

Sensory Representations in the Auditory Cortex and Thalamus

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Abstract

What are the similarities and differences between sensory representations in the auditory cortex and thalamus --- and what do they imply about thalamocortical transformations in the auditory system? This chapter reviews studies that have addressed these questions by comparing auditory cortical and thalamic sound representations at the single-neuron and neuronal population levels. The studies have used a diversity of stimulus sets and approaches: simple sounds to evaluate frequency tuning and modulation sensitivity; complex artificial sounds to estimate spectrotemporal receptive fields and nonlinear response functions; sound sequences to measure effects of stimulus probability and patterning; and natural sounds to examine responses to ecologically relevant vocalizations and ambient noise. However, key findings converge to the conclusion that like auditory brainstem nuclei and midbrain structures, the auditory thalamus and cortex are specialized for analysis of temporal information in sensory signals over multiple timescales.

Introduction

Over the past 50 years, research on sensory representations in the auditory cortex and thalamus has been motivated in part by a question inspired by research on the visual system. Hubel and Wiesel's discovery of simple and complex orientation-selective cells in visual cortex (Hubel and Wiesel 1959, 1962) inspired decades of research on the mechanisms by which orientation selectivity and other emergent features of visual cortical representations are generated by thalamocortical and intracortical interactions. In the auditory system, however, there are fewer obvious differences between cortical and thalamic sensory representations in any species, and there is little agreement on what receptive-field properties are “emergent” at the cortical or even thalamocortical level. The most striking and consistent of the differences between auditory cortical and thalamic sound representations tend to be quantitative rather than qualitative; for example, an increase in the timescale of forward suppression and adaptation to repeated stimuli.

Thus, while research on the visual cortex and thalamus was propelled in part by the search for mechanisms underlying receptive-field properties identified as thalamocortically emergent since the 1960's (at least in primates), research on the auditory cortex and thalamus over the same period has been driven more by the search for any thalamocortically emergent receptive-field properties at all. This search has inspired the use of increasingly complex stimulus sets and approaches to analysing receptive fields, as researchers have sought to determine whether the “right” stimulus set might reveal uniquely cortical or thalamocortical receptive-field properties. While it remains debatable whether any particular features of sound representations are truly emergent at the thalamocortical level in the auditory system, the diversity of stimulus sets used to probe these representations has provided rich insights

into more quantitative differences between cortical and thalamic neurons, particularly with regard to temporal response properties.

Here, I use the diversity of stimulus sets as an organising principle for discussing cortical and thalamic sensory representations. I begin by reviewing key findings regarding representation of relatively simple sounds, such as tones, clicks, and noise bursts. Next, I discuss insights gained from analysis of neuronal responses to complex artificial sounds, such as dynamic ripple stimuli and dynamic random chords. Then, I consider representation of more temporally extended sound sequences, such as those used to examine “stimulus-specific adaptation” and representation of regular or repeating sound patterns. Finally, I discuss cortical and thalamic representations of natural sounds, particularly animal vocalizations and naturalistic noise (see Chapter 8 for discussion of human speech representations).

The chapter focuses primarily on reviewing studies that have directly compared auditory cortical and thalamic sensory representations at the single-neuron and/or neuronal population levels. This constraint means that some features of auditory cortical representations are not discussed, because they have been minimally investigated in the thalamus. Additionally, following the literature, this review focuses mainly on spectral and temporal properties of cortical and thalamic responses, rather than binaural selectivity or other response properties. Topics such as the effects of activation or deactivation of cortex on thalamus; cortical and thalamic contributions to brain oscillations; and the roles of the cortex and thalamus in auditory plasticity and learning are addressed in other chapters.

Several limitations of this comparison of auditory cortical and thalamic sensory representations should be noted at the outset. First, most of the relevant papers have

compared neuronal response properties between the core (primary) auditory cortex (A1) and either the auditory thalamus as a whole (medial geniculate body, or MGB) or the lemniscal auditory thalamus (ventral MGB, or vMGB); previous work suggests that sensory representations differ substantially between lemniscal and non-lemniscal thalamic subregions (e.g., (Anderson et al. 2009; Antunes et al. 2010)). Second, even within primary auditory cortex, most research has focused on properties of neurons in layers 2-4, but there are known differences in sensory representation between superficial and deep layers (e.g., (Christianson et al. 2011)) and between deep-layer cell types projecting to different targets (e.g., (Williamson and Polley 2019)). Third, similarities and differences between cortical and thalamic sensory representations depend upon brain state; for example, response properties of auditory cortical and thalamic neurons differ between awake and sleep states (for reviews see (Edeline 2003; Hennevin et al. 2007)).

Finally, and perhaps most importantly, sensory representations in the auditory cortex and thalamus are surely somewhat species-specific, optimized for the sensory environment and behavioral goals of the animal. This point is well illustrated by the example of echolocating bats, where cortical and thalamic (as well as midbrain and brainstem) auditory representations are specialized for detection of sound combinations arising from the bat's sonar calls and their echoes (Wenstrup et al. 2012; Suga 2015). However, the literature on auditory cortical and thalamic sound representations is not extensive enough to permit conclusive analysis of species differences, so instead I have highlighted the issue by specifying the animal species for all key references, and by illustrating how the most common animal models used for auditory cortical and thalamic research have changed over time (Figure 1A).

