Enhancing sensitivity to interaural time differences to improve sound lateralization and auditory object formation in bilateral cochlear implant users

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Dedication

To my best friend, my mother, Smita Thakkar. She is the strongest, smartest, and most level-headed woman I know. I would not be the woman I am today if it weren't for her. I strive to be just like her every day.

To my father, Deepak Thakkar. To my two wild and wonderful sisters: Meghna and Tejal. My sisters have always taught me the art of a "healthy" competition. I am so proud of the women they have become.

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ABSTRACT

Everyday listening environments often require the ability to effectively locate sounds in space. Interaural time differences (ITDs) are acoustic cues which enable normal-hearing listeners to navigate in noisy environments and locate sounds in the horizontal plane. Patients with bilateral cochlear implants (BiCIs) have limited sensitivity to these cues, which explains why they experience difficulties locating sound sources, particularly in noise. These difficulties stem largely from a limitation in conveying of the fine timing of ITDs in the clinical devices. The objective of dissertation was to investigate the impact of a low stimulus rate on binaural sensitivity, lateralization, and auditory object formation of ITDs. While previous work has determined that BiCI listeners with adult-onset of deafness show binaural sensitivity to constant amplitude, low rate stimulation (~ 100 Hz) with consistent ITDs, these stimulus conditions are not representative of real-life stimuli which are typically more spectrally complex, dynamic, and varying in time. The studies described in this dissertation take a step towards providing a more realistic representation of the complex signals that BiCI listeners may face in everyday listening situations, as well as provide solutions for improving their ability to detect ITDs in the context of these complex signals.

CHAPTER I: Introduction

Chapter I, the introduction, provides a background for the four studies described in this dissertation. Chapter titles shown below:

(1) **Chapter II: Mixed stimulation rates to improve the sensitivity of interaural timing differences in bilateral cochlear implant listeners**

(2) **Chapter III: Lateralization of interaural time differences using mixed rates of stimulation in bilateral cochlear implant listeners**

(3) **Chapter IV: The impact of interaural time differences with asymmetric rates on lateralization and auditory object formation in bilateral cochlear implant listeners**

(4) **Chapter V: The importance of consistent onset cues for enhancing low-rate ITDs and establishing good sound lateralization and object formation**

I. Physical characteristics of sound

Sound propagates from the vibration of objects, and these vibration patterns travel through a medium (air) causing changes in pressure. The changes in pressure are periodic oscillations of condensed vs. expanded air that extend outwards from the object, propagating in a sinusoidal manner and producing a sound wave. An object whose vibration can be described by a simple sine wave corresponds to a tone of a single frequency. When the level of the pressure or intensity is plotted against time, a single cycle corresponds to a phase change of 360° or 2π radians, and the length of a single cycle is the wavelength of the tone. The time taken to complete one cycle is the period, and the inverse of the period is the frequency. When multiple sounds, having a sinusoidal pattern, complete a cycle at the same time, they are said to be "in-phase," while sounds with misaligned cycles in time are said to be "out-of-phase."

Sounds are generally periodic, but can also be more complex than a simple sine tone. When sounds reach the ear, the ear performs a Fourier analysis whereby a complex sound

representing a collection of sinusoids can be mathematically broken down into its individual frequency components. For example, a harmonic complex tone is one that is composed of many sinusoids where each frequency component is a multiple of the frequency of the lowest common component. A single sinusoid in the complex tone is said to be a component of the complex. Therefore, if a series of sinusoids produced a waveform with a harmonic structure (i.e., having components that are multiples of each other), the spectrum of the signal is generally continuous in the time domain but discrete in the frequency domain. Alternatively, a non-periodic signal generally has a spectrum that is continuous in the frequency domain, but discrete in the time domain (e.g., an impulse). In summary, the auditory system analyzes sounds both temporally and spectrally.

II. Sound transduction

Sound waves first reach the auricle or visible portion of the outer ear. This external portion of the outer ear amplifies and filters the incoming sound waves, directing them into the auditory canal. Once a sound has entered the ear canal it reaches the tympanic membrane, also called the eardrum. At this point, the sound has reached the middle ear. The middle ear is an air-filled cavity, which consists of the tympanic membrane and the ossicular chain. The ossicles consist of three small bones – the malleus, incus, and stapes – which are anchored between the tympanic membrane and the oval window of the cochlea, the main structure of the inner ear (see Figure 1). After sound enters the ear canal, it vibrates the thin tympanic membrane, which in turns activates movement in the ossicular chain, converting sound pressure into mechanical energy. These vibrations then transfer energy to the cochlea of the inner ear. The cochlea is a spiral-shaped structure, which includes a bony outer casing and an inner membranous labyrinth. The role of the cochlea is to transform physical sound waves into an electrical signal that the

brain can understand. The cochlea's two membranes, Reissner's membrane (RM) and the basilar membrane (BM), run along the length of the entire cochlea from the base (opening near the stapes) to its apex (opening near the top of the spiral). These membranes divide the cochlea into three chambers: the scala tympani, the scala media, and the scala vestibuli (Moore, 2013). The BM is a resonant structure residing in the scala media. It is narrowest, most stiff at the near the basal end, and widest, most flexible near the apical end (Fernández, 2005; Gummer et al., 2005), giving it unique physical properties. Once the fluid inside the cochlea is set in motion, it causes the BM to oscillate in a pattern known as a traveling wave (von Békésy, 1947; Cooper, 1999; Jacob et al., 2009). Because it is a resonant structure, different locations on the BM vibrate maximally to particular incoming frequencies. Lower frequency waves (down to ~ 20 Hz) travel farther on the BM and vibrate maximally near the apex. In contrast, higher frequency vibrations (up to ~ 20 kHz) do not travel far from the opening of the oval window and vibrate maximally near the base (Robles and Ruggero, 2001). In other words, the cochlea behaves as a Fourier or frequency analyzer which decomposes incoming complex signals into their individual component frequencies (Hartmann, 1997). This frequency arrangement of the BM is referred to as a "tonotopic organization" (Greenwood, 1990), which is retained throughout various stages of the ascending auditory pathway. Additionally, the tonotopic organization of the BM functions as a series of non-linear, overlapping band-pass filters. These band-pass filters correspond to each frequency-specific point in the cochlea, where the bandwidths of each filter change non-linearly from the base to the apex (Fletcher, 1940; Greenwood, 2005a).

To send electrical signals from the cochlea to the ascending auditory pathway, the BM houses the Organ of Corti, a structure which supports two types of nerve cells that interface with the auditory nerve. Inner hair cells (IHCs), of which humans have about 3,500, are mainly

responsible for transmitting electrical impulses caused by BM oscillation. Outer hair cells (OHCs), of which humans have about 20,000, actively enhance and sharpen the signal to be transmitted (Ruggero, 1992). When maximal vibration on the BM occurs, it deflects small fibers called ‘stereocilia’ which exist at the tips of the IHCs (Pickles et al., 1987). The deflection of these stereocilia opens transduction channels on the hair cell bodies and, due to the difference in electrical potential between the fluid in the hair cell and the surrounding endolymph, there is an influx of potassium ions into the hair cells. An influx of potassium rapidly depolarizes the hair cell (Pickles et al., 1984), and results in an action potential that is sent along to the auditory nerve (Ruggero, 1992).

The tuning and timing of the neurons in the auditory nerve is by far the most important peripheral process in the auditory system because it represents the decoded version of the acoustic signal that travels into the cochlea. One prominent feature of hair cells is the ability of the voltage potentials of certain hair cells and the firing of the electrical signal in the auditory nerve fiber to be able to follow stimuli of up to 3 kHz with each cycle, referred to as the “volley theory.” Therefore, the frequency information of a tone is said to be related to the firing rate of the auditory nerve. However, this does not explain how the auditory nerve decodes frequencies greater than 3 kHz. Conversely, the "place theory" says that frequency information is specified by preserving the tonotopy of the cochlea. Because the auditory nerve fibers innervate IHCs in an approximately one-to-one manner, it follows that the incoming acoustic signal will create maximum displacement of the basilar membrane in a frequency-specific manner. As a result, auditory nerve fibers towards the apical end of the cochlea respond to low frequencies and auditory nerve fibers near the basal end respond to high frequencies (von Békésy, 1956; Moore and Ernst, 2012; Zwislocki and Nguyen, 1999)

Another prominent feature of the auditory nerve response is the ability to follow the waveform of a low-frequency sound, or "phase-locking." IHCs have a biphasic response, meaning that they oscillate during the negative and positive phases of the sound wave cycle. The auditory nerve only fires during the positive cycle of the incoming waveform (Rose et al., 1967; Ruggero, 1992; Sellick et al., 2005). Phase-locking to low frequency sounds at the level of the auditory nerve provides an essential function for processing of temporal information between the ears (Carr and Köppl, 2004; Carr and Konishi, 1990), discussed in later sections.

III. The auditory pathway

The auditory nerve synapses in the brainstem, where it branches to innervate the three divisions of the cochlear nuclei. Within the cochlear nuclei, each ascending fiber from the auditory nerve reaches a point of contact that is also tonotopically organized (see Figure 2). Thus the tonotopic organization of the cochlea is maintained in the cochlear nucleus. Next, the individual fibers in the cochlear nucleus ascend to several auditory brainstem nuclei, where primary binaural functions occur. A bilateral set of nuclei, called the superior olivary complex, can be further separated into the lateral superior olive (LSO) and medial superior olive (MSO) (Fitzpatrick et al., 1997; Joris and Yin, 2007; Masterton and Imig, 2003; Yin and Kuwada, 1983). The binaural pathways are only one part of the output of the cochlear nuclei; a second major set of pathways bypass the superior olivary complex and terminate in the nuclei of the lateral lemniscus. These nuclei process other aspects of the sound such as onsets, intensity, and frequency.

The auditory pathways then ascend from the superior olivary complex and lateral lemniscus and project to the midbrain center, the inferior colliculus. Because space is not mapped on the surface of the hair cell receptor, the inferior colliculus processes auditory space as

well as complex temporal patterns. The pathways from the brainstem and midbrain are processed in parallel and ultimately reach the medial geniculate nucleus of the thalamus which receives convergent inputs from spectrally and temporally separate pathways. The medial geniculate nucleus is the site where spectral and temporal information is highly integrated. Finally, ascending projections from the medial geniculate nucleus reach the primary auditory cortex, which also has tonotopic organization maintained from the cochlea. The primary function of the auditory cortex is to processes highly complex signals, such as speech. Speech understanding and language is processed in Wernicke's area, which lies in the secondary auditory cortex. It is important to note that these processes also have descending projections which help to provide feedback to the auditory system when the stimulus or environment changes (Kandel et al., 1981).

IV. Perceptual processes of the auditory system

Signals decoded by the auditory pathway are the sensory function of the auditory system. However, once interpreted by the brain, the physical properties have a perceptual analog which we can describe using behavioral tasks. For instance, the amplitude of the pressure or intensity of a wave corresponds to a listener’s perception of loudness while the frequency of a signal corresponds to the perception of pitch. As mentioned in the “Sound transduction” section, the cochlea can be thought of as a series of overlapping band-pass filters, and several behavioral studies have determined that the perceptual response to sounds that are captured by each filter can be referred to as the “critical band.” In short, the critical band is a listener’s responses to complex stimuli, and the behavioral response corresponds directly to whether the component of a stimulus falls within a critical band or are spread over a number of critical bands. Generally, these bands increase in bandwidth from low to high frequency (Greenwood, 2005b; Zwicker et al., 1957; Zwicker and Terhardt, 1980). Additional processes such as the processing of temporal

information over time (Viemeister and Wakefield, 1991), mechanisms of masking, and perception of pitch and harmonicity have all been determined using psychophysical tasks. Each of these measures either a detection threshold (i.e., the ability of a listener to detection a sound in isolation) or a discrimination threshold (i.e., the ability of a listener to detect a relative change in a sound).

The studies in this dissertation are focused on the ability to localize sound sources in the horizontal plane, specifically for listeners who have cochlear implants. Before discussing, sound localization in listeners with cochlear implants. The next section with a focus on the basics of binaural hearing in listeners with normal hearing.

A. Functions of the binaural hearing system

One of the goals of the auditory system is to parse out different sound sources in an auditory scene. To accomplish this feat, the auditory system must be able to localize sounds, make across-ear comparisons, and suppress echoes. Binaural hearing facilitates our ability to localize sound, particularly in the left-to-right horizontal plane. Sound localization in the azimuthal (horizontal) plane occurs through a time-sensitive binaural network which encodes interaural time differences (ITDs) and interaural level differences (ILDs). As mentioned previously, most binaural processes occur in the superior olivary complex where the two sets of nuclei: the MSO and LSO process ITDs and interaural level difference ILDs, respectively. When auditory information arrives at both ears resulting in relative changes in time and level in auditory nerve fibers, ultimately reach the first point of contact in the brain, the superior olivary complex, for comparing the two signals between the ears. The spiking patterns from both sides can be cross-correlated and analyzed for differences in spectral information, timing, correlation, and pattern matching in order to observe the across-ear differences of a single sound source.

There are three primary functions of the binaural hearing system: sound localization spatial unmasking, and echo suppression (the precedence effect). Localization of sounds in the horizontal plane is achieved through a combination of ILDs and ITDs which inform the listener about the acoustic space. Locations of the sound sources are defined relative to the head. Typically, –90 degrees corresponds to the far left, 0 degrees corresponds to the center, and +90 degrees corresponds to the far right (Blauert, 1987; Feddersen et al., 1957; Mills, 1960; Wallach, 1938). Interaural cues are helpful when localizing sounds in the horizontal plane; they are also frequency-specific. For the case of simple sine tones or amplitude modulated tones, ITDs are most effective at lower frequencies (~500 – 1500 Hz) and ILDs at higher frequencies (> 1500 Hz). This result occurs because low-frequency sounds have larger wavelengths, making it easier to make comparisons in time across the ears. The amount of time it takes for sound to reach one ear before the other is approximately 690-760 μs. Therefore one cycle of the wavelength cannot be smaller than 690-760 μs (approximately 1500 Hz). If the wavelength is too small, this can result in comparisons across ears at different phases of the cycle. Smaller wavelengths do not provide a good temporal comparison across the ears, and this is the reason why ILDs are more effective at higher frequencies. The frequency-dependent sensitivity of binaural cues is known as the "Duplex Theory" (Rayleigh, 1896). For sine tones, this holds, but for more complex signals, transients, and speech signals, this can vary. An extension of localization is sound “lateralization” whereby sounds are perceived intracranially when presented over headphones, rather than in free-field (Toole, 2005).

