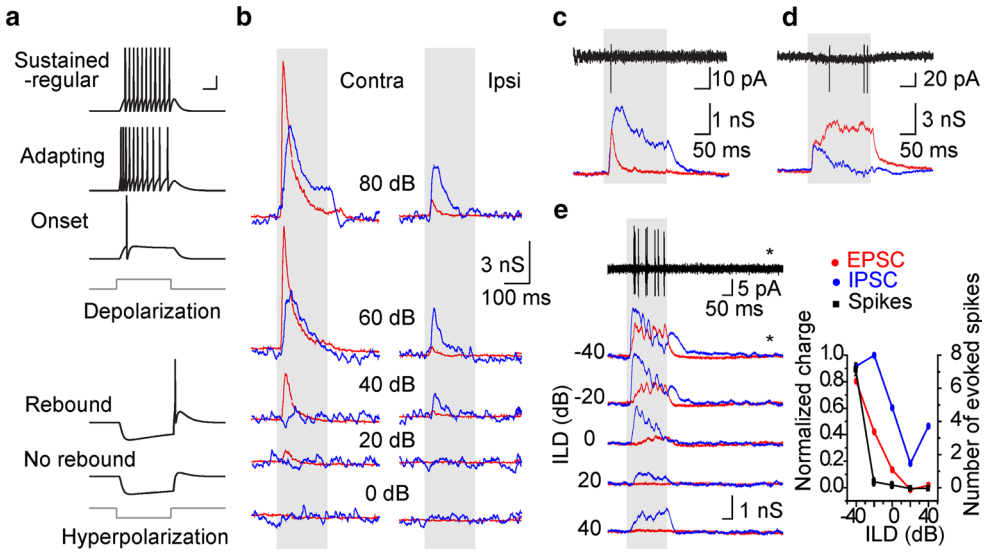

Fig. 2 Firing types and synaptic responses of IC neurons. **a** Illustration of representative discharge patterns of IC neurons in response to current. *Upper* and *lower traces* are responses to depolarizing and hyperpolarizing current (*gray traces*), respectively. These traces were modeled by MATLAB (Mathworks, Natick, MA, USA). *Scale bars*, 20 mV, 50 ms. **b–e** Synaptic responses of mouse IC neurons to sound. Adapted, with permission, from Refs. [53, 54]. These are recordings are from different neurons. **b** The synaptic responses of an IC neuron to contralateral (*left*) and ipsilateral (*right*) sound. *Gray boxes* indicate the timing of sound presentation. *Red* and *blue traces* are excitatory and inhibitory conductance, respectively. The excitatory and inhibitory conductances were separated under the voltage clamp by recording the sound-evoked currents at the reversal potentials of the inhibitory and excitatory inputs, respectively. The responses to different sound intensities ranging from 0 to 80 dB sound pressure level (SPL) are presented. **c**, **d** Spike (*upper black traces*) and synaptic responses to contralateral sound of IC neurons. The spike responses were recorded in gigaseal condition before break-in. Note that the time courses of the excitatory conductance are different. **e** Spike and synaptic responses of an IC neuron to binaural sound of which the interaural level differences (ILD) were varied. The ILD value is shown as negative when contralateral sound was stronger. The spike trace was the response to the sound with ILD of −40 dB (*asterisks*). The ILD tuning curve (*right panel*) of spike responses was more sharply tuned to contralateral side than to that of excitatory inputs (color figure online)

and from 39 to 615 MΩ (mouse, IC cortex) [42]. The R_i values in slice recordings were higher than those in vivo (Table 1), probably because of the immaturity of the tissue (see age in Table 1). R_i was reported to be inversely correlated with somatic size (Table 1) [42] whereas firing types were not well correlated with morphology [26, 43]. Importantly, neurons with different membrane properties were heterogeneously mixed in the IC. No relationship was observed between neuronal membrane property and spatial distribution (except for GABA module neurons [26]). Thus, a synaptic domain in the ICC is likely to contain a mixture of neurons with different intrinsic membrane properties. Interestingly, recent studies using tetrode recordings showed that the correlation of the temporal responses with sound was usually low for closely located ICC neurons [19, 23] and the degree of the correlation of their frequency tuning depended on distance between neurons [19]. These results suggested there might be a