Despite the limitations of the research literature, there has been notable progress toward understanding what the auditory cortex and thalamus are contributing to sound representation in the brain. Historical trends in the use of different stimulus types and response measures (Figure 1B) reveal not only diverse approaches with distinct strengths and limitations (Table 1), but also a growing appreciation for the role of adaptation to sound statistics. Key experimental insights are summarized in a final figure describing differences between auditory cortical and thalamic sensory representations (Figure 2).

Representation of Simple Sounds

Most investigations of cortical and thalamic responses to simple sounds have found modest or no differences in spectral response properties, with more profound differences in temporal properties and response reliability. Early studies described broader frequency tuning curves in cortex than thalamus, but this observation has not been upheld by later work. Cortical neurons tend to respond more phasically and less reliably to tones than thalamic neurons (Creutzfeldt et al. 1980) and therefore, frequency-intensity response areas are typically noisier and harder to measure in cortex than thalamus. However, frequency tuning is not consistently broader in A1 than MGB, even when thalamic recordings are restricted to the vMGB. For example, (Bartlett et al. 2011) found that selectivity of neurons for sound frequency was comparably narrow in the A1 and vMGB of awake marmoset monkeys, and often much narrower than observed in the auditory nerve. Proportions of narrowly tuned neurons were observed to be somewhat lower in A1 than vMGB, but quantitative comparisons are complicated by the fact that tone durations and analysis procedures used for defining the frequency tuning curve borders were different for A1 and vMGB (Bartlett et al. 2011). In anaesthetized mice, optogenetic silencing of intracortical activity during

intracellular recordings in A1 layer 4 neurons reduced the magnitude of responses to tones but did not affect spectral range or tuning (Li et al. 2013), indicating that tone responses in cortical cells preserve the frequency tuning of their thalamic inputs. Interestingly, responses to tone offsets are also similar in cortex and thalamus; (Solyga and Barkat 2021) found that offset responses in the auditory cortex of awake mice are largely inherited from the MGB. Even modulation of tone responses during different sound categorization tasks may be similar in cortex and thalamus. In rats performing a flexible high/low sound frequency categorization task, A1 and MGB neurons showed equivalent modulation of responses to the same tone by its category association (Jaramillo et al. 2014). Similar results were obtained in monkeys performing a frequency-step direction categorization task (Selezneva et al. 2017).

The most striking difference between auditory cortical and thalamic representations of simple sounds is that thalamic neurons respond with higher temporal fidelity to rapidly varying sounds. In an influential early paper on auditory thalamocortical transformations in awake guinea pig, (Creutzfeldt et al. 1980) recorded simultaneously from pairs of thalamic and cortical neurons with correlated spiking and showed that thalamic neurons were capable of following amplitude-modulated (or frequency-modulated) sounds at much higher rates than cortical neurons. Later investigations in marmoset monkeys confirmed this finding, and also demonstrated a transformation from more “synchronous” representation of repetition rate in the thalamus to a more predominantly “non-synchronous” rate-code representation in the auditory cortex (Bartlett and Wang 2007). More recent studies have also demonstrated increased temporal integration and adaptation from thalamus to cortex in mice, for example in the timecourse of forward suppression (Xiong et al. 2020). Thalamocortical transformation in the auditory system therefore seems to replicate a transformation that also occurs across the entire ascending auditory system, from cochlea to cortex: transition from temporal to rate

codes, with increasing rate-based representation of rapidly varying sound signals and temporal representation only of slower modulated signals (Wang et al. 2008).

Another prominent feature of thalamocortical transformation of simple sounds seems to be that the cortical representation is far less reliably stimulus-driven and less robust to major changes in brain state than the thalamic representation. Using two-photon calcium imaging to record from large ensembles of cortical and thalamic neurons in awake versus anaesthetised mice, (Filipchuk et al. 2022) recently found that patterns of evoked population activity were easily distinguished from patterns of spontaneous activity in the awake animal in both cortex and thalamus, but in the anaesthetised state, distinct differences between patterns of spontaneous and sound-evoked population activity persisted only in thalamus, not in cortex. This result echoes conclusions from earlier studies using electrophysiological recording methods in cat (Zurita et al. 1994; Cotillon-Williams and Edeline 2003) and rat (Cotillon-Williams and Edeline 2003), which found that different forms of anaesthesia could have profoundly different effects on cortical versus thalamic responses to simple sounds.

Thus, to a first approximation, cortical and thalamic representations of simple sounds are remarkably similar, with prominent differences observed mainly in temporal response properties such as forward suppression, and in less stimulus-related properties such as robustness of representations to changes in brain state. A caveat to this conclusion, of course, is that differences between cortical and thalamic representations of simple sounds may be evident in the projections of auditory cortical and thalamic neurons to particular targets even if they are obscured in the mixed population of projection neurons within the areas themselves. For example, in the mouse, optogenetic inhibition of projections from the auditory cortex to the striatum produces a more frequency-specific suppression than

inhibition of projections from the MGB to the striatum (Chen et al. 2019). Differences in amplitude modulation tuning between thalamostriatal and corticostriatal projections have also been observed (Ponvert and Jaramillo 2019).