Spatial unmasking is a process by which listeners can make small distinctions in the interaural phase between sounds. Spatial unmasking results in the perception of accurately detecting a coherent target sound in a mixture of incoherent noise sources (Freyman et al., 2002,

2005b; Shinn-Cunningham, 2002), in particular when a target source and noise source differ in their respective binaural cues. (Blauert, 1987; Feddersen et al., 1957; Mills, 1960; Wallach, 1938). While spatial unmasking can occur when a target sound and masking sound are out of phase from one another, interaural cues can facilitate the distinction between a target and masker even further (Freyman et al., 2005b; Garadat et al., 2009). Unmasking is also heavily influenced by monaural cues such as head shadow, fundamental frequency, temporal coherence, or similarity of acoustic information (Kidd et al., 2002, 2010; Lutfi et al., 2013; Micheyl et al., 2013). However, in multi-source environments, binaural processing is a significant contributor to spatial unmasking (Arbogast et al., 2016; Hawley et al., 2004).

The precedence effect, the underlying mechanism involved in echo suppression, is the third primary binaural function. The precedence effect is also referred to as the "Law of the First Wavefront" or "Haas effect." (Blauert, 1987). The precedence effect is the phenomenon by which spatial cues, carried by the first-arriving wavefront—the sound traveling from the direct source to the ears—are perceived as the most dominant, and those arriving later are suppressed or down-weighted (Litovsky et al., 1999; Litovsky and Shinn-Cunningham, 2002; Yost and Soderquist, 1984). The precedence effect is an essential by-product of the binaural hearing system which provides NH listeners the ability to achieve sound location in echoic environments with high accuracy. Wallach et al. (1938) discovered that by presenting a pair of impulses with different locations, and varied the delay between the two clicks, the later-arriving click is suppressed with a delay as small as 5 ms. For more complex stimuli, the delay can be as large as 40 ms (Litovsky et al., 1999). If two sounds played in succession (longer than ~ 1 ms) are heard as a single sound, then the location of the perceived source is primarily determined by the first sound. However, if two sounds that are played within 1 ms of each other, the sound of the

perceived source is an approximate average of the two locations (Litovsky and Shinn-Cunningham, 2002).

In summary, our acuity in locating sounds is greatest in the horizontal plane, and binaural hearing is extremely useful for parsing out a target sound from noise or echoes. The next few sections will discuss the perceptual processes of binaural hearing, but specifically for ITDs, as ITDs are the focus of the studies in this dissertation.

V. Research on interaural time differences

Studies on binaural hearing have uncovered the impact of controlled binaural stimuli on behavioral responses and neurophysiological responses. In the field of binaural psychoacoustics, a subset of psychophysics (the effect of physical properties on perceptual processes by systematically varying acoustic properties of a stimulus along one or more physical dimensions) (Irwin and McCarthy, 1998), various unique stimuli have been utilized to understand which properties of the signal play a role in localization and sound source segregation of ITDs.

Impulses or "clicks" are broadband signals (a signal having a wide range of frequencies) and are short in duration. Clicks can be a unique way of presenting binaural information because they represent a range of frequencies. When clicks are high-pass filtered above 1500 Hz, the ability to detect a change in location is much worse than when the click is low-pass filtered (Yost et al., 1971). Conversely, if a high-frequency masking noise is presented with a broadband click, the ability to detect a change in the location of the click does not deteriorate as much as it does with a low-frequency masking noise. These findings suggest that low-frequency sounds have salient ITDs, which appear to be heavily weighted in a sound localization task.

Due to previous work that suggests that listeners rely on the temporal fine structure of a low-frequency sinusoid, the dissociation between amplitude modulation rate and carrier frequency have been examined by imposing a sharp envelope or a specific modulation rate on a high-frequency carrier (Hafter and Buell, 1990; Nuetzel and Hafter, 1981). Nuetzel and Hafter investigated the effect of click modulation rate and the carrier frequency (which represents the temporal fine structure) on listeners' sensitivity to ITDs. They investigated whether high carrier frequencies of the envelope modulation rate facilitates ITD sensitivity. Their data suggested that modulation cycles lower than 150 Hz or greater than 350 Hz occurring over a short duration influenced ITD sensitivity the most, while the carrier frequencies (> 3 kHz) had no impact. Primarily, the number of information-bearing clicks was much higher for a low-rate click train than for a high-rate click train (Nuetzel and Hafter, 1981). Some studies have postulated that this occurs in part because the peripheral auditory system responds low-rate modulations in a phasic manner while the high-rate modulations do not (Hartung and Trahiotis, 2002).

In contrast, when click trains instead of single clicks are used, the ability to carry ITD information is not frequency-dependent. Human psychophysical studies have found that ITD sensitivity can be very good for a range of click-train stimuli paired with different carrier frequencies. Some of these stimuli include two-tone complexes (Mcfadden and Moffitt, 1977; McFadden and Pasanen, 1976), sinusoidally-amplitude modulated tones (Henning and Ashton, 1981; Nuetzel and Hafter, 1976), and pulse-modulated noise (Hafter and Ricard, 1973; Hafter et al., 1980). Each of these click trains has one common feature: the amplitudes of these signals change over time at a low rate, mimicking a low-frequency sinusoid. This low-rate pattern allows activity in the nervous system to synchronize with peaks in the envelope of the stimulus (Bibikov and Nizamov, 1996; Joris and Yin, 1992; Moore and Glasberg, 2005).

In summary, prior psychophysical literature supports the notion that a) low-frequencies relay salient ITD information, b) ITDs are highly dominant cues in relation to ILDs when presented as a click, and c) low-rate modulations are effective for relaying ITD information, as they can mimic a low-frequency pure tone. The literature demonstrates that ITDs provide useful information for locating and segregating a target form noise in a complex auditory scene.

A. Onset dominance of ITDs

The dominance of onset ITDs in spatial hearing has been investigated for a considerable number of studies in normal-hearing listeners. The phenomenon of onset dominance has a wide range of applications in the binaural hearing literature, but most are related to the precedence effect. The binaural auditory system prioritizes ITD information in the onset of a signal with repeated cycles due to possible adaptation, similar to how a direct sound suppresses a later-arriving echo (Brown et al., 2015; Freyman et al., 2005a; Keen and Freyman, 2009)

In the laboratory setting, experiments that investigate the onset dominance of ITDs often reveal information about the underlying mechanisms of sensitivity to temporal changes in the ITD information over time. Some of those experiments measure the perception of stimuli where the onset and post-onset portions are identical but experimenters may vary the duration or inter-click interval with each trial (Hafter et al., 1983; Stecker and Hafter, 2002), experiments which measure listeners' ability to detect the location of the first sound when the delay between a single pair of clicks (the "lead" and "lag", respectively) are varied (Brown et al., 2015; Litovsky et al., 1999; Tollin et al., 2004; Wallach, 1938; Yost and Soderquist, 1984), experiments which measure a listener's ability to tell the correct location when the onset and post-onset ITD are varied, and finally, experiments which vary the onset and post-onset inter-click intervals (Brown and Stecker, 2011; Freyman, 1997; Stecker, 2014; Stecker and Brown, 2010). Each of these

studies have suggested that the binaural system adapts to ITDs (Hafter et al., 1983; Hafter and Buell, 1990), suppresses ITD information in a later-arriving impulse (Freyman et al., 2005a; Gaskell, 1983), and that relative weights of each cycle or pulse in a stimulus often predict performance in an ITD task very well (Stecker, 2014; Stecker and Hafter, 2002). A common point which all of the above studies share is that the inter-click interval generally requires a low pulse rate. Using a low stimulus rate helps to uncover how ongoing ITD changes in a stimulus affect localization perception. Some of these studies are described in detail in the following sections.

Studies on the precedence effect have not only uncovered the binaural system's suppressive role of later-arriving clicks or transients in a click train, but prompted an investigation on "binaural adaptation," or the impact of temporal relationships of successive ITDs in the ongoing signal. Akeroyd and Bernstein (2002) found that when a short 5 ms window of a 50 ms series of clicks, or "click train," was filtered with a broadband noise, listeners' thresholds for detecting the ITD were best when the ITD was at the start of the sound, deteriorated when it was in the middle, and were restored when placed again at the end. These data suggest that ITD information in the temporal fine structure is weighted more at the start and end of a sound than in the middle.

Hafter and colleagues found that when click trains, filtered with high-frequency bandlimited tones (e.g., 4 kHz) were presented to listeners, this produced a relationship between the number of clicks in the train and the interval between successive clicks when the stimulus had either an ITD or ILD (Hafter et al., 1983; Stecker and Hafter, 2002). This result showed that the relationship is inversely proportional to the number of clicks (n) or,$\sqrt{n}$ which implies that all the clicks in the train contributed equal amounts of information to the resulting behavioral

response. However, this was only true for tones with a 10 ms period; in other words, a 100 Hz rate in the click train. Conversely, for a click rate of 1000 Hz, thresholds did not change much with an increasing number of clicks. This suggests that the binaural system processes ITDs in a rate-dependent manner, but only for low rates. For high rates, the binaural system favors the onset of a click train due to adaptation, resulting in zero-weighting of the later ongoing clicks. The down-weighting of later clicks would mean that information that is captured earlier is successful in creating localization accuracy when listening in noisy or echoic situations.

B. Across-frequency integration of ITDs: Binaural interference

Integration of ITD information across-frequency is just as important as the integration of ITD information across time for resolving a target sound in a noisy or echoic environment. Just like the importance of later-arriving ongoing pulses in an acoustic click train is down-weighted, across-frequency differences in ITD information can be down- or up-weighted in some frequency bands over others. This across-frequency comparison of ITD information is referred to as "binaural interference," whereby binaural information in a target frequency band is degraded by conflicting binaural information at other frequency bands (Best et al., 2007a; Dye et al., 1996). Binaural interference is generally characterized by presenting listeners with a target signal with either ITDs or ILDs to one frequency band and playing a conflicting ITD/ILD in another frequency band in a signal, and then asking listeners to lateralize where they heard the target sound. Binaural interference studies have shown that sensitivity to the ITD in the target frequency band can worsen as a result of having conflicting ITDs in other frequency bands (McFadden and Pasanen, 1976; Stellmack and Dye, 1993).

Numerous studies have found that when the conflicting ITD is in a lower frequency band than the target ITD, the influence of the conflicting ITD or ILD is much greater than that of the

target (Best et al., 2007b; Dye et al., 2005; Heller and Trahiotis, 1996). However, the primary conclusions from binaural interference studies were that the degree of fusion between the target and interfering sounds profoundly impacts sensitivity to the location of the target sound. For example, if a target frequency band of a complex tone has a leftward ITD, or interfering spectral bands have rightward ITDs, the degree of fusion of these components is dependent on how far the spectral bands are separated, the relative the onset times or synchrony, and the number of interfering spectral bands in the complex (Dye et al., 1996; Stellmack and Dye, 1993). Therefore, greater perceptual fusion based on these three factors could lead to worse performance in detecting the location based on the target ITD, given that the interfering components in the tone have conflicting ITDs.

Although perceptual fusion can preclude accurate detection of the ITD, there are cases where presenting conflicting ITDs at different spectral regions may not result in lowered detection of the ITD in the target frequency band. For example, a study where listeners were presented with synchronous and asynchronous frequency components in a complex tone, assessed how well listeners could detect a target ITD when two of those frequency components had conflicting ITDs (Woods and Colburn, 1992a). As a result, the amount of interference on the target sound was much less in the asynchronous condition than in the synchronous condition, but the authors of this study also found that listeners reported hearing two sound objects more often in the "asynchronous" case and just one object in the "synchronous" case. Fusion and segregation of auditory objects is, therefore, a double-edged sword for ITD detection. Depending on relative changes in the acoustics, this could lead to good detection of the target ITD, or lead to compromised ITD detection and greater separation of individual auditory objects.

C. Neurophysiology of ITDs

The underlying mechanisms for how ITDs are relayed to the two MSOs, and ultimately to the cortex, are a source of debate: On the one hand, some researchers argue that the physical path length of afferent neural fibers leaving the cochlear nucleus is longer from the contralateral side than the ipsilateral side of the sound source (Joris and Yin, 2007; McAlpine et al., 2001; Tollin, 2005). As a result, this pathway will maximally excite a neuron in the MSO, which accounts for the ITD of the sound source. This model is referred to as the "Jeffress Model," and assumes that there are several parallel fibers which reach the MSO and have varying lengths to account for the physical path difference of the sound source located to the ipsilateral vs. contralateral ear. Some anatomical evidence suggests that these "delay lines" exist in the mammalian MSO (Joris et al., 1998; Joris and Yin, 2007; Yin and Chan, 1990). In this model, the horizontal location is encoded by the activity profile of an array of binaural cells that are tuned to specific ITDs, their "best delay," based on different axonal lengths.

On the other hand, other scientists argue that rather than a physical path difference accounting for the delays between the two ears, there is an "internal delay" which varies with frequency (Goldberg and Brown, 2017; McAlpine et al., 2001). Frequency specificity is an important factor for this model because it can account for how the brain encodes an ITD at very high frequencies; a physical path difference mediated by the Jeffress model could not explain that. Assuming that there is a range of best delays for each neuron spanning from 0 μs to approximately 700 μs, the neurons in the MSO only have best delays corresponding to the period of the tone's frequency in order to account for the duplex theory. There is no such assumption for any frequency-dependency of the neurons in the MSO, at least for the Jeffress model. There is some evidence that there is a disproportionate distribution of neurons corresponding to different

delays, where more neurons are tuned to larger best delays. In other words, more neurons respond to lower frequency ITDs; yet there are still some that respond to best delays of higher frequency ITDs (McAlpine et al., 1996). This finding provides greater evidence towards the "internal delay" hypothesis as opposed to the Jeffress model.

Additional evidence towards the “internal delay” hypothesis was shown by Yin and Chan (1990) where 39 cells in the MSO were recorded in anesthetized cats in response to sine tones and broadband ITD stimuli. Yin and colleagues found that a majority of these cells were responsive to characteristic frequencies below 3 kHz and that 79% of all the cells were sensitive to either ITDs or interaural phase differences (IPDs). Furthermore, they observed that more than half of all cells responded to binaural and monaural responses that were phase-locked, meaning firing of the auditory nerve fibers fired at exactly the same phase of the signal with each cycle. Many physiological studies have shown that when low-frequency sinusoidally-amplitude modulated tones are played to just one ear, phase-locking of the auditory nerve fibers occur at the rate of the modulation (Rose et al., 2005). This is also true for neurons involved in processing binaural information at the level of the MSO (Yin and Chan, 1990). Whether there are delay lines or pre-coded "internal delays” in each neuron, the physiological evidence would suggest that neurons at the level of the auditory nerve and superior olivary complex are highly optimized to respond to lower frequencies, partially because those neurons respond to characteristic frequencies below 3 kHz. It also suggests that there are phase-locking properties of the neurons at the level of the auditory nerve that can contribute to ITD sensitivity.