Table 1 The input resistance (R_i) of IC neurons

Cell type	R_i (MΩ)[a]	No. of cells	Species	Age	Preparation	Ref.
Sustained-regular (SR)	393.45 ± 190.1	10	Rat	P8–17	Slice	[39]
Onset	643.71 ± 243.8	8	Rat	P8–17	Slice	[39]
Rebound	229.6 ± 88.0	19	Rat	P10–19	Slice	[62]
SR-GABA	413.0 ± 239.6	69	Mouse	P12–31	Slice	[26]
SR-nonGABA	280.7 ± 120.4	19	Mouse	P12–31	Slice	[26]
All types	106 ± 51	103	Mouse	P21–37	In vivo	[40]
Small (<15 μm)	214 ± 91	68	Mouse	P21–79	In vivo	[42]
Medium (15–25 μm)	144 ± 53	35	Mouse	P21–79	In vivo	[42]
Large (>25 μm)	82 ± 38	12	Mouse	P21–79	In vivo	[42]

[a] R_i is given as mean ± standard deviation. When the original value was given with the standard error, the standard deviation was calculated from the standard error

decorrelation in a synaptic domain that could increase coding capacity [44, 45]. Variability in the intrinsic membrane properties may contribute to decorrelation of the neural responses in the IC local circuit.

Compared with the neurons in the brainstem, the IC neurons have higher R_i (Tables 1 and 2). Neurons with extremely low R_i are seen in the brainstem nuclei (indicated with b in Table 2, i.e., VCN octopus neurons and MSO principal neurons) but not in the IC. Those low R_i neurons are highly specialized for coincidence detection over a sub-millisecond timescale [46]. For these neurons, extremely short membrane time constant makes EPSP brief, so that firing requires highly coincident synaptic summation. The high R_i of the IC neurons might make them less incapable of reproducing the temporal structure of their inputs with high fidelity compared with lower auditory brainstem neurons, and they are more likely to act as temporal integrators [47]. This notion is consistent with the observation that temporal synchronization to amplitude-modulated sound is degraded in the IC [48].

Integration of excitatory and inhibitory synaptic inputs shapes tuning to sound in an IC neuron

As shown above, anatomical studies have suggested that the synaptic inputs from different sources converge on an IC neuron. Reflecting their locations in different synaptic domains, IC neurons will receive synaptic inputs with different temporal patterns. Intracellular studies (cats, guinea pigs, and bats) have shown that interaction of excitatory and inhibitory inputs affects neural responses of IC neurons [49–52]. Recent in-vivo whole-cell recording of mice, rats, and bats have shown that virtually all the IC neurons receive excitatory and inhibitory synaptic inputs (Figs. 2b–e) [53–59]. Analysis of synaptic responses to binaural stimuli showed that many IC neurons receive inputs from several sources (Fig. 2b; note that contralateral and ipsilateral sounds evoked both excitatory and inhibitory responses) [54, 56, 59]. The excitatory inputs are temporally diverse and contribute substantially to the temporal pattern of action potential firing (Figs. 2c–e) [53, 55, 60]. Furthermore, the balance and timing of the excitatory and inhibitory inputs are crucial in shaping the spike responses [53, 55–59, 61]. Because the sound-evoked excitatory and inhibitory synaptic inputs temporally overlap (Figs. 2b–e), their relative size and timing affects spike generation profoundly [53, 58, 61] and determines the sound selectivity of the neuron [55–57, 61]. In binaural responses, nonlinear synaptic summation is also critically involved in shaping the selective responses to different binaural stimuli [54, 56, 59]. Nonlinear summation of monaural responses is observed for synaptic inputs; this sharpens selectivity to interaural level differences (ILD). Furthermore, extracellular and intracellular recordings from the same neuron showed that the ILD curve of spike responses was more sharply tuned than that of the synaptic responses (Fig. 2e). These observations suggest that the sound responses of IC neurons were determined by the complex interaction of synaptic inputs and postsynaptic processes that reflect the intrinsic membrane properties.