Representation of Complex Sounds

Spectrotemporally rich sounds, such as “dynamic ripple” or “dynamic random chord” stimuli, can be powerful tools for probing thalamic and cortical sound representations (Meyer et al. 2016). Techniques for estimating stimulus-response functions from neuronal responses to complex sounds (broadly, reverse-correlation techniques and related nonlinear approaches) have many strengths for analysis of sensory representations. Most importantly, these techniques provide a more stimulus-agnostic, less hypothesis-driven answer to the question: what sound features are represented by thalamic and cortical activity? Another strength is that complex artificial sounds are in some sense more “natural” than many simple sounds used in auditory experiments, at least in that the sounds are spectrally rich and temporally varying. A third, more practical, advantage of using complex sounds with stimulus-response function estimation techniques is experimental efficiency; the same stimulus and analysis procedures can be used to estimate response properties of all neurons (including simultaneously recorded neurons) systematically, without the online optimisation that is often necessary for efficient evaluation of response properties that depend (for example) on frequency tuning.

However, complex sounds and stimulus-response function estimation techniques also have limitations for analysis of sensory representations, especially in auditory cortex and thalamus. Most importantly, while the stimulus space explored is very large compared to that which can realistically be probed using simple sounds, the stimulus-response function model must be

constrained to make estimation of its parameters computationally tractable. The constraint is usually that the stimulus-response function is assumed to be linear in the stimulus spectrogram, or linear with well-defined nonlinearities applied at either the input or the output to the linear stage (Meyer et al. 2016). The approach is therefore relatively agnostic about stimulus sensitivities, but not agnostic about the nature of response nonlinearities --- which might ultimately be the most important features of thalamocortical transformations. A related limitation is that the complex sounds used for stimulus-response function estimation must not have higher-order autocorrelations in the space used for representing the “receptive field” of the neuron, because the receptive-field estimate can be distorted by artifactual structure arising from interactions between higher-order autocorrelations in the stimulus and unmodelled nonlinear aspects of the neuronal response (Christianson et al. 2008; Meyer et al. 2016). In practice, this means that stimulus-response function estimation techniques cannot be relied upon to produce conservative, unbiased depictions of neuronal receptive-field properties when natural sounds are used as the complex stimuli.

Both the strengths and the limitations of stimulus-response function estimation using complex sounds have helped to advance understanding of cortical and thalamic sound representations over the past two decades. In an influential early paper, (Miller et al. 2001) used dynamic ripple stimuli to estimate spectrotemporal receptive fields (STRFs) in anaesthetised cat, comparing STRFs between pairs of A1 and vMGB neurons with correlated firing. This analysis revealed significant transformation and reconstruction of sensory representations between thalamus and cortex. Cortical STRFs could be inherited from thalamic STRFs, constructed from smaller units, or assembled by cooperative activity (Miller et al. 2001). Key conclusions from previous studies using simple sounds also held for cortical and thalamic responses to complex sounds; STRF analysis revealed slower temporal

modulation preferences in cortex than thalamus and similar spectral modulation preferences (Miller et al. 2002). Importantly, analysis of dynamic-ripple modulation transfer functions revealed no differences in spectrotemporal asymmetry between cortical and thalamic STRFs (Miller et al. 2002), suggesting that frequency-modulation (FM) selectivity --- an obvious possible auditory analogue of visual orientation or direction selectivity --- is similar in auditory cortex and thalamus. However, since STRFs are linear in the spectrogram of the stimulus, this work left open the question of how nonlinear properties of responses to complex sounds might differ between cortex and thalamus.

More recent studies have attempted to address this question for response nonlinearities such as spectrotemporal context sensitivity and contrast gain control, using stimulus-response function models with input or output nonlinearities. For example, (Williamson et al. 2016) introduced stimulus-response functions with input nonlinearities designed to capture interactions between pairs of spectrotemporal inputs within a complex sound (e.g., nonlinear forward suppression and two-tone combination sensitivity). Analysing neuronal responses to dynamic random chord stimuli in anaesthetised mice, they found remarkably similar patterns of nonlinear context sensitivity in cortical and thalamic neurons. The only obvious difference was that the timecourse of nonlinear forward suppression was significantly more elongated in cortex than thalamus (Williamson et al. 2016). A different approach, using stimulus-response functions with an output nonlinearity dependent on spectrotemporal contrast, has revealed contrast gain control at multiple levels of the ascending auditory pathway in both ferrets and mice (Rabinowitz et al. 2013; Lohse et al. 2020). Again, the main difference observed between thalamus and cortex related to temporal aspects of the nonlinearities; time constants for adaptation to spectrotemporal contrast were longer in cortex than thalamus (Lohse et al. 2020). Thus, experiments using complex sounds and stimulus-response function estimation

techniques indicate that both linear and nonlinear properties of sensory representations in the auditory cortex and thalamus are qualitatively similar (or at least, similarly diverse), with consistent quantitative differences primarily in the temporal domain.