In summary, there are consistent findings from psychophysical and physiological studies. Much of the findings on binaural sensitivity are born out of highly-controlled, laboratory conditions. This format of testing can help understand the underlying mechanisms and individual

differences in sensitivity to ITD cues. As mentioned earlier, one such type of stimulus manipulation is the use of a click or transient, but more specifically, a click pair having different ITD cues. These types of stimuli have been necessary for understanding the impact of onset ITDs.

Taken together, the intricacies within the auditory system which process interaural time differences appear to interact highly with processing temporal changes and frequency changes. The analysis of ITDs in this dissertation highlights an essential part of assessing an auditory scene. The very basics of processing an auditory scene are postulated to involve a set of heuristics where the first step is to process information sequentially (i.e., temporal changes over time) or simultaneously (i.e., across frequency changes) (Bregman, 1982). ITDs are a crucial component to identifying a target sound amongst competing sounds that occur either sequentially or simultaneously. In Albert Bregman's text, *Auditory Scene Analysis,* he states that the scene analysis problem is:

"[Not] simply a laboratory curiosity - it is an oblique glimpse of a scene-analysis process doing the best it can in a situation in which the clues to the structure of the scene are impoverished."

Bregman is implying that outside of the laboratory setting acoustic cues can be degraded. An existing population for which this is an ongoing problem is in listeners with bilateral cochlear implants. The remainder of this introduction will describe how acoustic cues for bilateral cochlear implant listeners are degraded and what types of solutions have been proposed for overcoming those degraded cues.

VI. Cochlear implants

Cochlear implants (CIs) are the standard of care for individuals with severe-to-profound hearing loss. For many years, only single CIs were provided, as improving speech perception was the primary goal. In recent decades, there has been an impetus to also provide CI users with auditory cues that are beneficial for accurate localization and understanding speech in noise; hence bilateral implantation has become relatively routine in many clinics (Peters et al., 2007; Wilson and Dorman, 2008). Bilateral cochlear implant (BiCI) patients exhibit improvements in comparison to a patient with a unilateral implant (Kerber and Seeber, 2012; Litovsky et al., 2012a). However, BiCI patients still struggle to achieve the same level of performance that NH listeners perform within spatial tasks (Jones et al., 2014; Kerber and Seeber, 2012; Litovsky et al., 2009, 2012b; Loizou et al., 2009a). This dissertation encompasses a series of studies which aim to uncover processing solutions that could improve BiCI patients' ability to extract ITDs of target sources from an auditory scene; before describing those in detail, the next few sections will discuss the basics of cochlear implants and hearing impairment.

Candidates for cochlear implantation generally have severe-to-profound hearing loss (Peters et al., 2007), usually due to a sensorineural (cochlear hair cell damage) hearing loss. Sensorineural hearing loss generally means that the information from the traveling wave is not relayed to the auditory nerve because there are missing hair cell connections. In these patients, the auditory nerve is generally intact but could also be degraded to some extent. For these patients, it is possible to substitute the function of the hair cells with electrodes that send electrical stimulation to the auditory nerve. Because the auditory nerve is closely aligned with the bony fluid-filled cochlea, inputting an electrode array into the bony cavity can allow for a transfer of electrical current to auditory nerves cells. The electrode array is inserted into the

basal opening of the cochlea, where the end of the array does not reach the apex and attempts to send frequency-specific information to the appropriate regions on the cochlea (Loizou, 1998).

The translation from acoustic to electric information can be difficult to replicate because there are multiple mechanisms for relaying spectral information that exists in the normal hearing auditory system that is not easy to represent as an electric signal. As mentioned earlier, there are two proposed mechanisms for transmitting frequency information to the auditory nerve: the volley theory and the place theory. The difficulty with translating acoustic to electric signals for the cochlear implant is that a complex tone for typically-developed auditory systems generally requires both temporal and place information to be perceived accurately. In cochlear implants, it is still challenging to encode both of these pieces of information simultaneously.

When the acoustic information travels to the ears of a listener with CIs, the signal is picked up by a microphone, processed into electrical stimuli by an external component, transmitted to the electrode array, and finally, the processed information then stimulates the electrode array in a frequency-specific manner. Electrodes are generally placed in the scala tympani of the cochlea because it is closest to the auditory neurons, preserving the "place" mechanism. This organization suggests that low-frequency information is presented to the apical electrodes and high-frequency information is presented to basal electrodes. As a result, the implant can transmit information about the sound spectrum (via the magnitudes of the current values mapped for each individual electrode) and the pitch (via selection of the electrode's place of stimulation) to the auditory nerve. The three major cochlear implant manufacturers are Cochlear, Advanced Bionics, and Med-El. Each manufacturer uses a different number of electrodes for their devices, 22, 16, and 12, respectively. The CI listeners who participated in the studies described in this dissertation were all patients with Cochlear devices.

For the first multi-channel implants, open-set speech recognition was reported with multi-channel devices (Clark et al. 1981). Other studies showed that there were more significant improvements in speech understanding performance of multi-channel over single-channel devices (Gantz et al., 1988). However, **t**he signal processing step is the most important and most researched aspect of the cochlear implant, because the decisions made on improving spectral resolution, temporal resolution, and feature extraction (i.e., envelopes and formants) are still being investigated and involve manipulation of, number of electrodes, the rate of stimulation, and envelope extraction.

Current processing strategies encode the incoming acoustic signal by passing the sound into a series of bandpass filters corresponding to the number of electrodes on the cochlear array. The external processor of the cochlear implant filters the signal into approximately 12-22 bandpass channels. When the acoustic information is bandpass filtered, the envelopes of these waveforms are full-wave rectified and then low pass filtered, and the temporal fine structure is discarded. Then the envelopes are compressed to fit the dynamic range of each listener's range of sensitivity between a threshold level and a comfortable loudness level. Finally, these levels are used to modulate biphasic (i.e., the electrical current has both positive and negative deflections) pulses using monopolar (when the active electrode is located far from the reference electrode, acting as a ground for all electrodes) stimulation. The amplitudes of the pulses are equivalent to the amplitude of the extracted envelopes. Biphasic pulses, usually at a rate of ~ 900 pulses per second (pps) are presented to eight electrodes at a time; a higher pulse rate has been shown to yield better speech perception (Loizou et al., 2000; Wilson and Dorman, 2008).

The current state-of-the-art processing strategies employ an "n-of-m" strategy, formally referred to as ACE. While the processor is picking up the acoustic signal, it is continuously

estimating the outputs of the 22 electrode filters and selects eight of the ones with the largest amplitude. This strategy is a combination of previous strategies which attempted to improve temporal resolution (CIS), enhance speech features (F0/Fl/F2 strategy), and preserve spectral peaks in a signal (MPEAK). Continuous-interleaved sampling (CIS) uses non-simultaneous, interleaved pulses in order to prevent interaction across electrodes. In the CIS strategy, a series of biphasic pulses are delivered to each electrode such that they do not overlap, allowing for better representation of the speech envelope. However, there is no adaptive selection of the spectral peaks in this strategy. CIS exists in the current ACE strategies because preservation of the speech envelope is the driving factor for speech perception (Dorman, 2000; Iverson et al., 2006). The F0/Fl/F2 strategy is aimed at preserving the fundamental frequency (F0), the first formant (F1), and the second formant (F2); this information is extracted using zero crossing detectors at different frequency ranges using different bandpass filters. The amplitudes of F1 and F2 are then conveyed to the appropriate electrode in the 22-electrode array (for Cochlear systems). The fundamental frequency, or F0, is conveyed by stimulating the selected electrode at a rate of F0 pps, so the stimulation rate reflects the voicing of the speech signal. Finally, the MPEAK strategy, uses a bank of 16 bandpass filters combined with a spectral maxima detector adaptively simulated a set of electrodes at a time—where there was no feature extraction. Taken together, all older strategies have contributed to the current processing strategy, ACE. To date, a significant limitation in all processing strategies is the encoding of temporal fine structure (TFS)—a potential reason for why listeners with bilateral cochlear implants (i.e., two implants) do not receive ITDs (Ihlefeld and Litovsky, 2012). The dissertation will focus on the roles of stimulation rate and timing of low rate pulse trains to enhance sensitivity to ITD in postlingually-deafened adults with bilateral cochlear implants.

Bilateral implantation results in an improvement in spatial hearing tasks compared to hearing with just one implant, however, bilateral cochlear implants (BiCIs) still struggle to achieve the same spatial hearing tasks that NH listeners can perform with high accuracy via acoustic hearing (Hawley et al., 2004; Kerber and Seeber, 2012; Litovsky et al., 2012b; Loizou et al., 2009b; Seeber and Fastl, 2008). Both patient factors and device factors can limit performance in spatial hearing tasks for BiCI listeners. Patient factors, such as degraded neural substrates, can limit detection of ITDs even when ITDs are present in the acoustics (Hancock et al., 2012). This dissertation focuses on the device limitations which prevent detection of ITDs.

A major device limitation is that clinical processors primarily use high-rate pulsatile stimulation, which creates little opportunity to capture ITDs in the temporal fine structure of the signal (Jones et al., 2014; Kan and Litovsky, 2015; Laback et al., 2015). However, in a laboratory setting, the limitations from the clinical processors can be bypassed so that coordinated stimulation of electrodes can be presented to the two ears (Litovsky et al., 2017). However, BiCI listeners still vary drastically in their performance in ITD tasks and are far from achieving the same sensitivity as their normal hearing (NH) counterparts. With research processors, BiCI listeners with adult onset of deafness show ITD sensitivity, with thresholds ranging from 50-1000 μs when presented with very low stimulation rates (~100-300 pulses per second, pps) (van Hoesel, 2007; van Hoesel et al., 2009; Kan et al., 2015a). These thresholds are much higher than for NH listeners who have sensitivity ranging from from 10-75 μs depending on the stimulus type (Klumpp and Eady, 1956) However, these same listeners will still lack sensitivity at rates that are appropriate for good speech representation, which is typically around ~ 900 pps (van Hoesel, 2007; van Hoesel and Tyler, 2003).

Binaural hearing is vital in noisy or complex environments; however, the ITD cue, in particular, is the most robust in noisy situations. This dissertation focuses on an extension of ITD sensitivity in patients with BiCIs, whereby we investigate the impact of electrically stimulated ITDs and its influences on the ability to form coherent auditory objects. Perceiving independent objects, an aspect of sound source segregation, is known to enhance sensitivity to ITDs (Best et al., 2007b; Stellmack and Dye, 1993; Woods and Colburn, 1992b). Here we measured sound localization and auditory object formation of ITDs with psychophysical tasks. The approach in the current dissertation is unique in that we measured sensitivity to low-rate ITDs as well as the utility of low-rate ITD using a combination of discrimination, lateralization, and auditory object formation tasks.

Since bilateral implantation continues to grow as a clinical option, there is a critical need for restoring ITD cues to CI processing strategies in order to preserve spatial hearing abilities and improve patient outcomes. The following chapters focus on understanding unique stimulus features required for good performance in both lateralization and auditory object formation tasks. Here we have focused on the ITD cue because, in NH listeners, this is known to provide robust information for performing well in lateralization and hearing out individual sources, or "objects."

VII. Figures

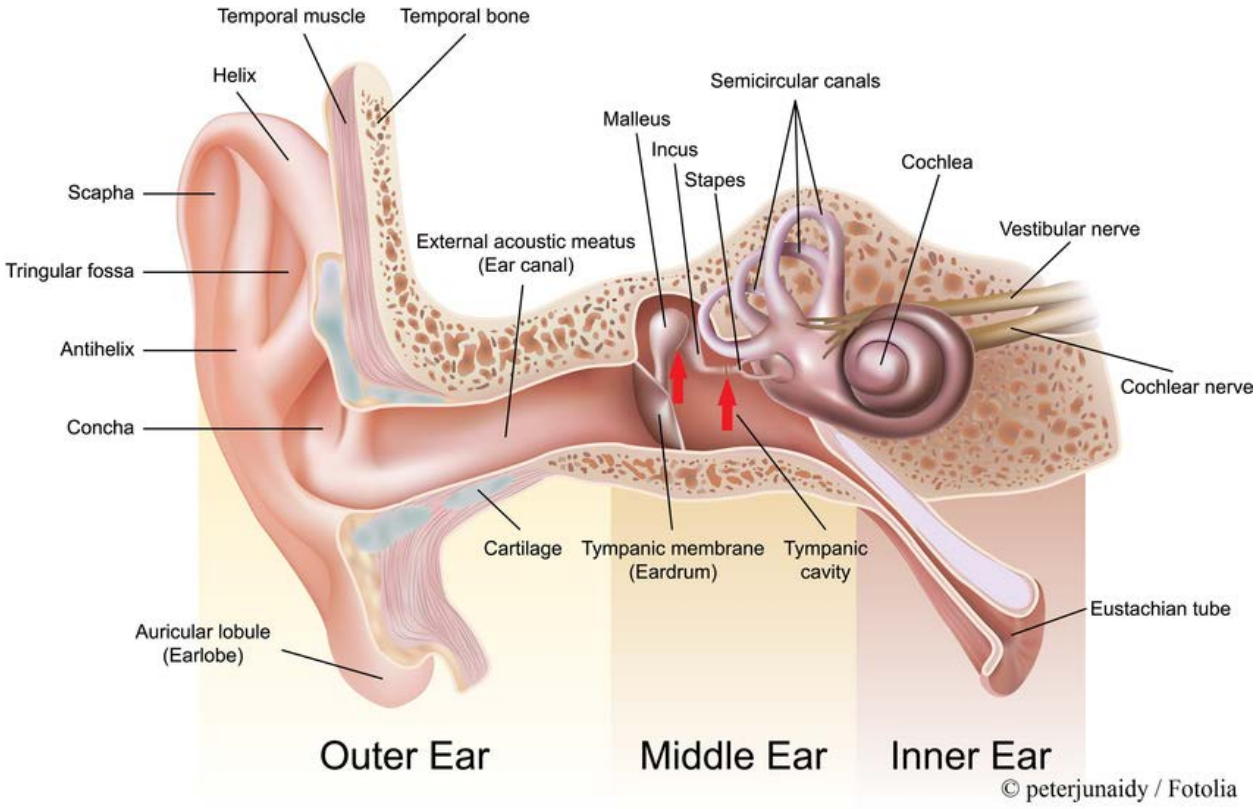

Figure 1: Image of outer, middle, and inner ear.