Table 2 R_i of auditory brainstem neurons

Nucleus	Cell type	R_i (MΩ)[a]	No. of cells	Species	Age	Ref.
VCN	Bushy	40.2 ± 9.8	24	Mouse	P29–39	[63]
VCN	T-stellate	81.5 ± 36.7	21	Mouse	P29–39	[63]
VCN	D-stellate	60 ± 17	11	Mouse	P16–18	[64]
VCN	Octopus[b]	6 ± 6	10	Mouse	P16–19	[65]
DCN	Fusiform	93.2 ± 49.5	21	Mouse	P15–25	[66]
DCN	Cartwheel	55.7 ± 18.6	5	Mouse	P16–24	[67]
DCN	Vertical	163.7 ± 53.8	27	Mouse	P16–23	[68]
DCN	Stellate	996 ± 749	29	Mouse	P15–32	[69]
MSO	Principal[b]	10 ± 9	18	Gerbil	P17	[70]
LSO	Principal	23.4 ± 19.0	7	Mouse	P23	[71]
MNTB	Principal	80.6 ± 23.4	10	Gerbil	P19–22	[72]
LNTB	Principal	56.5 ± 33.7	50	Gerbil	P18–22	[72]
VLL	Globular	108.3 ± 36.2	7	Gerbil	P25<	[73]
DLL	Principal	137 ± 26	7	Gerbil	P23–26	[5]

MNTB medial nucleus of trapezoid body, *LNTB* lateral nucleus of trapezoid body

[a] R_i is given as mean ± standard deviation. When the original value was given with the standard error, the standard deviation was calculated from the standard error

[b] The neurons with extremely low R_i in the brainstem

Concluding remarks

The mammalian IC is an auditory center that transforms its afferent inputs into excitatory and inhibitory outputs within local functional zones. IC is characterized by a complex neural circuitry in which IC neurons with a variety of physiological properties reside in functional zones that receive different combinations of afferent inputs from different sources. This generates neurons with a great variety of responses to sound. This complexity and diversity makes it challenging to elucidating the function of the IC. To truly understand the function of the IC, we require more basic knowledge to distinguish the unique phenotypes of IC neurons in vitro and in vivo. It will be also an important to investigate common and different interspecies features of the physiological characteristics of IC neurons, because most current knowledge of the cellular physiology on IC neurons is based on recordings from rodents.

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Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

