

Auditory processing in birds

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Over the past year, much progress has been achieved in the study of both the peripheral and the central auditory systems of birds. Significant advances have been made in the study of hair cells, including elucidation of the mechanisms of selectivity for sound frequency, functional differentiation, efferent innervation, and regeneration. Most of the studies of central auditory neurones have concerned the developmental and physiological correlates of vocal learning in songbirds and sound localisation in owls.

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Abbreviations

AFP	anterior forebrain pathway
BOS	bird's own song
DLM	medial portion of dorsolateral nucleus of anterior thalamus
GABA	γ -aminobutyric acid
HVC	high vocal centre
ICx	external nucleus of inferior colliculus
IID	interaural intensity difference
ITD	interaural time difference
LMAN	lateral portion of magnocellular nucleus of anterior neostriatum
NIF	interfacial nucleus
NL	nucleus laminaris
NM	nucleus magnocellularis
RA	robust nucleus of archistriatum
SHC	short hair cell
SOAE	spontaneous otoacoustic emission
UVA	uvaeform nucleus
X	Area X

Introduction

Auditory processing begins with the encoding of frequency, amplitude, and phase. The hair cells of the avian inner ear use both mechanical resonance and electrical mechanisms for their frequency selectivity, and the past two years have seen much progress in the study of the ionic bases for frequency tuning. New developments have also been reported in other aspects of hair-cell research, such as functional differentiation, efferent innervation, otoacoustic emissions, and regeneration. We will discuss these topics in the first section of this review.

The central auditory system synthesises representations of complex stimuli from the coded data provided by primary afferent fibres of the ear. The creation of auditory receptive fields and space maps in barn owls exemplifies how this synthesis proceeds. Encoding of interaural time differences (ITDs) by coincidence detection is an important component of these creative processes. We will briefly dis-

cuss the current state of research on this topic. The final section reviews recent studies on auditory responses within the avian song control system. Also presented is a brief discussion of neural plasticity in the auditory systems of both barn owls and songbirds.

Inner ear

Recent research into the avian basilar papilla has concentrated on four areas: hair-cell tuning mechanisms; the functional significance of hair-cell specialisation; the function of the efferent innervation that provides feedback from the brain; and hair-cell regeneration. For information deriving from earlier studies on the bird cochlea, readers are referred to recent more-general reviews [1,2].

Mechanisms of frequency selectivity in avian hair cells

In birds, frequency tuning depends on morphological and molecular gradients both along and across the basilar papilla; these gradients determine the micromechanical and electrical properties of the hair cells. Morphological gradients are seen in many parameters, for example the size and shape of the hair cells and the tectorial membrane, the size, shape and orientation of the mechanosensitive hair-cell bundles, and the number and size of afferent and efferent nerve terminals (for a recent review, see [1]). Considering the multitude of morphological gradients, it has been suggested that, in fact, every hair cell in the avian basilar papilla is a unique individual [3]. These morphological and molecular gradients also conform with expectations for a micromechanically resonant system at the frequencies known to excite the respective papillar locations (for example, see [4]), although this has not yet been modelled in sufficient detail. There is little doubt, however, that the gradients of bundle stiffness and tectorial mass, for example, would be large enough to establish resonant frequencies in the expected range.

Recent molecular studies of hair cells provide a remarkable parallel to these morphological data: with respect to their ion channel complements, every hair cell of the chicken's papilla may have a different phenotype [5]. Thus, it now seems that, in parallel to the morphological gradients, equivalent changes in molecular composition occur.

The resonant frequency of hair cells in non-mammalian papillae is also influenced by gradients in the number and kinetics of Ca^{2+} -dependent K^+ channels (K_{Ca} ; for a review, see [6•]). These are products of the *cSlo* gene [5]. Kinetic variations between channels — which affect the resonance frequency — are determined at least partially by alternative splicing of *cSlo* products. In the chicken's papilla, Rosenblatt and colleagues [5] have described numerous isoforms of K_{Ca} channels generated by alternative mRNA splicing at seven sites in *cSlo*. These isoforms vary in their Ca^{2+} and voltage

sensitivities and are differentially distributed along the papilla, which suggests that these properties contribute to the frequency map in the papilla [5]. The range of channel kinetics is extended by an accessory subunit that is preferentially expressed by apical hair cells (which are tuned to low frequencies). This subunit exaggerates the kinetic differences between alternatively spliced channel types [7,8^{*}]. Similarly, but less dramatically, the molecular determinants of the magnitude of the calcium current that activates the K_{Ca} channels result at least in part from cell-specific splicing of gene products for Ca^{2+} -channel subunits [9].