Representation of Sound Sequences and Statistics

Cortical and thalamic representation of sound sequences and long-term sound statistics accelerated in the early 2000's with the discovery of strong stimulus-specific adaptation (SSA) in the auditory cortex (Ulanovsky et al. 2003, 2004). A neuron is said to exhibit SSA if the magnitude of its response to a specific stimulus within a sound sequence depends on the probability of that stimulus occurring over many seconds. SSA differs from simple firing-rate adaptation in both its stimulus-specificity and its long timescale. Importantly, SSA can manifest not only as a stimulus-specific suppression of neuronal responses to frequently repeated sounds (“standards”), but also as a stimulus-specific facilitation of neuronal responses to rare sounds (“deviants”). Thus, SSA has been interpreted as a neuronal correlate of auditory expectation violation and prediction error.

Over the past two decades, multiple studies have found that SSA is stronger in auditory cortex than thalamus. The first two papers to describe SSA in the auditory cortex found no evidence for SSA in the auditory thalamus of anaesthetised cats (Ulanovsky et al. 2003, 2004). Later work, mostly in rats and mice, demonstrated that SSA does occur in both the MGB and the inferior colliculus (IC) (Anderson et al. 2009; Antunes et al. 2010; Ayala et al. 2012). However, SSA is strongest in the auditory cortex, and cortical neurons are also more likely than thalamic neurons to show “true deviance detection”: greater responsiveness to a stimulus occurring as a deviant in an otherwise predictable sound sequence than to the same

stimulus in an unpredictable sound sequence (Parras et al. 2017). Remarkably, cortical neurons exhibit robust SSA even to different instances of multi-frequency tone clouds, while MGB (and IC) neurons do not (Harpaz et al. 2021). These observations indicate that while SSA in thalamic (and midbrain) neurons might arise from relatively simple mechanisms, such as short-term adaptation of narrowly tuned synaptic inputs, such mechanisms cannot fully account for SSA in cortical neurons. More generally, the SSA results demonstrate that cortical neurons are more sensitive to long-term sound statistics than thalamic neurons.

Other studies of cortical and thalamic representation of sound sequences and long-term sound statistics have come to similar conclusions. For example, in anaesthetized rats, (Asari and Zador 2009) recorded auditory cortical and thalamic responses to sequences of different natural and complex artificial sounds and examined how responses to a particular sound segment depended on the preceding sound context. Time constants for adaptation to a change in sound statistics were approximately 1 second for synaptic inputs to A1 neurons but less than 100 ms for spiking activity in MGB, indicating that the prolonged cortical adaptation timescale arises from thalamocortical or intracortical mechanisms. Interestingly, (Cooke et al. 2020) recently reported very late "post-stimulatory" activity in auditory cortical neurons which persisted for hundreds of milliseconds after sound stimulation in awake, passive listening marmosets. This post-stimulatory activity was shorter in duration, longer in latency, and much less commonly observed overall in the MGB than A1, suggesting a thalamocortical, intracortical or corticocortical origin for prolonged cortical aftereffects of sensory stimulation.

Finally, in one of the most systematic comparisons of cortical and thalamic representational timescales to date, (Asokan et al. 2021) recorded simultaneously from neurons in A1, MGB

and IC of awake mice while presenting sequences of noise bursts in random or repeating inter-burst interval patterns. Neuronal ensemble activity in each area was used either to decode local inter-burst interval duration or to classify the global sequence as random vs. regular pattern. Decoding accuracy for identification of short intervals deteriorated across the IC-MGB-A1 hierarchy, while classification accuracy for discrimination of random vs. regular patterns improved (Asokan et al. 2021). These data clearly demonstrate that the thalamocortical transformation produces a loss in temporal fidelity at short timescales but a gain in context sensitivity at long timescales.

Representation of Natural Sounds

Natural sounds such as vocalizations and naturalistic noise are the signals that the auditory system evolved to perceive. In principle, then, differences between cortical and thalamic representations of natural sounds could provide particularly useful information for defining the nature of the auditory thalamocortical transformation. Here I consider this possibility, focusing on studies that have examined neuronal responses to vocalizations or naturalistic noise in both A1 and MGB of animals. (Cortical and thalamic processing of speech sounds in the human brain is discussed in Chapter 8.)

One of the most well-studied examples of vocalization processing in mammals is the representation of pulsed bio-sonar calls and their echoes in the auditory system of echolocating bat species. Combination-sensitive neurons in the auditory brainstem and midbrain, tuned to bio-sonar signal components and echoes at varying delays, are transformed through collicular and thalamic processing into topographic maps of echo delay in the auditory cortex (Wenstrup et al. 2012; Suga 2015). In the mustached bat, echo delay

tuning is sharper in the thalamus and cortex than in the midbrain (Yan and Suga 1996). However, thalamic and cortical representations of echo delay are similar (Suga 2015; Butman and Suga 2019), and evidence suggests that cortical combination sensitivity is largely inherited from the midbrain and thalamus (Wenstrup et al. 2012). Thus, differences between cortical and thalamic representations have been challenging to identify even in the case of an auditory system highly specialized for a distinctive vocalization-based, sound-guided behaviour.