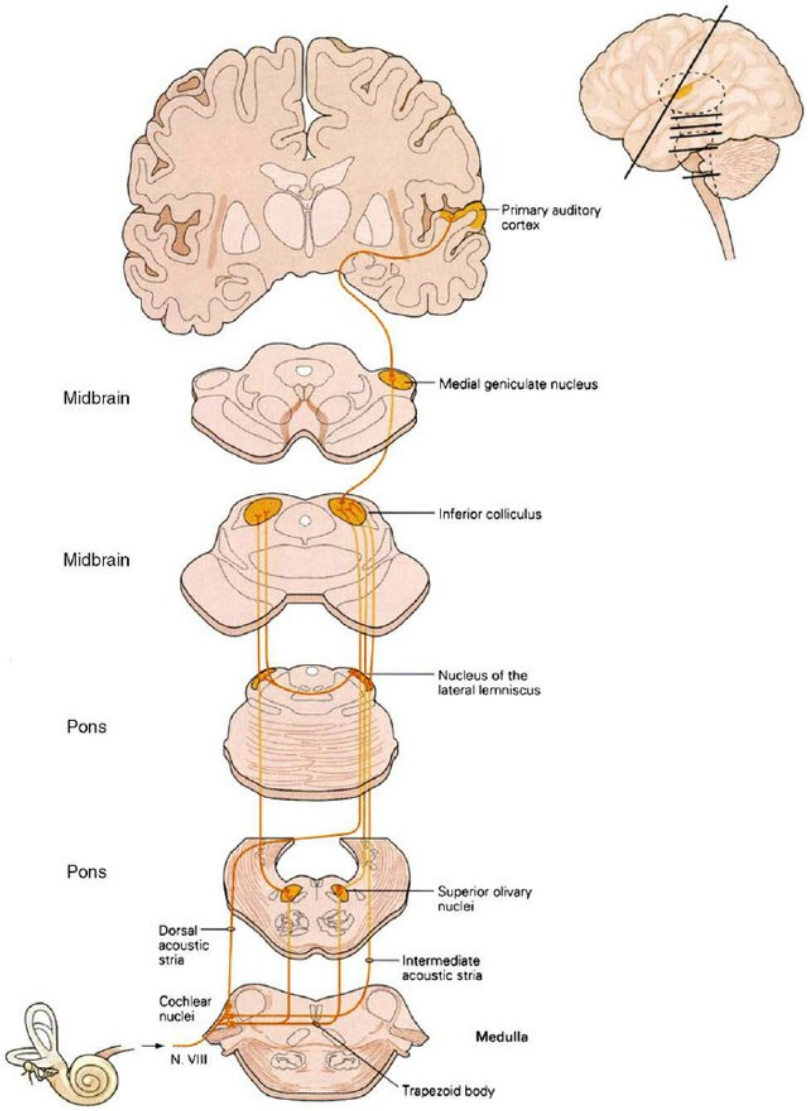

Figure 2: Crosss-sectional mage of the auditory pathway from the auditory nerve to the primary auditory cortex (Kandel et al., 1981)

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CHAPTER II: Mixed stimulation rates to improve the sensitivity of interaural timing differences in bilateral cochlear implant listeners

I. Abstract

Normal hearing listeners extract small interaural time and level differences (ITDs and ILDs, respectively) to locate sounds and segregate targets from noise. Bilateral cochlear implant listeners show poor sensitivity to ITDs when using clinical processors. This is because common clinical stimulation approaches use high rates (~1000 pulses per-second, pps) for each electrode in order to provide good speech representation, but sensitivity to ITDs is best at low-rate pulsatile stimulation (~100-300 pps). Mixing rates of stimulation across the array is a potential solution. Here, we examined ITD sensitivity for a number of mixed-rate configurations that were designed to preserve speech envelope cues using high-rate stimulation and spatial hearing using low-rate stimulation. Results showed that ITD sensitivity with mixed-rate configurations, with only one low-rate electrode, generally yielded ITD thresholds comparable to a configuration with low rates only. Low-rate stimulation at basal or middle regions on the electrode array yielded the best sensitivity to ITDs. This work provides critical evidence that supports the use of mixed-rate strategies for improving ITD sensitivity in bilateral cochlear implant users.

II. Introduction

Patients fitted with bilateral cochlear implants (BiCIs) generally show improvements on measures of speech understanding in noise and sound localization when using two vs. one implants (Kerber and Seeber, 2012; Litovsky et al., 2006, 2009a). However, performance in BiCI users is typically poorer when compared to performance in normal hearing (NH) listeners (Jones et al., 2014; Loizou et al., 2009; Majdak et al., 2011). NH listeners localize sound sources using interaural time differences (ITDs) and interaural level differences (ILDs). Sensitivity to these cues is best at low- and high-frequencies, for ITDs and ILDs, respectively. Sensitivity to ITDs is also provided at high frequencies in the envelope of the signal (Bernstein and Trahiotis, 2002, 2009; Macpherson and Middlebrooks, 2002; Wightman and Kistler, 1992a).

When using clinical processors to localize sound sources, BiCI listeners have been shown to rely primarily on ILD cues (Aronoff et al., 2010; Grantham et al., 2007). Numerous factors contribute to the limited ability of BiCI listeners to make use of ITDs when they listen through clinical processors (Kan and Litovsky, 2015; Laback et al., 2015). These factors include: (1) poor neural survival in one or both ears, resulting in neural asymmetries between the ears, (2) surgical limitations due to asymmetrical placement of electrodes in the two ears, (3) lack of synchronization between clinical speech processors in the two ears, and (4) reduction of binaural sensitivity from the envelope-extraction process and use of high rate pulsatile stimulation (van Hoesel and Tyler, 2003; van Hoesel, 2008; Kan and Litovsky, 2015; Laback et al., 2004). The present study used bilaterally synchronized research processors to overcome the limitations of the clinical processors, and was particularly aimed at understanding whether improvements in ITD sensitivity could be achieved while still providing the high stimulation rates required for

good speech understanding. As a first step, we measured ITD sensitivity, but with the intent of implementing future studies that will examine speech understanding as well.

Binaural sensitivity has been explored extensively in BiCI listeners using bilaterally-synchronized research processors. Bilateral research processors typically deliver controlled pulse timing, allowing for good delivery of the ITD cue. Earlier studies have determined that listeners have sensitivity to ITDs at single pairs of electrodes that are matched across the ears. Results in post-lingually deafened BiCI listeners show that ITD thresholds are best at low rates (<300 pulses per second, pps), and increase at higher rates with nearly no sensitivity at 600 pps and higher (van Hoesel et al., 2009; Kan and Litovsky, 2015; Laback et al., 2015). However, sensitivity improves again when very high rates (~1000 pps) are modulated by a low frequency component (van Hoesel, 2007a). Regarding place of stimulation along the electrode arrays, ITD sensitivity appears to be slightly better at the basal end of the electrode array (Best et al., 2011; Kan et al., 2015a), though large intra- and inter-subject differences in sensitivity exist. Hence, there is no systematic change in ITD sensitivity along the electrode array across the population of BiCI patients studied to date. Individual differences within and across subjects are likely due to factors such as etiology, hearing loss history and delay of implantation (Litovsky et al., 2010a), possible surgical trauma (Nadol and Eddington, 2006), and the placement of the electrode array within the cochlea (Stakhovskaya et al., 2007). To maximize the benefits of ITDs for BiCI users listening in the free-field, we must consider both the effect of rate of stimulation and the impact of individual variability across the cochlear array.

More recent studies have investigated ITD sensitivity with multi-electrode stimulation. Understanding the impact of multi-electrode stimulation on perception is paramount to BiCI outcomes because multi-electrode stimulation is necessary for good speech understanding.

Ihlefeld et al. (2014) found that, when two electrodes are stimulated with a 1000 pps, 100 Hz amplitude modulated pulse train, overall sensitivity to dual-electrode ITDs is at least as good as when a single-electrode pair with the *worst* sensitivity was stimulated. This provides evidence that BiCI listeners can resolve ITDs in the signal's envelope from dual-electrode stimulation. However, this appears to apply only for modulated pulse trains with 100% modulation depth, presented in quiet. While cochlear implant processing often retains the signal's envelope ITDs, in general, detection of envelope ITDs can still be limited by small modulation depths and synchrony in the across-electrode temporal envelopes (Francart et al., 2015). Thus, the effects of presenting ITDs in only the envelope at multiple electrode sites can have its limitations. Combining envelope limitations with the findings that ITD sensitivity is limited or absent at high rates, the current approaches to improving ITD sensitivity are precluded largely by poor fine-timing in the pulse trains.

An additional issue when presenting ITDs to multiple electrode pairs, is that sensitivity to multi-electrode ITDs can vary with a certain configuration of electrodes that are chosen along the electrode arrays. A recent study by Kan et al. (2015a) provided evidence that, when multiple places along the binaural cochlear arrays are stimulated at low rates (100 pps), ITD sensitivity can be at least as good as it is with a single pair of electrodes stimulated at low rates. In addition, sensitivity to ITDs was better when the set of electrodes is spread across the electrode array than when all stimulation is restricted to one region of the electrode array (basal or apical). The authors suggested that with multi-electrode stimulation, perceptual weighting is either dominated by a listener's ITD sensitivity to the best electrode pair in the set, or determined by a more complex mechanism that takes into account sensitivity to electrode pairs across the entire array. Hence, the fact that some interaural electrode pairs along the array can yield better ITD

sensitivity than others must be taken into consideration; it is likely that there are limitations on ITD sensitivity due to poor neural survival at specific places of stimulation. The open question now for multi-electrode presentation is how to optimize ITD sensitivity while also maintaining speech understanding, knowing that listeners exhibit differential performance when certain cochlear regions are stimulated. This can be achieved by understanding *which* electrode should convey ITD information to maximize overall ITD sensitivity.

One approach to improving ITD sensitivity while maintaining speech understanding is to combine low and high stimulation rates across the electrode array (Churchill et al., 2014; Hochmair et al., 2006; van Hoesel, 2007a). Some studies have explored this approach using "naturally-occurring" ITDs, where ITD information delivered to each pulse are derived from the acoustic stimulus. This is in contrast to the work examining ITD sensitivity described above, where ITDs have been constant throughout the entire stimulus. In these studies, the approach has been to extract the ITDs at low frequency channels from some acoustic feature and conveyed them at a low rate to apical electrodes. At the basal electrodes, high rate stimulation is maintained.

A clinical strategy which aims to capture ITDs in the signal, and present the ITDs with fidelity to electrodes in the cochlear arrays, is Med-El's FS4 strategy; low rate stimulation which follows the temporal fine structure of the acoustic signal is applied to the apical four electrodes. Evaluation of this strategy compared to a constant high rate strategy (HDCIS) suggests that there is some improvement in ITD sensitivity, where ITD thresholds using either HDCIS or FS4 improves from an average of 3.3 ms to 2.2 ms, respectively (Zirn et al., 2016). However, note that even with an improvement, ITD thresholds are still above the physiological range of 700 µs. One reason for the modest improvement in ITD sensitivity with FS4 may be due to the fact that

electrodes of the same number across the ears may be exciting different neural populations along the cochlea due to differences in insertion depth (i.e. a mismatch of stimulation across the ears). Previous studies have shown that an interaural place-of-stimulation mismatch has a detrimental effect on ITD sensitivity (Kan et al., 2015b; Poon et al., 2009). A second possible reason is that each processor's clocks are not synchronized between the two ears. Synchronization would be necessary to ensure precise encoding of ITDs with low rate pulses.

Using research processors that control both place and timing of stimulation, Churchill et al. showed a much larger improvement in ITD sensitivity with a mixed-rate strategy compared to a strategy with only high rates (Churchill et al., 2014). In that study, an 8-channel temporal fine structure strategy was examined where low and high stimulation rates were presented at four apical and basal electrodes, respectively, and both ITD sensitivity and speech understanding were evaluated. When all electrodes received low stimulation rates, speech understanding was poor and ITD discrimination was good. The ITD discrimination measures, or just noticeable differences (JNDs) averaged at ~135 μs. Conversely, when all electrodes received high stimulation rates, speech understanding was good, but as expected, ITD discrimination was poor (average JND ~1430 μs). With mixed stimulation rates, performance on ITD discrimination improved compared to performance where all-high rates were presented across the array (average JND ~278 μs). However, this outcome was suboptimal because with only low rate stimulation, many listeners achieved better sensitivity than with the mixed-rate method. One hypothesis for this suboptimal performance is that low rate ITDs were only presented to the apical-most regions of the electrode array.

In the present study, we explore whether alternate configurations of low rates presented to regions along the electrode array, other than the apex, can lead to better ITD sensitivity than

previously observed. Specifically, we used mixed stimulation rates to understand a) how the position of low rate stimulation affected overall ITD sensitivity, and b) how many electrodes with low rate stimulation are necessary, in the context of otherwise high-rate stimulation, to achieve comparable performance to that with low rate stimulation only.

III. Methods

A. Listeners

Ten postlingually-deafened BiCI listeners with demonstrated sensitivity to ITDs from prior experiments volunteered to participate in this study. Listeners traveled to the University of Wisconsin-Madison for 3-5 days for testing and were paid a stipend for their participation. Listener demographics are displayed in Table 1. All listeners had Cochlear Ltd (Sydney, Australia) implants (CI24 and CI512 family of implants). These devices have 24-electrodes (22 intra-cochlear and 2 ground electrodes), with approximately 0.75 mm center-to-center inter-electrode spacing. Electrodes are numbered such that 22 is the apical-most electrode and 1 is the basal-most electrode. All experimental procedures followed the regulations set by National Institutes of Health and were approved by the University of Wisconsin's Human Subject Institutional Review Board.

B. Equipment and Stimuli

Stimuli were delivered via direct stimulation using bilaterally-synchronized Lara34 research processors or a RF GeneratorXS interfaced with MATLAB (Mathworks, Natick, MA) via the Nucleus Implant Communicator (version 2 for Lara34s, version 3 for RF Generator). All testing was performed on a personal computer with custom-made software written in MATLAB. Stimuli were checked using an oscilloscope prior to beginning experiments with listeners.

Responses to stimuli were made on a touchscreen connected to the same computer. Stimuli were anodic-phase leading, biphasic pulse trains presented in monopolar (MP 1+2) configuration. All stimuli were 300-ms duration, 8-μs phase gap, and 25-μs phase duration (with the exception of listener ICP who was mapped with a phase duration of 75 μs), constant amplitude pulse trains. Electrodes were either stimulated at 100 or 1000 pps. Because Nucleus implants are unable to stimulate on multiple electrodes simultaneously, stimulation was staggered in time along the array by 70 μs for each electrode. Stimulation was presented in an apex-to-base order.