Alternative splicing can potentially generate thousands of channel phenotypes [10] that, when combined with variations in calcium sensitivities, modulation by β subunits and differing channel numbers per cell, could easily account for a large range of frequency responses. This raises the very interesting issue of whether the factors determining the unique morphologies and those determining the molecular make-up of avian hair cells develop independently of each other, or whether the variation in splicing is a consequence of the mechanical tuning of the hair cells [10] or vice versa. The avian auditory papilla will, in the future, provide one of the most interesting examples of genetic flexibility for the creation of a wide spectrum of functional variations within one type of cell.

Cochlear amplification and the specialisation of hair-cell populations in birds

There are two principal hair-cell populations (tall and short) in the avian basilar papilla, which show several interesting structural and functional similarities to the inner and outer hair cells of mammals, although they are not identical to those (for reviews, see e.g. [11,12]). The short hair cells (SHCs), which comprise up to 35% of all hair cells, totally lack afferent innervation, but receive large efferent synapses [13]. This was an unexpected and exciting discovery that raised important questions relating to function. It is the only known case of sensory cells routinely lacking an afferent innervation: in this respect, hair-cell differentiation has evolved further in birds than in mammals, as mammalian outer hair cells are afferently innervated, albeit by only about 5% of afferent nerve fibres. Recent work on the papilla of a primitive bird, the emu [4,14], suggests that this differential innervation of hair-cell populations may have arisen earlier than other hair-cell morphological specialisations.

The function of SHCs may be to modify the micro-mechanical environment of other hair cells [1,12] by acting as cochlear amplifiers. In mammals, this function is well accepted for the outer hair cells, whose active contractions are thought to be a central element in a complex positive feedback loop (for example, see [15]). Evidence for a cochlear amplifier in non-mammalian ears is widespread, but often indirect (for example, see [12,16,17]). It is thus not yet generally accepted that such amplification is the rule, for the mechanisms underlying it, as well as the implications for the mammalian case, are highly controversial. Spontaneous

otoacoustic emissions (SOAEs; faint tones produced by the inner ear under quiet conditions) are evidence for active processes in the cochlea and they were recently demonstrated in the barn owl at frequencies up to 10.5 kHz [18]. New work on primary auditory neurones in two bird species, the emu and the barn owl, has further strengthened the argument for an active mechanism operating in the avian basilar papilla. Rate–intensity functions of single auditory-nerve fibres of both species have been studied in detail and reveal a characteristic non-linear response component indicating amplification at low sound levels and compression at medium to high levels [19^{*},20^{*}]. Although this is similar in its effect to the cochlear amplifier of mammals, the underlying mechanisms in birds are unknown and unravelling them will be an exciting task for the future.

Complexity of the efferent cochlear system

The function of the efferent cochlear system in birds, which provides neural feedback from the brain, is largely unknown. All hair cells receive efferent input; however, the existence of the specialised group of SHCs, having only efferent (and no afferent) connections [13], suggests that different sub-populations of efferents may exist. Physiologically, there is evidence for different types of efferents. Recordings from presumed efferent neurones in the brainstem of chickens revealed several types of responses, including both excitation, i.e. an increase in spike rate, and inhibition, i.e. a decrease in spike rate, to sound stimulation [21]. Together, these different types could form a complex modulatory system, depending on exactly how they connect to the hair cells of the cochlea, which is largely unknown. Each cochlea receives approximately equal numbers of ipsilateral and contralateral efferents (for example, see [22]). Recent experiments testing the influence of contralateral-sound-activated efferents on otoacoustic emissions in the barn owl have provided a first glimpse of the potentially diverse role of efferent fibres [23^{*}]. In the absence of contralateral stimulation, the amplitudes of distortion-product otoacoustic emissions drift over time. The amplitudes of the emissions sometimes gradually increase, sometimes decrease, over periods of many minutes. The effect of efferent activation via noise to the contralateral ear often appeared to be a stabilising one. Depending on the direction of the drift behaviour of the emission, efferent activation could suppress (if the emission had drifted up in amplitude) or enhance (if it had drifted down in amplitude) the emission. When using pure tones for efferent activation, their effect was highly frequency selective, indicating the ability for regional modulation by efferents. Clearly, this is only the beginning of our understanding of the cochlear efferent system in birds.