References

1. Ohmori H (2014) Neuronal specializations for the processing of interaural difference cues in the chick. Front Neural Circuit 8:47
2. Schnupp JW, Carr CE (2009) On hearing with more than one ear: lessons from evolution. Nat Neurosci 12:692–697
3. Young ED, Oertel D (2004) Cochlear nucleus. In: Shepard GM (ed) The synaptic organization of the brain, 5th edn. Oxford University Press, Oxford, pp 125–163
4. Grothe B, Pecka M, McAlpine D (2010) Mechanisms of sound localization in mammals. Physiol Rev 90:983–1012
5. Ammer JJ, Grothe B, Felmy F (2012) Late postnatal development of intrinsic and synaptic properties promotes fast and precise signaling in the dorsal nucleus of the lateral lemniscus. J Neurophysiol 107:1172–1185
6. Oliver DL (2005) Neuronal organization in the inferior colliculus. In: Winer JA, Schreiner CE (eds) The inferior colliculus. Springer, New York, pp 69–114
7. Winer JA, Schreiner CE (2005) The central auditory system: a functional analysis. In: Winer JA, Schreiner CE (eds) The inferior colliculus. Springer, New York, pp 1–68
8. Saldana E, Merchan MA (2005) Intrinsic and commissural connections of the inferior colliculus Chapter 5. In: Winer JA, Schreiner CE (eds) The inferior colliculus. Springer, New York, pp 155–181
9. Winer JA (2005) Three systems of descending projections to the inferior colliculus. In: Winer JA, Schreiner CE (eds) The inferior colliculus. Springer, New York, pp 231–247
10. Ayala YA, Udeh A, Dutta K et al (2015) Differences in the strength of cortical and brainstem inputs to SSA and non-SSA neurons in the inferior colliculus. Sci Rep 5:10383
11. Ayala YA, Malmierca MS (2012) Stimulus-specific adaptation and deviance detection in the inferior colliculus. Front Neural Circuit 6:89
12. Yamauchi K, Yamadori T (1982) Retinal projection to the inferior colliculus in the rat. Acta Anat 114:355–360
13. Itaya SK, Van Hoesen GW (1982) Retinal innervation of the inferior colliculus in rat and monkey. Brain Res 233:45–52
14. Itoh K, Kaneko T, Kudo M et al (1984) The intercollicular region in the cat: a possible relay in the parallel somatosensory pathways from the dorsal column nuclei to the posterior complex of the thalamus. Brain Res 308:166–171
15. Oliver DL, Morest DK (1984) The central nucleus of the inferior colliculus in the cat. J Comp Neurol 222:237–264
16. Malmierca MS, Blackstad TW, Osen KK et al (1993) The central nucleus of the inferior colliculus in rat: a Golgi and computer reconstruction study of neuronal and laminar structure. J Comp Neurol 333:1–27
17. Schreiner CE, Langner G (1997) Laminar fine structure of frequency organization in auditory midbrain. Nature 388:383–386
18. Loftus WC, Bishop DC, Oliver DL (2010) Differential patterns of inputs create functional zones in central nucleus of inferior colliculus. J Neurosci 30:13396–13408
19. Chen C, Rodriguez FC, Read HL et al (2012) Spectrotemporal sound preferences of neighboring inferior colliculus neurons: implications for local circuitry and processing. Front Neural Circuit 6:62
20. Oliver DL (1984) Dorsal cochlear nucleus projections to the inferior colliculus in the cat: a light and electron microscopic study. J Comp Neurol 224:155–172
21. Oliver DL, Beckius GE, Bishop DC et al (1997) Simultaneous anterograde labeling of axonal layers from lateral superior olive and dorsal cochlear nucleus in the inferior colliculus of cat. J Comp Neurol 382:215–229
22. Cant NB, Benson CG (2006) Organization of the inferior colliculus of the gerbil (*Meriones unguiculatus*): differences in distribution of projections from the cochlear nuclei and the superior olivary complex. J Comp Neurol 495:511–528
23. Seshagiri CV, Delgutte B (2007) Response properties of neighboring neurons in the auditory midbrain for pure-tone stimulation: a tetrode study. J Neurophysiol 98:2058–2073
24. Ito T, Hirose J, Murase K et al (2014) Determining auditory-evoked activities from multiple cells in layer 1 of the dorsal cortex of the inferior colliculus of mice by in vivo calcium imaging. Brain Res 1590:45–55
25. Chernock ML, Larue DT, Winer JA (2004) A periodic network of neurochemical modules in the inferior colliculus. Hear Res 188:12–20
26. Ono M, Yanagawa Y, Koyano K (2005) GABAergic neurons in inferior colliculus of the GAD67-GFP knock-in mouse: electrophysiological and morphological properties. Neurosci Res 51:475–492