C. Pitch-matched electrodes

For this study, five bilateral, pitch-matched electrode pairs were found for each listener individually. There have been many approaches to match the place of stimulation across the ears (Hu and Dietz, 2015; Long et al., 2003), these techniques are important for achieving good ITD sensitivity. Previous studies from our lab have shown that interaural pitch-matching techniques can also be used as a proxy to identify pairs of electrodes that can lead to relatively good ITD sensitivity (Kan et al., 2015b), we used the pitch-matching approach to be consistent with our prior work. Pitch matched electrodes were identified using two tasks, a pitch magnitude estimation and a direct pitch comparison task. The stimulus for the pitch-matching tasks were 300-ms, 100-pps electrical pulse trains presented at a comfortable loudness level as determined by the listener prior to testing. From these tasks, the pair that yielded the highest number of "same" results was chosen as the pitch-matched pair for testing (see Litovsky et al., 2012 for further details on methodology). The five pitch-matched pairs found for each listener is shown in Table 2. The pairs were selected to roughly span the entire electrode array at the following locations: base, mid-base, mid, mid-apex, and apex. ITD sensitivity on these electrode pairs were determined in prior studies.

D. Calibration of multi-electrode mixed-rate configurations

Seven multi-electrode configurations were created for the experiment. These are shown in Figure 1. Within the seven configurations, two had the same stimulation rates on all electrodes. These were “High5” and “Low5”, which had 1000 and 100 pps stimulation, respectively. Three configurations had a single low rate (100 pps) at either apex, middle, or base (“Apex1,” “Mid1,” and “Base1,” respectively) and 1000 pps at the remaining four bilateral pitch-matched pairs. The final two mixed-rate configurations had three low-rate electrodes at either the three apical-most pitch-matched pairs, or spread across the array (“Apex3,” and “Spread3,” respectively). The remaining two pairs were stimulated at 1000 pps.

To ensure that all configurations were equally loud, a loudness map for stimulation at 1000 pps was first determined for each ear. The loudness map defines the range of current units that generates an audible percept between threshold (T) and most comfortable (M) loudness levels at each electrode. Within this range, a comfortable (C) level was also measured, which we defined as the stimulation level that a listener is willing to be tested at for an extended period of time. C levels were compared across electrodes within an ear to ensure the same loudness. This was achieved by stimulating the electrodes one at a time with an inter-stimulus interval of 100 ms. Listeners indicated which electrodes were noticeably louder than others and those C levels were adjusted.

Because concurrent stimulation across multiple sites has the potential to generate louder percepts because of summing of currents and broader recruitment of auditory nerve fibers (Egger et al., 2016), the C levels found in the previous step were reduced by 15% at each electrode (20% for listener ICS, and by 25% for listener ICP) during multi-electrode stimulation. Equal loudness at these new levels were again ensured unilaterally by playing the five electrodes sequentially to

the listener. Once the new levels were found to be equally loud, we ensured that multi-electrode stimulation would still be comfortable by playing the five electrodes in each side, simultaneously to the listener. Because Nucleus implants are unable to stimulate on multiple electrodes simultaneously, stimulation was staggered in time along the array by 70 μs for each electrode.

For measuring ITD thresholds, it is important to establish that listeners perceived a fused, centered auditory percept when each interaural pair of electrodes was played together. Each pitch-matched electrode pair was stimulated simultaneously and the C levels found in the previous step were adjusted as needed to obtain a centered auditory percept. Typically, only a small adjustment of 2-3 current units (CU) were necessary to center the auditory image. No listener reported hearing multiple auditory images when pitch-matched electrode pairs were simultaneously stimulated.

The C-levels for 1000 pps found using the previous steps were used to create the High5 configuration loudness map. Mixed-rate loudness maps were created by systematically changing the stimulation rate from 1000 pps to 100 pps one electrode at a time. For each mixed-rate map, we ensured that the loudness was the same as the High5 map when all electrodes in one ear were stimulated simultaneously. Because our mapping software only allows across ear comparisons, loudness matching was conducted across ears. On average, the amount of change in CUs from 1000 to 100 pps were approximately the following: Apex, Left = ~146 μAs, Right = ~146 μAs; Mid-Apex, Left = ~247 μAs, Right = ~253 μAs; Mid, Left = ~250 μAs, Right = ~260 μAs; Mid-Base, Left = ~109 μAs, Right = ~71 μAs; Basal, Left = ~86 μAs, Right = ~60 μAs. These values were determined by averaging the microamperes across listeners in Table 2, and then taking the difference between the 100 pps and 1000 pps values. Details for converting CUs to amperes can be found in the Nucleus Implant Communicator documentation (Cochlear Ltd., 2006).

E. ITD Discrimination Task

ITD discrimination was tested using a 2-interval, 2-alternative forced-choice paradigm with a 300 ms inter-stimulus interval. For the task, each interval had a bilateral stimulus consisting of multi-electrode stimulation of five electrode pairs. On each trial, the first interval had a left- or right-leading ITD, and the same whole-waveform ITD shift was applied to all electrode pairs, and to all biphasic pulses in the 300 ms stimulus. In the second interval, an ITD of the same magnitude was applied but in an opposing direction to that of the first interval. Subjects responded by indicating the direction of the second interval relative to that of the first interval. A method of constant stimuli was used to test ITDs of 100, 200, 400, and 800 μs in all listeners. In some instances, additional ITDs were included (such as 50 μs) to complete a psychometric function, based on percent correct, so that JNDs determined at 70.7% (Levitt, 1971) could be estimated. The data were fit using the psignift MATLAB tools version 2.5.6 (Wichmann and Hill, 2001). It should be noted that the ITD JNDs reported in this paper are 50% smaller than that typically reported for discrimination tasks with a center reference. Each ITD was tested 40 times with 20 left-leading and 20-right leading trials. The experiment was conducted in blocks, where each block consisted of 10 trials at each ITD (5 left-leading and 5 right-leading). ITDs within each block was tested in random order. No training or feedback was provided to the listeners because all listeners had prior experience with the task.

ITD JNDs were measured in all seven configurations shown in Figure 1. JNDs were first measured in the Low5 and High5 configurations to establish the range of performance. Subsequently, performance was measured for Apex1, Mid1, Base1, Spread3, and Apex3 in a pseudo-random manner.

IV. Results

Figure 2 shows examples of psychometric functions for two of the ten listeners, with model fits for each configuration, where percent correct (converted to proportion correct) in the discrimination task is plotted as a function of the nominal ITD presented in each interval. It can be seen that the psychometric functions fit the listener data well. To ensure that the JNDs estimated in our data are accurate, we estimated listener bias and goodness-of-fit for the psychometric functions (see Table 3). It can be seen that in all cases, the amount of bias was small and that the psychometric functions fit the data well. For the goodness of fit, the deviance, *D*, was calculated (Wichmann and Hill, 2001). *D* is the log-likelihood that a saturated model (a model with no residual error between the fit and the real data) and the best-fitted model are different. In all cases where the D is greater than 2, (i.e., the log-likelihood ratio is greater than 1 which indicates a difference between the two models), a chi-square test revealed no significant differences (α=0.05). Additionally, biases in all psychometric functions were calculated, values with biases are considered to be greater or less than zero (Macmillan, 2002). These values are reported as *c* in Table 5. Hence, it can be concluded that our psychometric functions fit the data well.

Overall, these data suggest that listeners achieved ITD sensitivity with mixed rates comparable to the sensitivity achieved in the Low5 configuration. Considering the upper bound of physiological ITDs to be ~700 μs, we find that the Spread3, Apex3, Mid1, Base1, and Low5 not only produced similar performance, but also yielded JNDs within the physiological range (compare to results in Table 4) for every listener. These effects suggest that mixed-rate ITDs offer a unique and feasible way to improve ITD sensitivity for listeners without needing low rate stimulation to be presented at all electrodes.

To determine whether there was a significant difference in ITD sensitivity between stimulation configurations, statistical analysis was conducted with a non-parametric Friedman's test, which is most appropriate for data sets with a small sample size. There was a significant difference between configurations [χ^2 (6, 30.25) = 39.03, $p<0.001$] and post-hoc testing with Bonferroni correction revealed that the High5 and Apex1 configurations were significantly different from all other configurations. There were no significant differences between the Mid1, Base1, Apex3, Spread3, and Low5 configurations. This means that mixed-rate configurations where a single low rate electrode was presented in either the middle or basal region of the electrode array resulted in ITD JNDs that were smaller (i.e. better) than the JND obtained with High5, and comparable to that obtained with the Low5 configuration.

To estimate the magnitude of these differences, we conducted a pairwise comparison of the different configurations using a Wilcoxon signed-rank test, and the effect size was calculated by dividing the test statistic by the square root of the number of observations in each pairwise comparison, according to Field et al. (2013). The effect sizes are shown in Table 5. Using Cohen's scale for interpreting the magnitude of effect sizes, it can be seen that there was a moderate improvement from High5 when listening with the mixed rates configurations other than Apex1. Conversely, when comparing to the Low5 configuration, the magnitude of the differences were small mixed-rate configurations other than Apex1. A Kendall's W test was also conducted to determine whether the JNDs across configurations were ordered similarly across listeners. Results suggest that JNDs for the different configurations were ordered in a similar fashion across listeners (W = 0.763).

Individual data should also be highlighted. Figure 3 shows the individual ITD JNDs estimated from the psychometric functions, as well as a group boxplot showing the inter-quartile

range and medians for each of the tested configurations. There was clear variability in JNDs across listeners, ranging from listener ICP who showed JNDs as large as 1000 μs, to listener IBF who could discriminate ITDs at approximately 50 μs. JNDs that were "Not Determined" (ND) are represented with a diamond symbol. When comparing across configurations, there was no systematic performance changes within subjects, such that a particular configuration yielded the best JNDs for all subjects (see Table 4). To further illustrate this, Figure 4 shows individual ITD JNDs for the Low5 configuration compared to each of the other six configurations. Here, we made the assumption that the Low5 configuration would yield the best ITD JND, and was therefore Low5 used as a baseline for comparison to all other configurations. The dotted red line denotes unity between JNDs across the two compared configurations. The High5 and Apex1 configurations generally yielded higher (worse) JNDs than the Low5. However, for the other configurations, individual differences in JNDs are noteworthy. For example, listener ICD had data points below the line of unity for all mixed-rate conditions except for Apex1. Interestingly for most listeners, best JNDs were generally observed in the Spread3 or Apex3 conditions, suggesting that a single channel of low rate ITDs may be sufficient to deliver ITDs, but that more channels of low rate information would be necessary to provide the best possible sensitivity. In fact, with the Spread3 or Apex3 configurations, some listeners had lower JNDs than the Low5 configuration. This can be seen in Figure 5 where the differences in ITD JNDs between the High5 (left panel) and Low5 (right panel) are shown. Values falling below the dashed line indicate that the JND in a mixed-rate configuration was smaller (better) than a JND in either the High5 or Low5 configuration. Values falling above the dashed line indicated the reverse: that the mixed configuration produced higher (worse) JNDs than the High5 or Low5 configuration. Some listeners who had a High5 JND that was "ND" consequently had a ITD JND difference value

that was also ND (listeners ICJ, IBQ, and ICI). As a group, participants generally displayed improved ITD sensitivity (indicted by negative values below the dashed lines in Figure 5, panel A) in the mixed-rate configurations when compared to the High5 configuration. This improvement is marked by the introduction of at least one low rate electrode (see also Figure 3). Conversely, in the Low5 configuration, most data points did not deviate far from the dashed line, indicating that the difference in performance in a mixed-rate configuration from the Low5 configuration was negligible. Most mixed-rate configurations yielded improved or comparable performance in all listeners, however the Apex1 configuration did not (Figure 5, panel B).

V. Discussion

The goals of the current study were to a) understand the influence of stimulating a low-rate ITD in the context of high-rate ITDs, on different places along the cochlear array and b) to determine how many low-rate electrodes are required to achieve comparable ITD sensitivity with that of low-rate stimulation only.

The present experiment was designed as a “proof of concept” to show how well the auditory system of BiCI listeners can extract low rate ITD information in the presence of high rate stimulation. We demonstrated that, when presenting high rates on all but one electrode pair (see Fig. 3), ITD sensitivity improved relative to a configuration in which all the electrodes were stimulated with high rates. We showed that configurations with one electrode pair receiving low rate stimulation yielded average JNDs of 253 μs and 239 μs, which was significantly better than the configuration with only high rates (High5) (see Fig. 3). Notably, the mixed-rate configurations and the Low5 configuration (average: 260 μs) were not significantly different. Results showed that selection of the place for low rate stimulation does not need to be restricted to the apical region of the electrode array, as the tonotopicity of low-frequency information in the

cochlea would typically suggest. Rather, low rates can potentially be delivered to any place of stimulation along the electrode arrays that has capacity (i.e., sufficient neural health and neural-electrode interface) to promote ITD sensitivity. These findings provide evidence that multi-electrode stimulation with mixed rates is a feasible way of conveying binaural cues, without any tonotopic-driven restrictions regarding place of stimulation.

Our work was motivated by the knowledge that while speech representation in clinical processors requires high rates of stimulation, binaural cues needed for better speech unmasking and for sound source localization require low rates of stimulation. By utilizing multi-electrode, mixed-rate ITDs, here we have demonstrated a potential approach for retaining high-rate stimulation in multiple electrodes, while simultaneously providing ITD information through low rate electrodes.

A. Prior Research on Mixed Rates and Implications

Previous work has demonstrated that mixed rates can be implemented in research processors and clinical strategies; however, there is little evidence of improved ITD sensitivity with mixed-rate stimulation. Prior approaches to creating mixed rate stimulation involved a processing strategy that aims to time electrical pulses according to low-frequency components in the acoustic temporal fine structure. The “peak-derived timing” (PDT) strategy (van Hoesel, 2007b) is an example of a strategy that was intended to improve encoding of ITDs in the fine structure and also in the speech envelope. To date, the actual utility of the PDT strategy remains to be demonstrated. BiCI users have not shown improved performance in speech unmasking or sound lateralization tasks of a signal with a 700 μs ITD (van Hoesel et al., 2008). More recently, Churchill et al. (2014) implemented mixed-rate stimulation by controlling the timing of electrical pulses calculated from zero-crossings of the Hilbert transform to provide low-rate timing

information to convey ITDs. In that study, low rates were presented only to apical electrodes and the results showed that ITD JNDs in the mixed-rate configurations were smaller (better) than JNDs obtained in all-high rate conditions, and as good as ITDs with all-low stimulation rates. In that study, four low-rate electrodes were presented only to the apical portion of the electrode array, this assumption limits our understanding of the potential benefits to low-rate channels presented to regions without anatomical restrictions.