The regeneration of hair cells

The capacity of birds to replace hair cells fatally damaged by loud sounds or by drugs, and the ability of this replacement to restore hearing, has spurred great interest since its discovery 13 years ago. Initial efforts focused on docu-

menting the time course and the extent of the generation of new hair cells as well as the accompanying changes in hearing thresholds (for recent reviews, see [24••,25••]). It is now well known that traumatising of the avian auditory papilla (either by sound overexposure or by aminoglycoside antibiotics) that leads to hair-cell death initiates both the proliferation, and the differentiation into new hair cells, of supporting-cell populations. New cells differentiate in a manner that conforms to their specific location in the epithelium; they then connect to the tectorial membrane and establish contact with nerve fibres. Little information is available on the molecular triggers that initiate and guide the regeneration processes.

Current work is increasingly concentrating on the details of functional recovery, as well as on the fate of the neurones that innervate the damaged hair cells and presumably reconnect appropriately. Single-unit recordings in the auditory nerve after severe acoustic trauma have confirmed the initial devastating effects and the subsequent recovery, as seen previously in evoked-potential recordings. However, residual deficits do become apparent at the single-unit level. Thus, whereas sensitivity and frequency tuning are restored completely after acoustic trauma, rate–intensity functions remain abnormal within the damaged and repaired area [25••,26]. Interestingly, the remaining deficits are more pronounced if the initial damage is effected with aminoglycosides. This has been delineated more clearly and in more detail by recent single-unit recordings in the pigeon [27]. After treatment with aminoglycosides, neuronal thresholds and frequency selectivity never reach control values and the rate–intensity functions remain steeper than normal. The different extent of functional recovery correlates with the known differences in the damage patterns produced by loud sounds and by aminoglycosides. Aminoglycosides kill all hair cells at the affected sites but spare the tectorial membrane, whereas sound preferentially destroys the subpopulation of short hair cells and leaves a lesion in the tectorial membrane. The damage to the tectorial membrane is never completely repaired, so this may account for some of the residual functional deficits after sound damage [25••]. The re-innervation of regenerated hair cells, especially by efferent fibres, takes considerably longer after aminoglycoside damage than after sound damage, which suggests that defects in innervation may be responsible for the remaining functional deficits in this case [24••,25••]. Detailed investigations of damage and recovery patterns thus promise not only to reveal the mechanisms of regeneration, but also to shed light on the roles of different elements in the normal functions of the avian cochlea and the functions of the different hair-cell populations.

In undamaged ears of normal canaries, Gleich *et al.* [28] found a very low rate of supporting-cell proliferation. The rate is much higher in normal ears that have sustained noise damage but also in undamaged ears of a race of genetic mutants known as Waterslager. The increased proliferation

rate is associated with the presence of immature, regenerating hair cells. Waterslager canaries thus show spontaneous, continuous hair-cell loss and regeneration and provide a promising model for hair-cell regeneration processes. Although bird species are differently susceptible to noise damage, this is partly a result of variations in the regulation of middle-ear pressure during sound exposure [29].