27. Gocho Y, Sakai A, Yanagawa Y et al (2013) Electrophysiological and pharmacological properties of GABAergic cells in the dorsal raphe nucleus. J Physiol Sci 63:147–154
28. Winer JA, Saint Marie RL, Larue DT et al (1996) GABAergic feedforward projections from the inferior colliculus to the medial geniculate body. Proc Natl Acad Sci USA 93:8005–8010
29. Ito T, Bishop DC, Oliver DL (2009) Two classes of GABAergic neurons in the inferior colliculus. J Neurosci 29:13860–13869
30. Oliver DL, Winer JA, Beckius GE et al (1994) Morphology of GABAergic neurons in the inferior colliculus of the cat. J Comp Neurol 340:27–42
31. Coote EJ, Rees A (2008) The distribution of nitric oxide synthase in the inferior colliculus of guinea pig. Neuroscience 154:218–225
32. Tongjaroenbuangam W, Jongkamonwiwat N, Phansuwan-Pujito P et al (2006) Relationship of opioid receptors with GABAergic neurons in the rat inferior colliculus. Eur J Neurosci 24:1987–1994
33. Nakagawa H, Ikeda M, Houtani T et al (1995) Immunohistochemical evidence for enkephalin and neuropeptide Y in rat inferior colliculus neurons that provide ascending or commissural fibers. Brain Res 690:236–240
34. Wynne B, Harvey AR, Robertson D et al (1995) Neurotransmitter and neuromodulator systems of the rat inferior colliculus and auditory brainstem studied by in situ hybridization. J Chem Neuroanat 9:289–300
35. Ito T, Oliver DL (2010) Origins of glutamatergic terminals in the inferior colliculus identified by retrograde transport and expression of VGLUT1 and VGLUT2 genes. Front Neuroanat 4:135
36. Ito T, Bishop DC, Oliver DL (2011) Expression of glutamate and inhibitory amino acid vesicular transporters in the rodent auditory brainstem. J Comp Neurol 519:316–340
37. Ito T, Oliver DL (2014) Local and commissural IC neurons make axosomatic inputs on large GABAergic tectothalamic neurons. J Comp Neurol 522:3539–3554
38. Ito T, Hioki H, Sohn J et al (2015) Convergence of lemniscal and local excitatory inputs on large GABAergic tectothalamic neurons. J Comp Neurol 523:2277–2296
39. Sivaramakrishnan S, Oliver DL (2001) Distinct K currents result in physiologically distinct cell types in the inferior colliculus of the rat. J Neurosci 21:2861–2877
40. Tan ML, Theeuwes HP, Feenstra L et al (2007) Membrane properties and firing patterns of inferior colliculus neurons: an in vivo patch-clamp study in rodents. J Neurophysiol 98:443–453
41. Xie R, Gittelman JX, Li N et al (2008) Whole cell recordings of intrinsic properties and sound-evoked responses from the inferior colliculus. Neuroscience 154:245–256
42. Geis HR, Borst JG (2013) Large GABAergic neurons form a distinct subclass within the mouse dorsal cortex of the inferior colliculus with respect to intrinsic properties, synaptic inputs, sound responses, and projections. J Comp Neurol 521:189–202
43. Peruzzi D, Sivaramakrishnan S, Oliver DL (2000) Identification of cell types in brain slices of the inferior colliculus. Neuroscience 101:403–416
44. Chen C, Read HL, Escabi MA (2012) Precise feature based time scales and frequency decorrelation lead to a sparse auditory code. J Neurosci 32:8454–8468
45. Friedrich RW (2013) Neuronal computations in the olfactory system of zebrafish. Annu Rev Neurosci 36:383–402
46. Golding NL, Oertel D (2012) Synaptic integration in dendrites: exceptional need for speed. J Physiol 590:5563–5569
47. Konig P, Engel AK, Singer W (1996) Integrator or coincidence detector? The role of the cortical neuron revisited. Trend Neurosci 19:130–137
48. Joris PX, Schreiner CE, Rees A (2004) Neural processing of amplitude-modulated sounds. Physiol Rev 84:541–577
49. Nelson PG, Erulkar SD (1963) Synaptic mechanisms of excitation and inhibition in the central auditory pathway. J Neurophysiol 26:908–923
50. Pedemonte M, Torterolo P, Velluti RA (1997) In vivo intracellular characteristics of inferior colliculus neurons in guinea pigs. Brain Res 759:24–31