Mixed-rate methods for clinical processors such as MED-EL's Fine Structure Processing (FSP, Hochmair et al., 2006) and FS4 strategies have introduced low rate information that is timed to the instantaneous fine structure frequency of the signal and then presented to the apical-most electrodes. Results on binaural sensitivity with the FS4 strategy have shown that improvements for interaural phase difference (IPD) thresholds in BiCI listeners were moderate, and that improvement on other binaural processes such as binaural speech intelligibility level differences were not observed (Zirn et al., 2016). Nonetheless, some evidence suggests that FSP/FS4 strategies do not lead to a decrement in speech understanding, suggesting that there are perhaps untapped potential benefits of using mixed rates for speech understanding with this approach (Riss et al., 2014).

The common thread in previous work regarding mixed rates is the assumption that low rate stimulation should occur in the apical region of the cochlea. However, our work would suggest that one cannot assume that stimulating *only the apical region* of the electrode array will lead to the best ITD sensitivity. Here we deliberately and systematically investigated various mixed-rate configurations where low rate ITDs were presented at any of the cochlear regions (apical, middle or basal), with the remaining electrodes conveying high rate ITDs. Our overall findings suggest that ITD sensitivity with mixed rates was generally comparable to ITD

sensitivity observed in the Low5 configuration. One notable exception was the Apex1 configuration where sensitivity was significantly worse. This finding suggests that there is no particular reason to assume that the low rates should be presented at the apical cochlear region in order to yield best binaural sensitivity.

B. Potential advantages to mixed-rate stimulation

We have observed that all mixed rate configurations, apart from the Apex1 configuration, showed improved ITD sensitivity from the High5. However, a notable observation in this study is that many BiCI listeners exhibited some improvements in ITD sensitivity in the mixed-rate configurations compared to the uniform-rate "Low5" configuration. In the Spread3 and Apex3 configurations, JNDs were *better* in at least six of the listeners with mixed rates compared with Low5. This suggests that there may be some benefits to mixing high and low rates as opposed to presenting low rates only. For example, listener ICS (Figure 4, magenta-filled symbol), had an improved JND in four of the five mixed-rate configurations when comparing to the Low5 configuration. This means that a mix of high and low rates has the potential to be better for ITD sensitivity rather than having low rates alone for this listener. A case where an all-low stimulation would be maladaptive would be if some regions along the electrode array have poor ITD sensitivity, due to factors such as poor neural health or poor electrode-neuron interface (Ihlefeld et al., 2015). It appears that presenting low rates to all electrode pairs could lead to good ITD representation to at least some of the electrodes while also yielding poor ITD representation at other electrodes. The outcome of improved sensitivity in some mixed-rate configurations compared to the Low5, resembles a situation of binaural interference, whereby a perceptual response to a stimulus with conflicting binaural cues across frequency can impair ITD sensitivity and lateralization abilities (Best et al., 2007b; Stellmack and Dye, 1993; Woods and Colburn,

1992b). A key observation from our work is that the same ITD was presented to all electrodes. Thus, it could be argued that a mix of high and low rates creates a "release from interference" because the high rate channels do not transmit useful ITD cues and are essentially ignored by the listener, ultimately reducing interference from poorer channels. Conversely, the configuration with all low rates across the array may force listeners to integrate the ITD across channels even if there are regions that may be transmitting a poorer ITD cue, thus causing interference. Finally, from a practical perspective, a potential benefit of reducing rates on some channels relative to the all-high rates would be a reduction in battery power needed, due to the replacement of some of the high rate channels with low-rate channels.

C. Importance of low rates for ITD processing in the context of physiology

The findings from the current study can be considered in the larger context of physiological mechanisms of neural ITD coding. Because our data suggest that place-specific low-rate stimulation of ITDs is crucial for good ITD sensitivity, it is important to recognize the underlying mechanisms when considering development of processing strategies aimed at transmitting binaural cues with fidelity to BiCI users. A number of physiological studies have provided insights into ITD coding with electrical stimulation. Single neurons in the inferior colliculus of rabbits respond to electrical stimulation of ITDs, particularly at rates as low as 100 pps (Hancock and Delgutte, 2004; Smith and Delgutte, 2007), and this is also true for amplitude modulated stimuli (Wang et al., 2014). Hancock and Delgutte (2004) found that "best delays" of neural units (a physiological equivalent of the JND) at low rate pulse trains are around 300μs. This is equivalent to the range of psychophysical ITD JNDs that we see in our BiCI listeners from the current study. Further, Smith and Delgutte (2007) showed that the binaural system is highly tuned to low rate sharp modulations of pulsatile stimuli, like our low-rate electrical pulse

trains, and that sensitivity degrades with higher stimulation rates. Specifically, when recording from a population of neurons, the neural spike rate as a function of the number of pulses in a low rate signal (an equivalent measure to behavioral ITD JNDs) will increase overall ITD sensitivity (i.e. the neural ITD JNDs decrease from ~500 μs to ~ 100 μs); this is similar to responses seen with acoustic stimulation in NH animals. This suggests that a low-rate electrical stimulus may be ideal for conveying ITDs because it reflects the neural response of ITD perception to acoustic pulsatile stimuli.

The auditory nerve response to low frequencies of a sinusoidally-amplitude modulated tone, a half-wave rectified, or "transposed tones" yields the greatest sensitivity at lower frequency components on the basilar membrane (Yin and Chan, 1990) and will ultimately display phase-locking to low rate information. Using these sharply-modulated acoustic signals (tones that relay good low rate envelope information to the auditory nerve) appears to enhance sensitivity to ITDs when compared to a low frequency pure tone. This means that the low frequency sharp modulations of a transposed tone, much like a low rate pulsatile stimulus has the potential to enhance sensitivity to ITDs. In the current study, we are mimicking this neural response to a transposed tone by introducing low rate ITDs in place-specific electrode configurations, and constraining those low rates at certain place-specific electrode frequency specific information at the level of the auditory nerve that is needed for sensitivity at the level of the brainstem. This may be, in part, why sensitivity is so good with mixed rates.

D. Importance of low rates for ITD processing in the context of psychophysics

Our results are also consistent with behavioral data which suggest that listeners can detect ITD cues that are peripherally optimized by the low frequency components of a complex tone,

analogous to our multi-electrode mixed-rate stimulation in BiCI listeners (Bernstein and Trahiotis, 2002, 2009; McFadden and Pasanen, 1976b; van de Par and Kohlrausch, 1997; Stecker and Brown, 2010). There is a notable connection between the physiological data discussed above and the psychophysical data on low-rate ITDs. Using strategies that induce common neural mechanisms with electrical or acoustic stimulation, we can maximize our understanding of stimulation approaches for BiCI listeners that would optimize ITD cues using mixed rates of stimulation.

At present, the mechanism for perception of mixed-rate ITDs is unknown, but the introduction of low rates maximizes the use of low frequency ITDs. One possible explanation for the effectiveness of mixed rates is the is the idea that the simultaneous stimulation of high and low rates promotes a "restarting" of the auditory nerve, as suggested by Laback and Majdak (2008) where electrical pulses stimulated closer in time at high rates can lead to improved ITD sensitivity, but caN inadvertently create large low-rate fluctuations in time, similar to an amplitude modulate tone. However, this is unlikely with our study because the low rate stimuli were not presented in the same channel. An alternative explanation is that the brain is able to extract the most salient ITD information from across the electrode array. This is more likely since data from Ihlefeld et al. (2014) and Kan et al. (2015a) would suggest that BiCI listeners do not behave as ideal observers when combining ITD information across the electrode array, but rather sensitivity appears to be more influenced by the electrodes that yield better ITD sensitivity. A note of caution is warranted because a realistic speech processing strategy will stimulate more than five electrodes at a time, and the electrodes are likely to be physically spaced closer together than the spacing that was used in this study. Further, the signal envelopes

carried on these electrodes may be highly different, which may affect the overall saliency of ITD cues (Francart et al., 2015).

E. Limitations, Caveats and Future Directions

While a mixed-rate strategy appears to be a potential solution for providing good ITDs to the auditory nerve fibers, it is unclear how this will translate into real-world benefits such as improved sound localization and speech-in-noise understanding. Though modeling data presented in Nicoletti et al. (2013) would suggest that electrical stimulation that follows the temporal fine structure of the acoustic signal, such as PDT and FS4, elicits neural responses that are more similar to what is seen with acoustic stimulation than with CIS. However, given that both these strategies use only the apical channels for conveying ITDs, there is potential for interchannel crosstalk because of spread of current. The Lindemann cross-correlation model described in Nicoletti et al. suggests that interchannel crosstalk is detrimental to ITD coding on the auditory nerve (Nicoletti et al., 2013). Our paradigm which spreads the low rate ITD information along the length of the electrode array is likely to mitigate some of these problems while being able to elicit ITD sensitivity. A caveat to the current study is that ITD cues in complex environments are often combined with other cues such as ILDs, spectral profiles, pitch cues and speech modulations. These aspects of audition are better understood when asking a listener to make more complex judgements regarding *identification* of the sound source, such as determining its coherency, or identifying its true location, rather than making *discrimination* judgements. The present study was restricted to measuring discrimination abilities to better understand ITD sensitivity when using mixed rates. If future cochlear implant processing strategies have the goal of relaying “sparse” temporal coding of ITDs (i.e. low rates), our current experiment using discrimination tasks is an important first step in understanding how many

electrodes are necessary for conveying ITDs at low rates. The next step beyond measuring ITD discrimination thresholds would be to examine how mixed-rate, multi-electrode stimulation affects perceived auditory object formation, lateralization, and more complex perceptual tasks. These questions are important because differential sensitivity on various electrodes may lead to lack of fusion of across-frequency components and a blur in the perceived location of the auditory object. Experiments conducted in NH have shown that sounds that have conflicting or degraded binaural cues lead to poorer perceived locations (Stellmack and Dye, 1993). Beyond localization testing, it would be important to introduce a speech envelope to the set of configurations we have tested here to see the impact of mixed-rate stimulation on speech perception and spatial hearing abilities.

A final note, and perhaps another caveat to the paradigm in the current study is the impact of pulse rate on perceived loudness. Dynamic range (DR) at individual electrode sites determine the range of current units from threshold to comfort level mapped for each individual electrode. DR has been shown to vary at different stimulation rates with larger dynamic ranges being associated with higher pulse rates (McKay et al., 2001). This can have a number of implications: (1) Sensitivity to binaural masking level differences (BMLD), a psychophysical test for binaural sensitivity in the presence of noise, has been shown to be best at larger dynamic range of current levels (Todd et al., 2016). Hence, this would suggest that with the introduction of low rate stimulation on some electrodes, there may be a possibility that BMLD thresholds will increase. While this is not desirable, the effect of rate of stimulation on BMLD thresholds is yet to be determined. (2) While loudness growth may remain the same at for different rates, DR does not and current processing strategies do not account for these differences across the electrode array. That is, current processing strategies assume that the mapping of envelope levels to current

levels are the same across all electrodes. In moving to mixed rates, greater care will be needed to account for loudness growth for the different stimulation rates. Otherwise, there is a potential for envelope distortions or fluctuations in the loudness in a mixed-rate stimulus. In NH listeners, it has been shown that large loudness fluctuations between the ears can reduce overall ITD sensitivity (Goupell and Litovsky, 2015). Recent work by Hu et al. (2017) has demonstrated that at 200 pulses per second, BiCI listeners have the greatest sensitivity to ITDs during the peak of the envelope modulation. This implies that in a reverberant situation where ITDs are more salient at the onset, than in the ongoing parts of the signal, ITD sensitivity in BiCI listeners will be more degraded by reverberation than their NH counterparts who use the signal onset for extracting ITDs. Though the impact of rate of stimulation on loudness perception and ITD sensitivity is a valid concern in a mixed-rate strategy, loudness-balanced stimuli appears to be highly effective in yielding good sensitivity to ITDs.

VI. Conclusions

The present study investigated the impact of a mixed-rate processing strategy in a multi-electrode paradigm on ITD sensitivity in bilateral cochlear implant listeners. Findings reported here demonstrate that introducing a low rate cue in at least one interaural pair of electrodes raised performance of ITD discrimination comparable to their ability to discriminate when all electrodes pairs possess a low rate ITD cue. Furthermore, stimulation of low rates at the apical region of the electrode array appears to yield the poorest ITD sensitivity in all listeners. The observation that mixed-rate ITDs yield performance comparable to having only low-rate ITDs suggests that the binaural system of BiCI listeners can extract pertinent cues to achieve ITD sensitivity even when high rate ITD information is presented at the majority of the cochlear locations; this lends support to the possibility of implementing mixed-rate ITD cues in current

cochlear implant speech processing strategies to improve localization performance while maintaining good speech understanding.

VII. Tables and Figures

Listener ID	Age	Sex	Years of CI experience (left/right)	Implant Type (left/right)	Etiology
IBF	64	F	(8/9)	(CI24RE/ CI24RE)	Hereditary
IBK	75	M	(12/6)	(CI24R (CS)/ CI24RE)	Hereditary, noise exposure
IBQ	84	F	(9/12)	(CI24RE/ CI24R (CS))	Meniere's
IBY	51	F	(7/3)	(CI24RE/CI512)	Unknown
ICB	64	F	(12/12-15) *listener was reimplanted in the right ear after 3 years	(CI24RE/ CI24R (CA))	Hereditary
ICD	57	F	(6/7)	(CI24RE/ CI24R (CS))	Hearing loss at 3 years old
ICI	57	F	(6/5)	(CI24RE/ CI24RE)	Hearing loss at 31 years, etiology unknown
ICJ	65	F	(4/4)	(CI512/CI512)	Hearing loss at 13 years, perhaps due to illness
ICP	52	M	(6/3)	(CI24RE/ CI24RE)	Hearing loss at 3 years old
ICS	87	M	(4/12)	(CI512/ CI24R (CS))	Gradual hearing loss

Table 1: Listener demographics and etiology. Table lists age at testing, sex, years of experience with a CI, and etiology.