Coincidence detection in the brainstem

Coincidence detection is the basic mechanism by which differences in the arrival times of a sound signal at both ears are determined, which is in turn the major cue for localising sound in the azimuth. Briefly, the ongoing temporal structure of a signal is coded separately in each frequency channel of the cochlear output by phase-locking of the primary afferents. In birds, phase-locked spikes from both ears are then conveyed, via the nucleus magnocellularis (NM), to neurones of the nucleus laminaris (NL) for binaural comparison. Spikes from one side (as in chickens) or both sides (as in owls) are systematically delayed in their arrival along an array of NL neurones such that the range of possible ITDs is systematically compensated for and leads to coincident arrival of the spikes from both sides at particular subsets of neurones. NL neurones thus act as coincidence detectors, and a map of azimuthal sound-source locations is formed (for a recent review, see [30]). Although partially understood for a long time, some crucial problems of coincidence detection in NL neurones still remain unsolved. Among these are how their relative independence of changes in overall sound intensity is achieved, and how coincidence detection is maintained at all at higher frequencies, where temporal jitter in the input spikes severely degrades the performance of models (for example, see [31]). Extensive data from the barn owl have shown that phase-locking and coincidence detection can be operational for frequencies of up to 9–10 kHz (for example, see [32,33]) and that coincidence detection is largely independent of overall sound level [34].

Recent work on brain slice preparations from embryonic or very young chickens has concentrated on the effects of inhibitory inputs and has revealed several interesting features that may contribute to improve coincidence detection and intensity independence. Activation of known sources of GABAergic input triggers a long-term depolarisation of both NM and NL neurones, and an inhibition of spike discharges results from a shunting effect of the activated currents [35••,36]. In NL neurones, GABAergic input also significantly shortens the time course and reduces the amplitude of excitatory postsynaptic potentials, thereby also potentially reducing temporal overlap between excitatory inputs and improving the precision of coincidence detection. A narrowing of the temporal coincidence window for a response in the presence of GABA was indeed shown directly by Funabiki *et al.* [37]. The GABAergic input to NL thus appears to provide both a sharpening of the temporal coincidence window and, as had been suggested on the basis of its cir-

cuitry and known physiological responses, a gain-control system [34,38]. Interestingly, experiments using a range of GABA concentrations suggest that at very low concentrations (i.e. very low sound levels under *in vivo* conditions) the effects of GABA may even be reversed, making the gain control very sophisticated indeed [39]. The challenge now remains to confirm all these effects in the mature auditory system *in vivo* (for a related review, see Grothe and Klump, pp 467–473, this issue).

Behaviour and central neurones

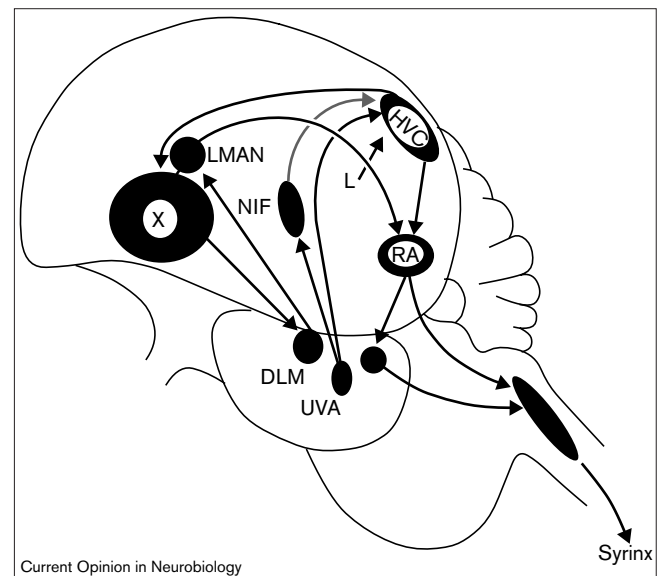
The majority of recent publications on the avian central auditory system concern the neural mechanisms of vocal learning in songbirds and sound localisation in owls. In this review of recent papers on birdsong research, we now focus on findings that require changes in existing views.

Auditory feedback

The view that auditory feedback is necessary for song development in young birds but not for the maintenance of song by adult birds is changing. Both deafening and non-invasive manipulations of auditory feedback cause large changes in the song of adult zebra and Bengalese finches [40–42,43••]. Of particular interest is the bird's ability to recover its original song when normal feedback is restored [43••]. These findings are also inconsistent with the view that song crystallisation marks the end of vocal plasticity in age-limited learners which cease to learn new song after the first year. A word of caution is, however, in order: it is important to consider species and age differences in the effects of feedback removal or perturbation.