Cortical and thalamic representations of conspecific social vocalizations have been compared most often in guinea pigs, which have a large repertoire of species-specific communication calls and a hearing range similar to that of humans. (Wallace et al. 2005) compared responses of cortical and thalamic neurons to the low-frequency "purr" call presented to anaesthetised guinea pigs; no differences in neuronal response types or temporal fidelity were observed between A1 and MGB. (Huetz et al. 2009) reported similar observations in their investigation of cortical and thalamic vocalization selectivity, studying responses to 4 different types of conspecific vocalizations in both anaesthetized and awake guinea pigs. There were no differences between A1 and MGB in the percentage of neurons that were informative about vocalization identity, nor even in the percentage of neurons that carried vocalization-related information primarily in spike timing rather than spike count (Huetz et al. 2009). (Suta et al. 2013) also found largely similar A1 and MGB responses to 4 types of vocalizations in anaesthetized guinea pigs. Recently, (Montes-Lourido et al. 2021) compared cortical and thalamic representations of a wider range of 8 conspecific vocalizations in awake guinea pigs; they also examined differences between the thalamorecipient layer 4 and supragranular layers 2/3 (L4 & L2/3) in auditory cortex. Interestingly, vocalization selectivity was similar in MGB and A1 L4, but substantially higher in A1 L2/3 (Montes-Lourido et al. 2021). Together,

these results suggest that representations of conspecific vocalizations in guinea pigs are surprisingly unaffected by thalamocortical transformation, but refined by intracortical processing.

Perhaps the thalamocortical transformation contributes more significantly to the separation of vocalizations from noisy background sounds? Recordings in cortex and thalamus (and midbrain) of anaesthetized ferret have revealed that A1 neurons respond most robustly to naturalistic noise with a $1/f$ power spectrum, whereas MGB neurons are less selective for natural noise characteristics (Garcia-Lazaro et al. 2011). Vocalizations and other ecologically important signals often have temporal envelopes that are more slowly modulated than natural noise backgrounds. Does greater sensitivity to long-term sound statistics and naturalistic noise characteristics in cortex than thalamus mean that cortical neurons distinguish vocalizations from background noise more effectively than thalamic neurons do?

This question has been addressed in a few studies so far, with intriguing results. One particularly influential paper (Chechik et al. 2006) compared A1, MGB and IC responses in anaesthetized cat to natural bird chirps in noise and to various decompositions of the natural sounds into signal and noise components. For all forms of neural representation examined (spike-count, spike-timing, or latency codes), informational redundancy between the stimulus representations was highest in the IC and lower in both the MGB and A1 (Chechik et al. 2006). Further work revealed that IC neurons preserved the largest amount of information about both abstract entities (e.g., bird chirp, echoes, ambient noise) and detailed spectrotemporal features, but the ratio of abstract to spectrotemporal information was higher in A1 and MGB (Chechik and Nelken 2012). Again, however, minimal differences were

observed between A1 and MGB; thus, there was no evidence for a special role of the thalamocortical transformation in separating signal and noise components in natural sounds.

More recent experiments have provided evidence that both MGB and IC contribute at least as significantly as A1 does to separation of ecologically relevant signals from noise. Recording in the cochlear nucleus, the central nucleus of the IC, the ventral MGB, A1, or the secondary auditory cortex in anaesthetized guinea pigs, Edeline and colleagues examined neuronal discrimination of 4 examples of a guinea pig alarm call masked by frozen noise, either vocalization "chorus" noise or vocalization-shaped stationary noise (Souffi et al. 2020, 2021, 2022). The 4 alarm call examples were more effectively distinguished by neurons or neuronal populations in subcortical than cortical structures, even in noise (Souffi et al. 2020). Cortical responses to the vocalizations were more robust than subcortical responses to increasing noise, but even at the highest noise level tested (-10 dB SNR), MGB and IC neurons retained more vocalization-related information than A1 (Souffi et al. 2020, 2021). Furthermore, the proportion of neurons that were more sensitive to vocalization signals than noise was highest in the MGB and IC, not in the cortex (Souffi et al. 2021).

Thus, separation of vocalizations from background noise appears to be a distributed function of the entire central auditory system, not a specific function of the thalamocortical transformation or the cortex itself. Indeed, (Souffi et al. 2022) found that neurons throughout the auditory system (not just in the cortex) maintained good ability to track slow modulations in the stimulus as noise increased. Neuronal discrimination of vocalizations deteriorated with increasing noise not because of changes or differences in modulation tracking at cortical vs. subcortical levels, but because the temporal envelopes of vocalizations degraded by noise were more similar acoustically than temporal envelopes of noise-free vocalizations (Souffi et

al. 2022). Notably, different conclusions were obtained from an earlier study in ferrets using variable rather than frozen noise tokens; cortical representations were found to be more noise-invariant in this context than IC representations (Rabinowitz et al. 2013). The differences may depend critically upon the answer to an almost philosophical question about how to define auditory "noise": is it an acoustic waveform with particular spectral and temporal properties, or the component of the sound that is most variable?