ID	Electrode Location														
	Apical			Mid-Apex			Mid			Mid-Base			Basal		
	El #	**100 pps** (CU/μA)	**1000 pps** (CU/μA)	**El #**	**100 pps** (CU/μA)	**1000 pps** (CU/μA)	**El #**	**100 pps** (CU/μA)	**1000 pps** (CU/μA)	**El #**	**100 pps** (CU/μA)	**1000 pps** (CU/μA)	**El #**	**100 pps** (CU/μA)	**1000 pps** (CU/μA)
IBF	**L4**	197/ 613.9	150/ 262.7	**L8**	197/ 613.9	166/ 350.7	**L12**	206/ 722.3	168/ 363.6	**L16**	199 /636.5	171/ 383.9	**L21**	173/ 398.0	167/ 357.1
	R5	187/ 512.5	152/ 272.3	**R10**	198/ 625.1	168/ 363.6	**R12**	205/ 709.3	171/ 383.9	**R17**	202/ 671.9	180/ 451.6	**R21**	186/ 503.3	175/ 412.6
IBK	**L6**	228/ 1012.8	208/ 675.4	**L11**	227/ 992.5	210/ 703.4	**L14**	227/ 992.5	213/ 747.4	**L15**	230/ 1054.7	212/ 732.4	**L18**	229/ 1033.5	212/ 732.4
	R6	220/ 930.1	190/ 541	**R10**	219/ 913.4	198/ 625.1	**R13**	215/ 849.7	194/ 581.5	**R16**	213/ 819.6	202/ 671.9	**R22**	205/ 709.3	199/ 636.5
IBQ	**L8**	223/ 981.8	185/ 494.3	**L12**	215/ 849.7	185/ 494.3	**L14**	207/ 735.4	182/ 468.2	**L16**	214/ 834.5	181/ 459.8	**L20**	213/ 819.6	184/ 485.4
	R1	220/ 861.3	196/ 529.7	**R3**	212/ 732.4	192/ 488.5	**R7**	210/ 703.4	186/ 432.6	**R9**	205/ 635.6	188/ 450.5	**R11**	212/ 732.4	185/ 423.9
IBY	**L4**	212/ 804.9	170/ 377.0	**L8**	213/ 819.6	181/ 459.8	**L12**	222/ 964.3	190/ 541.0	**L16**	202/ 671.9	192/ 560.9	**L20**	204/ 696.6	188/ 521.8
	R7	204/ 696.6	178/ 435.6	**R11**	214/ 834.5	183/ 476.8	**R12**	217/ 881.0	180/ 451.6	**R14**	216/ 865.2	183/ 476.8	**R18**	201/ 659.9	182/ 468.2
ICB	**L4**	222/ 964.3	172/ 390.8	**L8**	224/ 999.7	199/ 636.5	**L12**	237/ 1264.3	205/ 709.3	**L15**	233/ 1176.2	208/ 748.8	**L18**	230/ 1114.1	208/ 748.8
	R4	221/ 878.9	190/ 469.1	**R9**	230/ 1054.7	198/ 551.6	**R12**	234/ 1143.7	204/ 622.9	**R14**	225/ 953.1	208/ 675.4	**R18**	220/ 861.3	202/ 598.1
ICD	**L4**	179/ 443.5	161/ 320	**L8**	195/ 592.1	175/ 412.6	**L12**	189/ 531.3	178/ 435.6	**L16**	196/ 602.9	174/ 405.2	**L20**	198/ 625.1	176/ 420.1
	R2	193/ 498.5	177/ 360.5	**R6**	201/ 586.1	187/ 441.4	**R10**	201/ 586.1	194/ 508.7	**R14**	200/ 574.4	191/ 478.7	**R18**	194/ 508.7	194/ 508.7
ICI	**L2**	178/ 435.6	132/ 189.8	**L4**	174/ 405.2	127/ 173.4	**L8**	181/ 459.8	134/ 196.8	**L12**	180/ 451.6	134/ 196.8	**L18**	155/ 287.5	134/ 196.8
	R4	156/ 292.8	120/ 152.8	**R8**	171/ 383.9	132/ 189.8	**R10**	170/ 377.0	138/ 211.5	**R16**	172/ 390.8	134/ 196.8	**R18**	145/ 240.0	132/ 189.8
ICJ	**L4**	180/ 451.6	161/ 320.4	**L8**	179/ 443.5	157/ 298.1	**L12**	175/ 412.6	153/ 277.3	**L16**	173/ 398.0	146/ 244.4	**L20**	174/ 405.2	142/ 227.3
	R6	168/ 363.6	153/ 277.3	**R8**	175/ 412.6	159/ 309.1	**10**	172/ 390.8	159/ 309.1	**R15**	168/ 363.6	144/ 235.7	**R16**	142/ 227.3	143/ 231.5
ICP	**L4**	194/ 581.5	145/ 240.0	**L7**	166/ 350.7	135/ 200.3	**L12**	146/ 244.4	126/ 170.3	**L16**	140/ 219.3	118/ 147.4	**L20**	117/ 144.7	115/ 139.6
	R8	196/ 602.9	165/ 344.4	**R11**	169/ 370.2	141/ 223.3	**R14**	166/ 350.7	139/ 215	**R18**	156/ 292.8	124/ 164.2	**R20**	129/ 179.8	117/ 144.7
ICS	**L4**	187/ 512.5	173/ 398.0	**L8**	177/ 427.8	157/ 298.1	**L12**	175/ 412.6	162/ 326.3	**L16**	188/ 521.8	175/ 412.6	**L18**	179/ 443.5	167/ 357.1
	R5	186/ 432.6	165/ 282.7	**R7**	169/ 306.5	168/ 300.4	**R12**	197/ 540.5	185/ 423.9	**R17**	205/ 635.6	188/ 450.5	**R19**	197/ 540.5	180/ 383.1

Table 2: Pitch-matched electrode pairs. Summary of pitch-matched electrode pairs for all listeners. Also shown are comfortable (C) levels in current units (CUs) for each electrode and microamperes (see Cochlear Ltd., 2006 for details on how CUs are converted). These are loudness-balanced CUs that were determined for all mixed rate multi-electrode configurations.

Estimated bias(c) and goodness-of-fit (D)														
	High5		**Apex1**		**Mid1**		**Base1**		**Apex3**		**Spread3**		**Low5**	
Listener ID	***c***	***D***	***c***	***D***	***c***	***D***	***c***	***D***	***c***	***D***	***c***	***D***	***c***	***D***
IBF	0.11	5.1	0.42	1.7	0.22	0.2	-0.55	1.2	0.45	1.3	0.42	0.3	-0.26	2.5
IBK	0.46	3.1	0.37	1.8	0.06	2.6	0.03	1.1	-0.1	2.8	0.07	2.8	0.20	6.0
IBQ	0.51	-	0.4	1.3	0.27	5.0	-0.05	5.4	0.23	0.5	0.35	2.2	-0.04	0.9
IBY	0.36	3.1	0.28	0.6	0.2	3.1	-0.08	0.5	-0.08	7.0	0.15	10.1	0.43	6.8
ICB	-0.05	5.9	0.74	5.1	0.31	4.6	0.25	4.4	0.25	3.3	0.12	0.6	0.58	3.9
ICD	0.52	1.1	0.79	1.6	1.6	2.6	0.11	0.7	0.24	2.5	0.01	8.0	0.37	1.4
ICI	-0.16	-	0.13	-	-0.23	2.9	0.09	2.4	-0.38	3.6	-0.16	1.3	0.07	1.0
ICJ	-0.17	-	0.46	8.6	0.86	4.7	0.95	3.1	0.62	3.1	0.06	4.6	-0.29	1.7
ICP	-0.21	0.7	-0.13	-	-0.09	2.6	0.19	0.2	0.16	2.0	0.1	1.2	0.01	2.4
ICS	0.27	2.0	0.48	2.7	0.25	3.4	0.08	1.1	0.26	1.9	0.55	3.1	0.38	1.2

Table 3: Estimated bias and goodness of fit. The criterion location, c, for estimating bias is shown, along with the deviance value, D, indicating goodness-of-fit of the psychometric functions. D is the log-likelihood that a saturated model (a model with no residual errors between the fit and the real data) and the best-fit model are different. For some conditions, the deviance was not estimated because a threshold was not measured. This is indicated by a dash.

	ITD thresholds (μs)						
Listener ID	**High5**	**Apex1**	**Mid1**	**Base1**	**Apex3**	**Spread3**	**Low5**
IBF	98	273	27	65	77	48	40
IBK	219	77	35	52	44	56	63
IBQ	-	273	149	120	90	230	156
IBY	725	118	55	75	75	59	129
ICB	1029	731	143	39	252	65	40
ICD	164	163	60	47	49	37	73
ICI	-	-	880	228	178	258	206
ICJ	-	1613	671	942	302	163	455
ICP	945	-	220	411	166	253	929
ICS	818	428	177	300	141	112	368
Mean	**571**	**460**	**242**	**228**	**137**	**128**	**246**
Median	**882**	**351**	**146**	**97**	**116**	**88**	**143**

Table 4: ITD JNDs for all listeners under all seven configurations. Missing values indicate JNDs that could not be determined.

	High5	Low5	Apex1	Mid1	Base1	Apex3	Spread3
High5	0	0.63	0.30	0.63	0.47	0.63	0.60
Low5	0	0	0.56	0.10	0.03	0.35	0.17
Apex1	0	0	0.00	0.63	0.60	0.63	0.40
Mid1	0	0	0	0	0.26	0.15	0.15
Base1	0	0	0	0	0	0.25	0.13
Apex3	0	0	0	0	0	0	0.03

Table 5: Effect sizes for pairwise comparisons of all configurations.

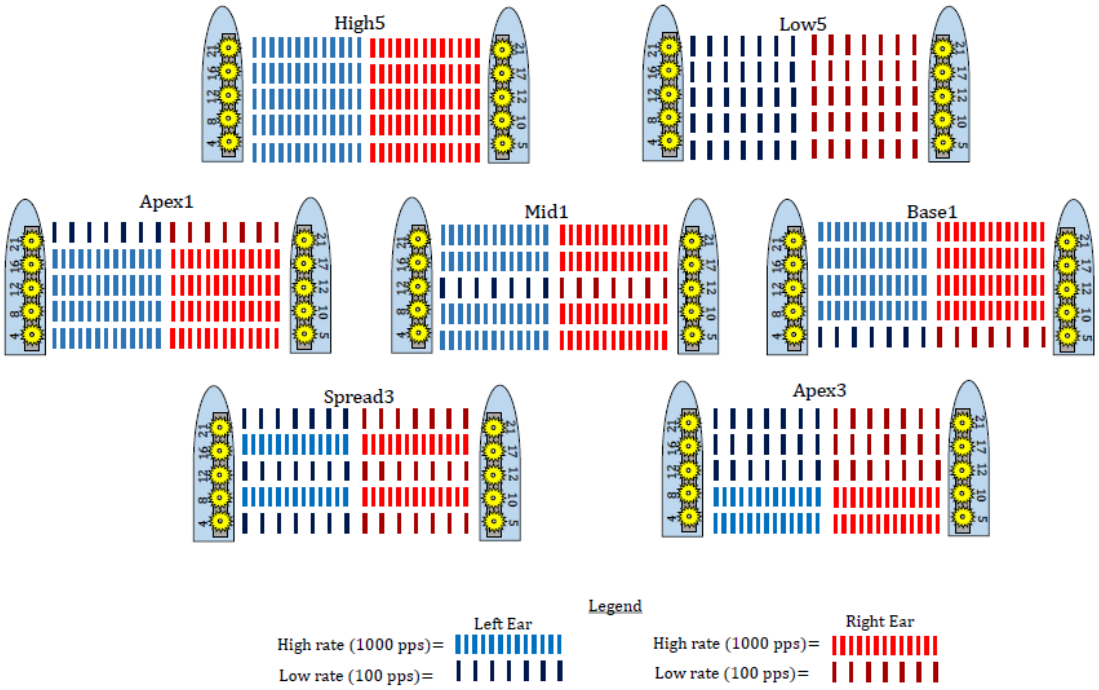

Figure 1: A schematic depicting the seven testing configurations used in the study. Using listener IBF as an example, the multi-electrode configurations reflect their pitch-matched electrodes of a Cochlear array, where lower numbered electrodes (i.e. electrode 4) are basal and higher numbered electrodes (i.e. electrode 21) are apical. The label for each testing configuration is listed above each configuration. The legend below shows the light blue and light red pulse trains as the high rate stimulus (1000 pps) and the dark blue and dark red pulse trains as the low rate stimulus (100 pps).

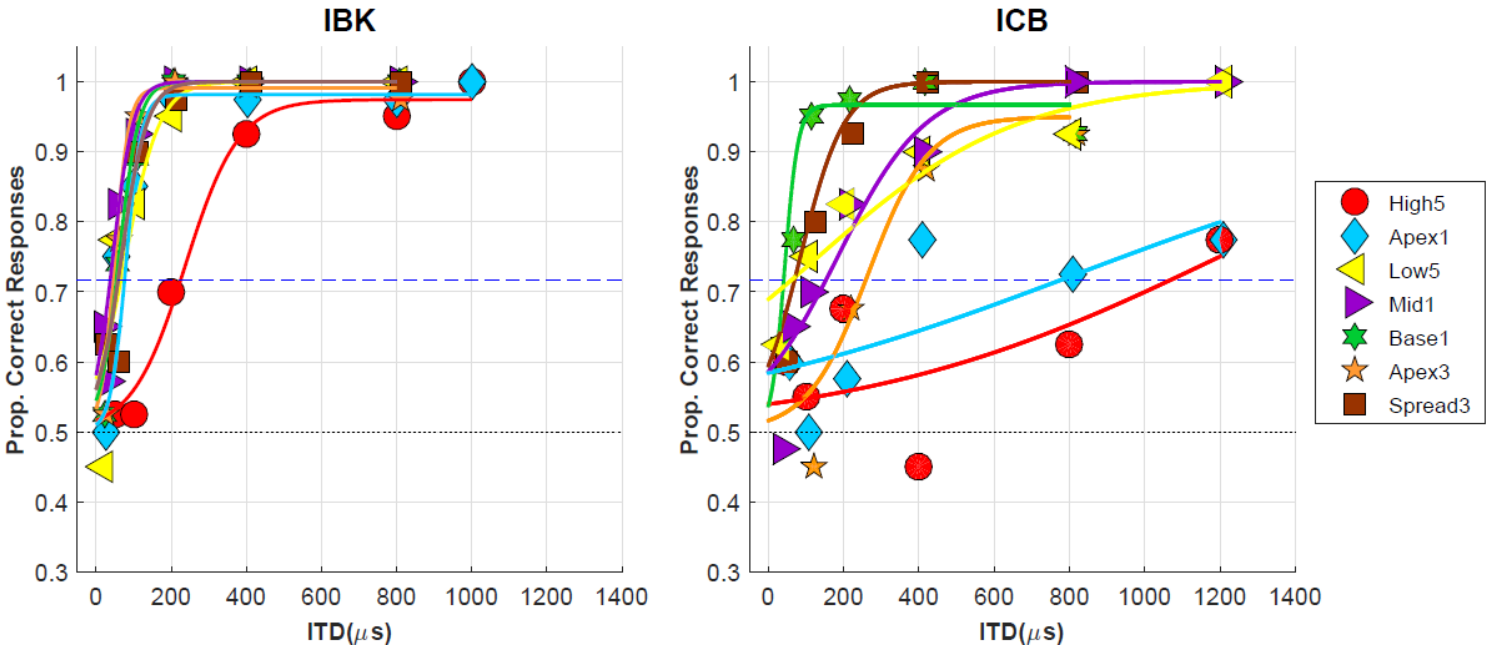

Figure 2: Shown are psychometric functions for two listeners (IBK and ICB) in all tested configurations. Proportion correct is plotted as a function of ITD (μs) and the model fits for each tested configuration are shown in different colors. The dashed blue line denotes the 70.7% mark and the dotted black line denotes the 50% mark.