51. Kuwada S, Batra R, Yin TC et al (1997) Intracellular recordings in response to monaural and binaural stimulation of neurons in the inferior colliculus of the cat. J Neurosci 17:7565–7581
52. Covey E, Kauer JA, Casseday JH (1996) Whole-cell patch-clamp recording reveals subthreshold sound-evoked postsynaptic currents in the inferior colliculus of awake bats. J Neurosci 16:3009–3018
53. Ono M, Oliver DL (2014) Asymmetric temporal interactions of sound-evoked excitatory and inhibitory inputs in the mouse auditory midbrain. J Physiol 592:3647–3669
54. Ono M, Oliver DL (2014) The balance of excitatory and inhibitory synaptic inputs for coding sound location. J Neurosci 34:3779–3792
55. Kuo RI, Wu GK (2012) The generation of direction selectivity in the auditory system. Neuron 73:1016–1027
56. Xiong XR, Liang F, Li H et al (2013) Interaural level difference-dependent gain control and synaptic scaling underlying binaural computation. Neuron 79:738–753
57. Gittelman JX, Li N, Pollak GD (2009) Mechanisms underlying directional selectivity for frequency-modulated sweeps in the inferior colliculus revealed by in vivo whole-cell recordings. J Neurosci 29:13030–13041
58. Gittelman JX, Pollak GD (2011) It's about time: how input timing is used and not used to create emergent properties in the auditory system. J Neurosci 31:2576–2583
59. Li N, Pollak GD (2013) Circuits that innervate excitatory-inhibitory cells in the inferior colliculus obtained with in vivo whole cell recordings. J Neurosci 33:6367–6379
60. Kasai M, Ono M, Ohmori H (2012) Distinct neural firing mechanisms to tonal stimuli offset in the inferior colliculus of mice in vivo. Neurosci Res 73:224–237
61. Gittelman JX, Wang L, Colburn HS et al (2012) Inhibition shapes response selectivity in the inferior colliculus by gain modulation. Front Neural Circuit 6:67
62. Sun H, Wu SH (2008) Physiological characteristics of postinhibitory rebound depolarization in neurons of the rat's dorsal cortex of the inferior colliculus studied in vitro. Brain Res 1226:70–81
63. Xie R, Manis PB (2013) Target-specific IPSC kinetics promote temporal processing in auditory parallel pathways. J Neurosci 33:1598–1614
64. Rodrigues AR, Oertel D (2006) Hyperpolarization-activated currents regulate excitability in stellate cells of the mammalian ventral cochlear nucleus. J Neurophysiol 95:76–87
65. Cao XJ, Oertel D (2011) The magnitudes of hyperpolarization-activated and low-voltage-activated potassium currents co-vary in neurons of the ventral cochlear nucleus. J Neurophysiol 106:630–640
66. Apostolides PF, Trussell LO (2014) Control of interneuron firing by subthreshold synaptic potentials in principal cells of the dorsal cochlear nucleus. Neuron 83:324–330
67. Bender KJ, Ford CP, Trussell LO (2010) Dopaminergic modulation of axon initial segment calcium channels regulates action potential initiation. Neuron 68:500–511
68. Kuo SP, Lu HW, Trussell LO (2012) Intrinsic and synaptic properties of vertical cells of the mouse dorsal cochlear nucleus. J Neurophysiol 108:1186–1198
69. Apostolides PF, Trussell LO (2013) Regulation of interneuron excitability by gap junction coupling with principal cells. Nat Neurosci 16:1764–1772

70. Magnusson AK, Kapfer C, Grothe B et al (2005) Maturation of glycinergic inhibition in the gerbil medial superior olive after hearing onset. J Physiol 568:497–512
71. Walcher J, Hassfurth B, Grothe B et al (2011) Comparative posthearing development of inhibitory inputs to the lateral superior olive in gerbils and mice. J Neurophysiol 106:1443–1453
72. Roberts MT, Seeman SC, Golding NL (2014) The relative contributions of MNTB and LNTB neurons to inhibition in the medial superior olive assessed through single and paired recordings. Front Neural Circuit 8:49
73. Franzen DL, Gleiss SA, Berger C et al (2015) Development and modulation of intrinsic membrane properties control the temporal precision of auditory brain stem neurons. J Neurophysiol 113:524–536