Important and Unanswered Questions

For decades, much research on sensory representations in the auditory cortex and thalamus has been driven by the question: what thalamocortically emergent property of auditory receptive fields might be analogous to orientation selectivity in the primate visual system? This question still remains unanswered, even after many years of research utilising diverse stimulus sets, including complex sounds, sound sequences and natural sounds. To a first approximation, neuronal response properties in the auditory cortex and thalamus have been found to be surprisingly similar, with differences primarily in the extent of temporal integration, temporal adaptation, representational stability, and sensitivity to long-term sound statistics. Temporal processing timescales generally lengthen across the entire central auditory system, from brainstem to cortex (for a recent review, see (Kopp-Scheinflug and Linden 2020)). Thus, differences in temporal processing between cortex and thalamus are not an emergent thalamocortical phenomenon like orientation selectivity in primates, but a continuation of a transformation that occurs throughout the ascending central auditory pathway in all species studied.

Where, then, to go from here? The strongest evidence for a special role for cortical or thalamocortical processing in sound representation has come from studies of sensitivity to sound sequences and global temporal patterns. To the extent that identifying an emergent thalamocortical phenomenon is still the goal, then understanding thalamocortical, intracortical and corticocortical mechanisms enabling sensitivity to long-term sound statistics is clearly an important focus for future investigation.

However, it is possible that Hubel and Wiesel's seminal discoveries in the visual system have not only inspired but also obscured the most important research questions in the auditory system. Functionally and physiologically (and even histologically), the primary auditory cortex may be more analogous to visual association areas than to primary visual cortex (King and Nelken 2009). Moreover, as discussed in other chapters, extensive research on central auditory plasticity already suggests that the most emergent role of the auditory cortex and thalamus relates not to representation of particular sound features, but to *learning* about sound features. Perhaps equivalently from a computational viewpoint, the emergent role of auditory cortex and thalamus may be learning to discount spectrotemporal detail that varies within but not between auditory objects in the real world. Thus, the most important unanswered questions about sensory representations in the auditory cortex and thalamus may not be what those representations are, but how invariances in the representations arise through sensory experience.