The control of vocalisation by auditory feedback requires direct or indirect links between the vocal and auditory systems. Auditory responses of neurones within the vocal control system have been recorded in songbirds, bats, and a type of parrot [44]. The forebrain part of the song system contains two pathways that start from the high vocal centre ([HVC], the caudal part of the ventral hyperstriatum) and converge in the robust nucleus of the archistriatum (RA; see Figure 1). The anterior forebrain pathway (AFP) travels from HVC to RA by way of Area X, the medial portion of the dorsolateral nucleus of anterior thalamus (DLM), and the lateral portion of the magnocellular nucleus of the anterior neostriatum (LMAN). This pathway has been thought to be necessary only for song learning in young birds [45]; however, this view is also subject to revisions. Lesions of LMAN cause significant changes in the song of adult white-crowned sparrows [46]. LMAN is also essential for the restoration of song after modification by injuries to the syringeal nerve in adult zebra finches [47]. Here, again, the distinction between age-limited and open-ended learners becomes obscure, because both groups are now known to need the AFP to maintain adult song. Also, the view that the sole function of the AFP is to mediate the use of auditory feedback for vocal control may not hold. Lesions in the pathways appear to have some effects on the discrimination of conspecific songs in zebra finches

Figure 1



The song system. A schematic drawing of the song system showing only the nuclei and their connections mentioned in the text. Arrows indicate the direction in which neural signals travel. Note that HVC projects to RA both directly and indirectly by way of X, DLM, and LMAN. L, field L.

and the retention of learned discrimination of auditory stimuli in female canaries [48,49].

The assumption that lesions of the AFP disrupt only the flow of signals within it also needs to be re-examined. Ablation of LMAN in young birds induces a premature transformation of synapses from juvenile to adult forms in RA, including those that connect HVC axons to RA neurones [50]. This change alone can explain the disruption of vocal learning without invoking any mechanisms unique to the AFP. On the other hand, this finding cannot explain why lesions of the AFP in adult birds prevent restoration of distorted song, if the pathway were to affect song only by acting on RA.

The relationships between the motor and auditory aspects of the song system remain to be clarified. Most of the song nuclei in which recordings are made under anaesthesia show responses to auditory stimuli, particularly the bird's own song (BOS). Early studies reported that auditory neurones in HVC tended to project to Area X, implying that RA-projecting neurones do not receive auditory input [51,52]. This claim partly contributed to the old view that the AFP dealt with auditory feedback, whereas the other pathway carried vocal motor signals. Recent studies, however, show that both the X- and RA-projecting neurones of HVC respond to BOS [53••]. If auditory neural signals descend both pathways, how about pre-motor signals? Multi-unit recordings in LMAN show both pre-motor discharges in the singing bird and some responses to playback of BOS in the awake adult bird. This pre-motor firing may

be an efference copy of the signals going to RA. As in the direct pathway, the temporal pattern of the pre-motor discharges does not change after deafening [54*].

Auditory gating

The question of whether the same neurones carry both pre-motor and auditory signals has not been answered, although auditory responses in motor neurones innervating the syringeal muscles indicate dual functions [55]. However, mixing of auditory and motor signals does not appear to happen, even if the same neurones convey both. Early studies reported that HVC neurones responded to playback of BOS in awake and silent canaries. However, it has been observed that neither natural feedback nor playback of BOS can elicit responses during, and for a period (10–20 secs) after, singing [56]. Recent studies also show in zebra finches that more HVC or RA neurones respond to BOS when the birds are anaesthetised or asleep than when they are awake [57,58]. These findings suggest that the entry of auditory neural signals to the song system is gated. We do not know where this gating takes place, although neurones of Field L2, from which HVC receives direct or indirect input, respond well to playback of BOS in the awake bird [58]. Thus, the site of the gate may be within HVC or between this nucleus and Field L2. Interestingly, stimulation of the uvulaeform nucleus (UVA) abolishes auditory responses in HVC under anaesthesia. UVA may, therefore, send signals to block auditory responses in the HVC of the singing bird [59].