Figures and Tables

Figure 1

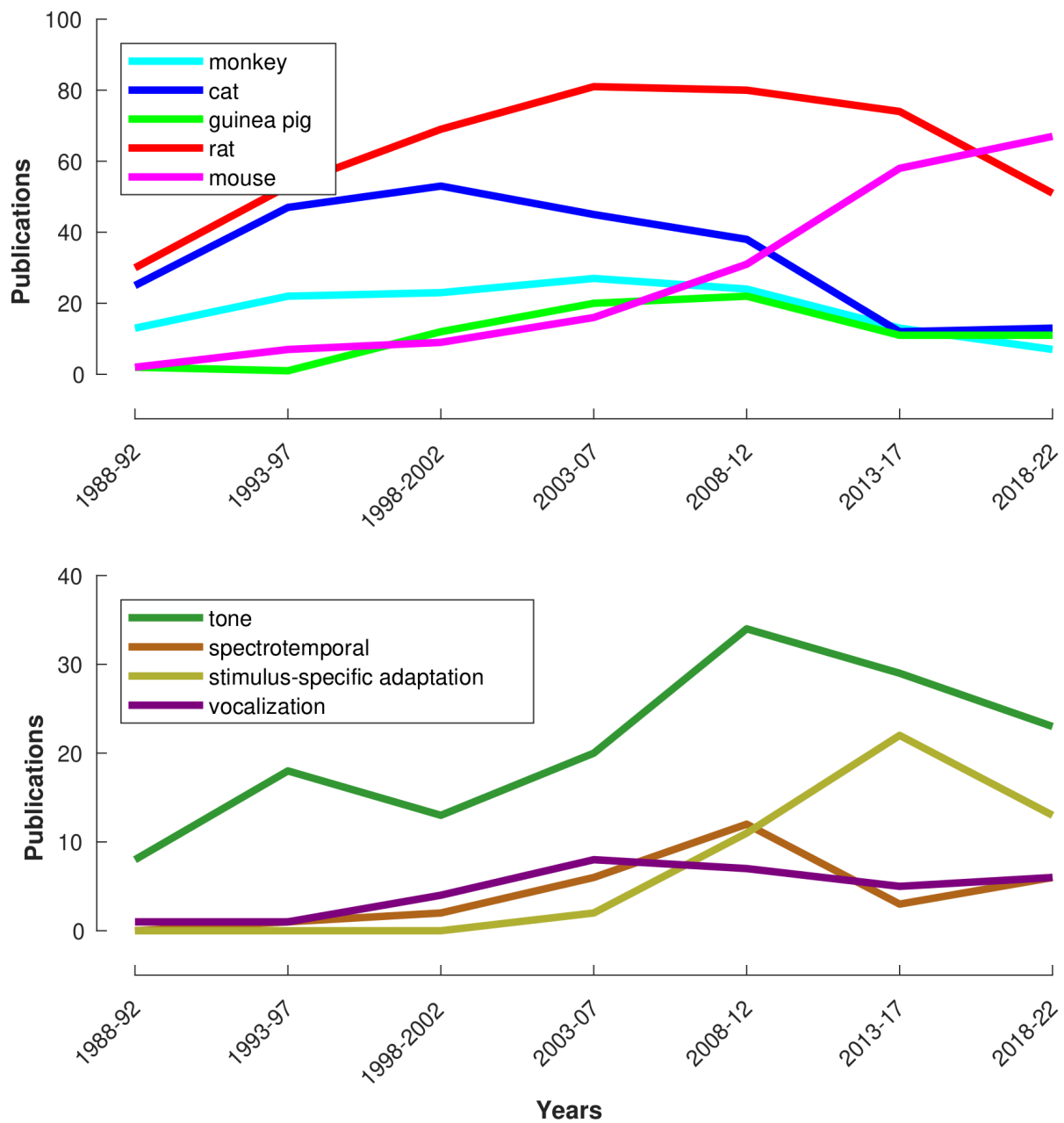


Figure 1. Historical trends in research comparing neuronal response properties between the auditory cortex and thalamus. Plots show results from Clarivate Web of Science searches in 5-year intervals for Topic (title/abstract/keywords) "auditory AND (cortex OR cortical) AND (thalamus OR thalamic) AND neuron*", plus one of the terms shown in

legends. **Top**, Number of publications using the mouse has increased greatly over the past 15 years at the expense of several other model systems with hearing ranges more similar to that of humans. (Ferret, gerbil, bat, and other auditory models excluded for small numbers overall.) This shift follows, of course, the 21st century development in mice of powerful genetic tools for manipulating neural circuitry, such as optogenetics. Until these genetic tools become easier to use in other species, the reduction in diversity of model systems could increase the risk that species-specific phenomena may be misinterpreted as fundamental characteristics of mammalian thalamocortical transformations. **Bottom**, Number of publications with topic words commonly associated with different stimulus types: “tone” representing simple stimuli; “spectrotemporal” for complex stimuli used for spectrotemporal receptive field estimation; “stimulus-specific adaptation” for sound sequences; and “vocalization” for natural sounds. The “tone” category includes many publications that also appear in the other categories. Note the surge of interest in stimulus-specific adaptation, reflecting the possibility that sensitivity to long-term sound statistics is dependent on cortical activity.

Table 1

Stimuli	Response Measures	Strengths	Limitations
Simple sounds (tones, noise bursts, clicks, click trains, FM sweeps, AM tones or noise).	Frequency-intensity response areas, modulation transfer functions, synchronization, FM/AM tuning.	Detailed description of stimulus-response function for selected stimulus parameters. Computationally simple.	Strong assumptions required about what relevant stimulus parameters are. Often experimentally inefficient.
Complex artificial sounds (dynamic ripples, dynamic random chord stimuli).	Spectrotemporal receptive fields (STRFs), nonlinear stimulus-response functions.	Comparatively unbiased and agnostic exploration of stimulus sensitivities. Experimentally efficient.	Requires assumptions about nature of nonlinearities in stimulus-response function. Often computationally intensive.
Sound sequences (oddball stimuli, regular versus random patterns).	Stimulus-specific adaptation, regularity sensitivity.	Allows analysis of representation and adaptation over a wide range of timescales.	Experimentally very time-consuming, so stimulus parameters must be tightly constrained.
Natural sounds (vocalizations, ambient environmental sounds).	Vocalization selectivity, categorical perception, noise invariance.	Ecologically relevant to animal studied. Possibly, also relevant to human language perception.	If used for stimulus-response function estimation, higher-order autocorrelations can produce misleading results.

Table 1. Key strengths and limitations of different stimulus types and response measures for investigating sensory representations in the auditory cortex and thalamus.

Figure 2

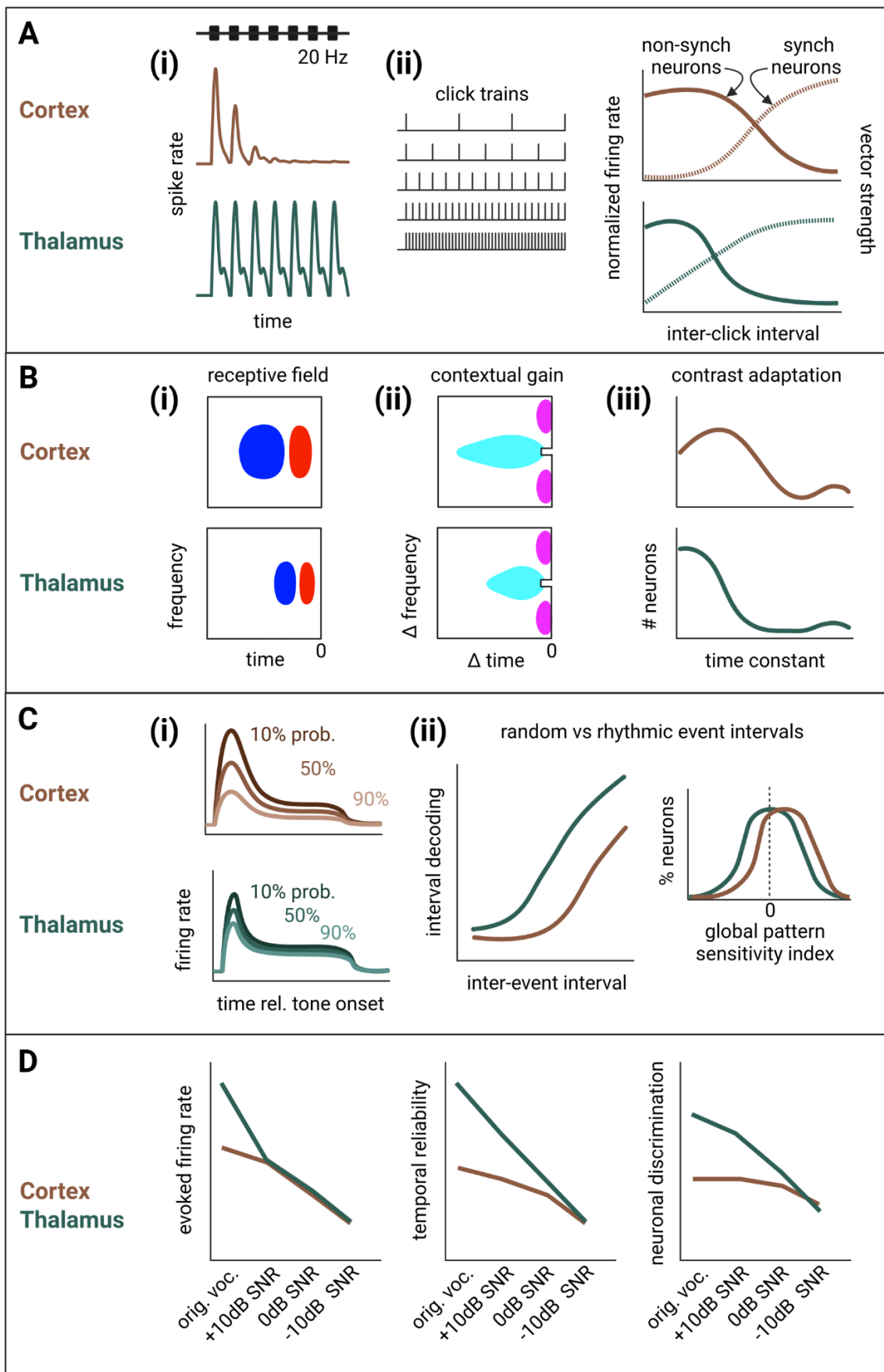


Figure 2. Key differences between sensory representations in A1 and MGB. A,

Differences revealed using simple sound stimuli. **A(i)**, Cortical neurons are less capable of following high rates of amplitude modulation than thalamic neurons (Creutzfeldt et al. 1980).

A(ii), Cortical and thalamic neurons typically encode inter-click intervals either with synchronized firing (synch neurons) or by increasing firing rate in a non-synchronized manner as the inter-click interval decreases (non-synch neurons). The transition between synchronized and rate coding in neuronal population activity occurs at longer inter-click intervals in cortex than thalamus (Bartlett and Wang 2007). **B**, Differences revealed using

complex artificial stimuli, such as dynamic ripples and dynamic random chords. **B(i)**, Spectrotemporal receptive fields are typically more temporally extended in cortex than thalamus (Miller et al. 2001, 2002). Plots can be interpreted as spectrograms of the typical stimulus preceding a spike. X-axis, time to spike; red, excitatory subfield; blue, inhibitory subfield. **B(ii)**, Contextual gain modulation, and specifically delayed suppression, is more temporally extended in cortex than thalamus (Williamson et al. 2016). Notch in plots signifies the target tone, which can be any spectrotemporal element in a complex stimulus; colours indicate modulatory effects of neighbouring sounds on the gain of the neuronal response to the target tone. X- and y-axes, time and frequency relative to the target tone; magenta,

positive gain (facilitation); cyan, negative gain (suppression). **B(iii)**, Time constants for adaptation to changes in spectrotemporal contrast are longer in the cortex than thalamus (Lohse et al. 2020). **C**, Differences revealed using sound sequences and patterns. **C(i)**, Stimulus-specific adaptation is stronger in the cortex than thalamus (Ulanovsky et al. 2003; Parras et al. 2017). Plots illustrate typical responses to the same tone when presented with 10% (deviant), 90% (standard), or 50% (control) probability in a sound sequence with a tone of another frequency that evokes similar responses from the neuron under control conditions.

C(ii), Analysis of neuronal population responses to sequences of noise burst events with

either rhythmic or random inter-event intervals shows that thalamic neurons represent local intervals (time between noise burst events) more accurately than cortical neurons do, while cortical neurons are more sensitive to the existence of global patterns (Asokan et al. 2021). **D**, Differences revealed using vocalizations with or without naturalistic noise. Without noise (orig. voc.), thalamic neurons respond more strongly and more reliably to conspecific vocalizations than cortical neurons, and neuronal discrimination of different examples of the same type of vocalization is better in thalamus than cortex. However, as the signal-to-noise decreases (+10 to -10 dB SNR), evoked firing rates, temporal reliability, and neuronal discrimination become more similar in thalamus and cortex (Souffi et al. 2020). Thus, cortical neurons represent vocalizations more poorly than thalamic neurons overall, but are less sensitive to changes in noise level. All illustrations are original cartoons of phenomena shown in data in the cited references. Created with BioRender.com.

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