Auditory plasticity

The selectivity for BOS is the clearest example in which neuronal responses to complex stimuli develop as a result of experience. Several studies have shown that this selectivity emerges as song develops [60,61]. These findings indicate that the selectivity develops as a result of either hearing or producing the song or both. Cutting the syringeal nerve before the onset of singing can prevent birds from reproducing tutor songs. A few Area X neurones of zebra finches that had received this operation responded to both the tutor song and the distinctly different BOS [62*,63*]. This is the first case in which song-selective neurones have been shown to respond to a tutor song that is heard but not vocally reproduced. These neurones are, however, much less selective for songs than Area X neurones of normal birds. The extent to which the reduced selectivity contributes to their dual responses to BOS and tutor song is not clear. This brings up another issue. The physical cues to which these neurones respond are not known. This problem must be addressed in all studies of neuronal selectivity for song [64,65*]. The selectivity for BOS is thought to emerge in HVC and thence it is conveyed to the rest of the song system. A recent study shows, however, that neurones of the interfacial nucleus (NIF) are sensitive for BOS, although as a population these neurones are not as song-selective as HVC neurones [66]. It should also be pointed out that

song stimuli induce early immediate genes such as *fos* and *Zenk* in areas other than the song system [67,68].

Barn owls offer another illustrative example of developmental plasticity within the avian auditory system [69*]. The owl's external nucleus of the inferior colliculus (ICx) contains a map of auditory space in which neurones respond selectively to the direction of sound sources. This selectivity is attributable to the tuning of neurones to combinations of the ITD for azimuth and the interaural intensity difference (IID) for elevation. The ICx map projects to the optic tectum to form an auditory–visual map of space. A displacement of the visual field by prisms in young owls causes their ICx auditory space map to shift towards the displaced visual map. The spatial receptive field of an ICx neurone consists of an excitatory centre with an inhibitory surround [70]. A recent study suggests that an ICx neurone's preferred ITD shifts, because the balance between excitation and inhibition changes [71*]. Visually induced shifts of best ITDs also occur in the forebrain pathway that bypasses the tectal pathway but includes ICx and the optic tectum [72]. This finding is surprising for two reasons; first, because neurones in this forebrain pathway do not form maps of auditory space; and second, because the only known site of plasticity is ICx [73]. Lateral inhibition that mediates shifts of best ITDs requires mapping of ITDs. The lateral shell, which projects to both ICx and the thalamus, may contain ITD–IID sensitive neurones which also respond to shifts in the visual field.

The avian central auditory system shares many properties with the mammalian one, despite a general ignorance of this fact. For example, mammals including humans and birds use a process similar to cross-correlation to measure ITDs in order to localise sound. If interaural correlation is important for the derivation of ITDs, decorrelation should affect it. Humans perceive blurred images when they listen to partially correlated signals through earphones [73]. Humans and owls perform similarly when attempting to localise partially correlated signals [74,75]. In owls, the response of an ensemble of neurones can account for some of the statistical characteristics of behavioural responses to decorrelation [76].

Conclusions

Several interesting facts and questions have emerged from the study of avian hair cells. The use of mechanical and electrical methods of frequency tuning is particularly interesting in birds, because some birds can hear frequencies as high as 10 kHz. The extent to which these tuning methods are weighted according to frequency, and whether electrical tuning functions up to the highest frequencies, are still open questions. The presumed match in frequency in individual hair cells between the two tuning methods also calls for an explanation. The SHCs that receive only efferent innervation are unique to birds. The signals they receive from the brain and their function in the hearing epithelium still require clarification. Regarding the regeneration of hair

cells, further open questions relate to the genetic regulation of this process, and whether the expression of the relevant genes can be re-activated in the mammalian organ of Corti.

In mammals (except for bats), the central auditory system above the inferior colliculus has been much less studied than have the lower-order systems. On the other hand, the auditory physiology of songbirds has concentrated on the forebrain song nuclei, some of which perhaps serve as the interface between the auditory and vocal systems. The fundamental question remaining in this field is why auditory input enters most of the song nuclei. As preliminary studies suggest, recording from single neurones in behaving birds is essential if this question is to be answered. Also, circuit level analyses of cell types and connectivity using intracellular electrodes will settle many other important questions. In the barn owl's auditory system, it is important to know how and to what extent the inputs to the tectal and forebrain pathways from the inferior colliculus differ from each other. Lastly, the biophysical and ionic mechanisms of coincidence detection in NL remain the Holy Grail of this research field.

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