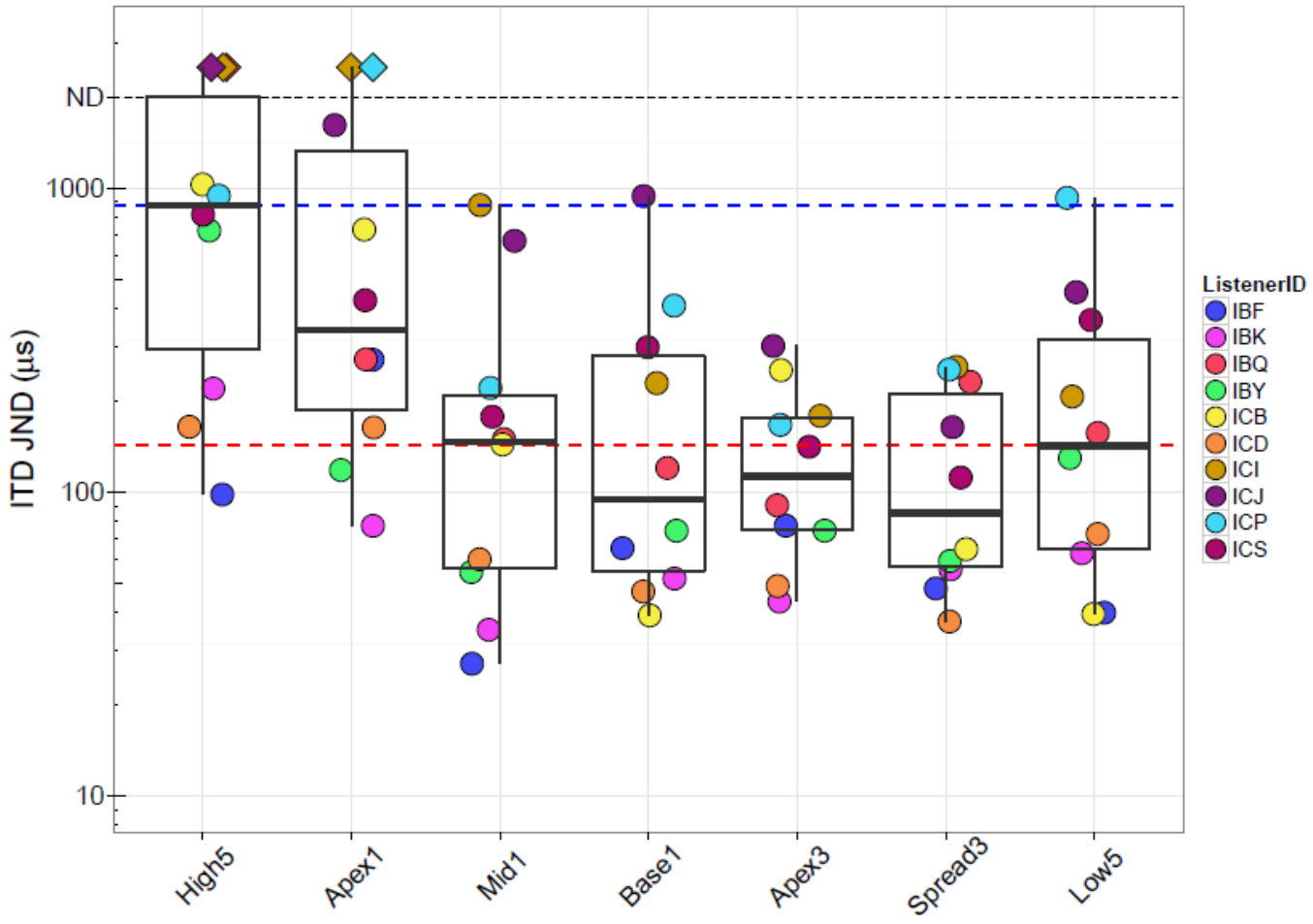

Figure 3: ITD JNDs (in microseconds) per listener and per condition. The five mixed-rate configurations are ordered from worst to best average ITD sensitivity, while the High5 and Low5 configurations are placed at the left and right ends, respectively. Each filled-circle depicts a different listener. Box plots are overlaid on the individual points to show distribution of data. JNDs are plotted on a logarithmic scale to better illustrate the range of performance. The dotted blue line illustrates the median value for the High5 configuration and the dotted red line illustrates the median value for the Low5 configuration. Listeners with diamond symbols are plotted as "ND" to show JNDs that were not determined.

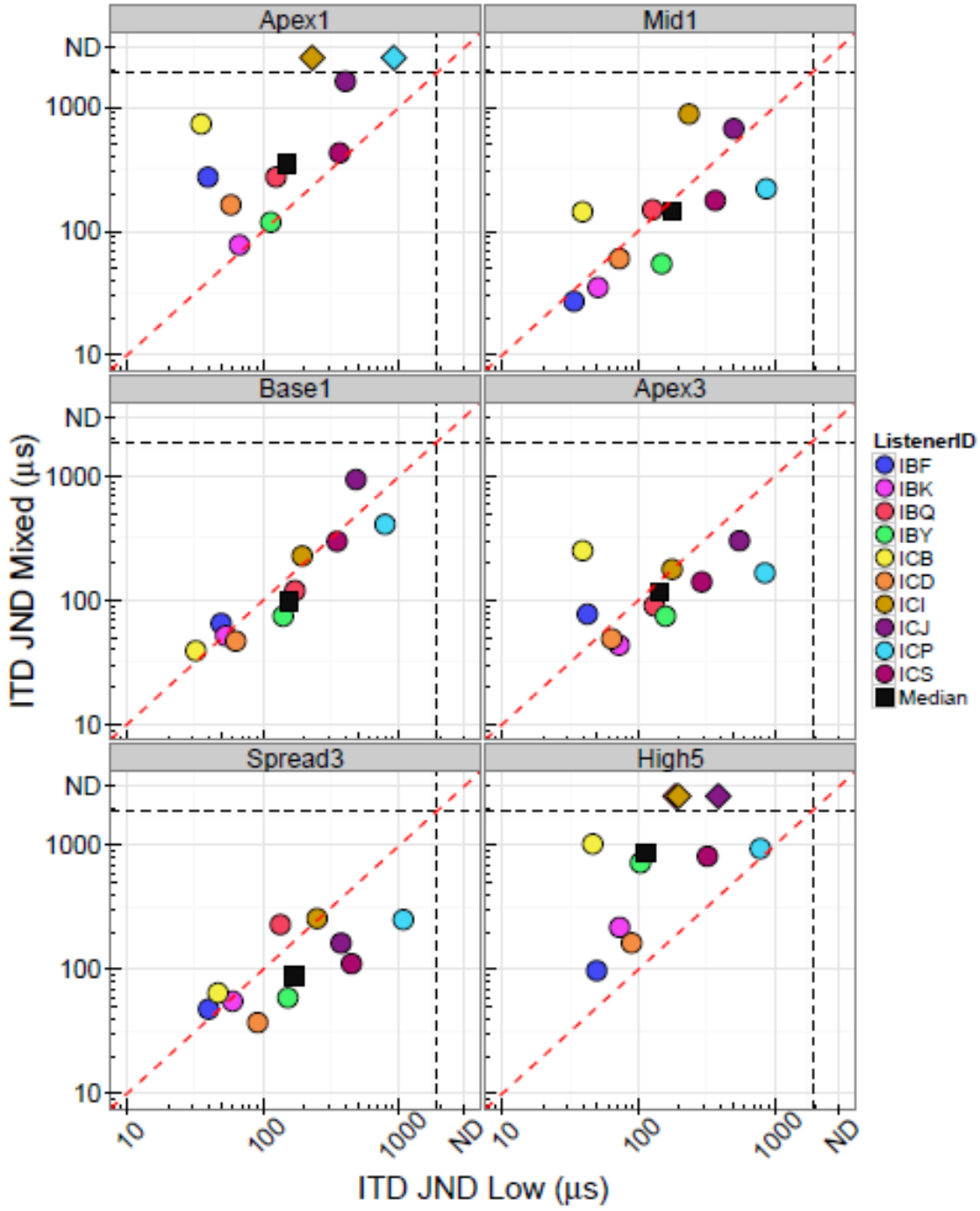

Figure 4: ITD JND comparison plots. Each mixed-rate JND (y-axis) is plotted as a function of the Low5 JND (x-axis). The diagonal represents the line of unity, where JNDs are identical in the two conditions plotted. Points that fall below the line depict JNDs in the mixed-rate configuration were better than the Low5 configuration, and points that fall above the dotted line depict JNDs that were worse compared with the Low5 configuration. JNDs are plotted on a logarithmic scale. Listeners with diamond symbols are plotted as “ND” (Not Determined).

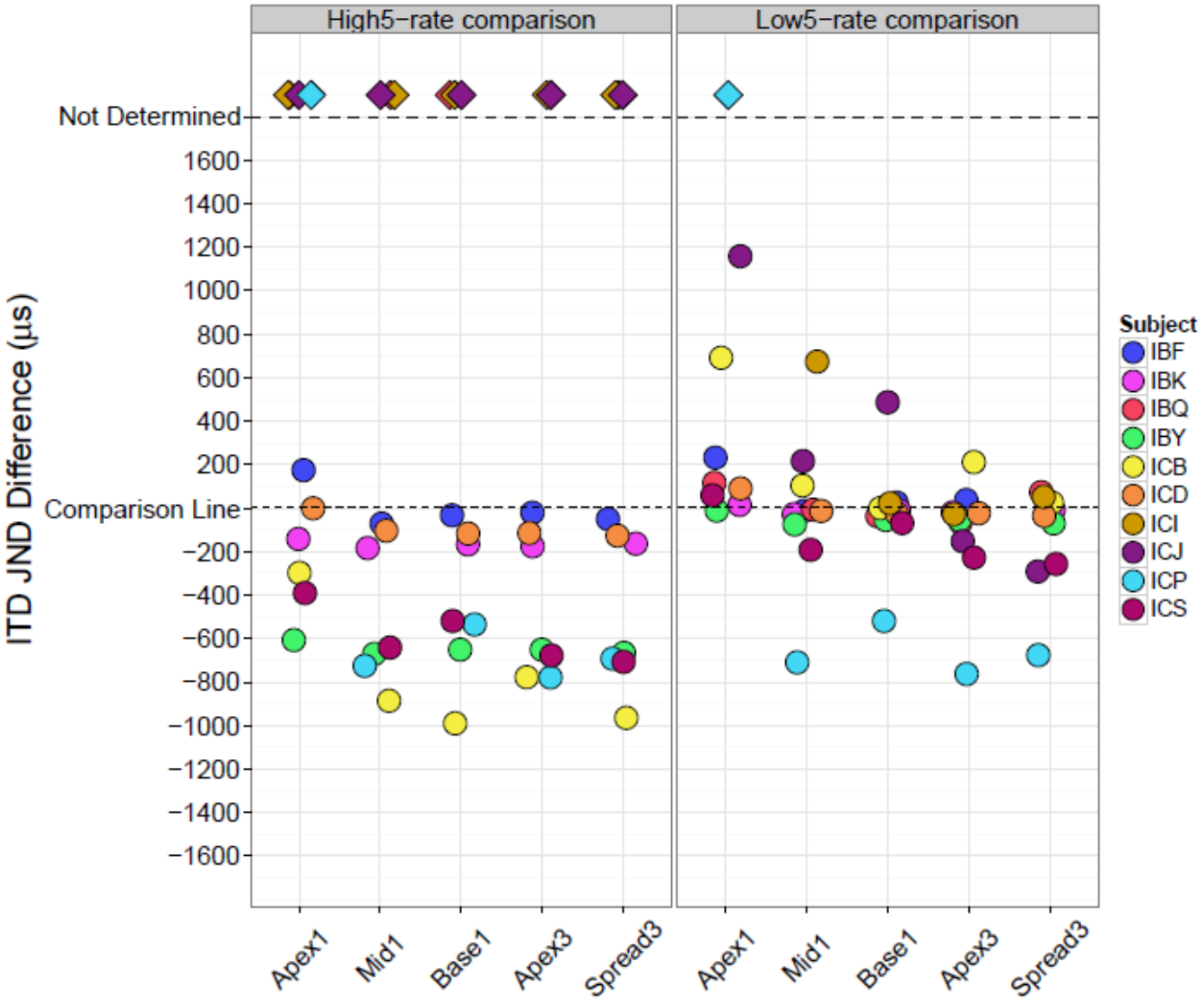

Figure 5: ITD JND *difference* values on a linear scale. Panel a) shows a comparison of each of the mixed-rate JNDs to the High5 JND, and panel b) shows a comparison of each of the mixed-rate JNDs to the Low5 JND. The dashed horizontal line is the line of unity, or point of comparison, whereby JNDs in the two conditions would be equal. Positive values depict cases in which ITD sensitivity in a mixed-rate condition is higher (worse) than in the High5 or Low5 conditions. Conversely, negative values depict cases in which ITD sensitivity in a mixed-rate condition is lower (better) than in the High5 or Low5 conditions. Differences where a JND was "Not Determined" is shown by a diamond symbol.

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CHAPTER III: Lateralization of interaural time differences using mixed rates of stimulation in bilateral cochlear implant listeners

I. Abstract:

Bilateral cochlear implants (BiCIs) result in improved spatial hearing compared with unilateral implants. However, spatial hearing is worse than in normal-hearing listeners. One problem is that clinical processors deliver stimulation at high rates to represent speech envelope cues accurately, but at high rates interaural time difference (ITDs) cues are unusable. Ideally, both high and low rates would be available in BiCIs. To overcome this dilemma, here we implemented a stimulation approach that delivers different stimulation rates to different electrodes. Using research processors, electrical pulse trains were presented to five pitch-matched pairs of electrodes; ITDs ranged from 100-1000 μs. Stimulation rates were either uniformly high-only, low-only or mixed such that some electrodes had high and others had low rates. Perceived intracranial lateralization was measured in eight post-lingually deafened adults. Range of lateralization was calculated as an index of appropriate ITD-to-azimuth mapping. The largest ranges were seen in low-rate only conditions. The high-rate only condition yielded smallest ranges and mixed-rate configurations varied with number and cochlear location of low-rate stimulation. All listeners but one perceived a single coherent auditory object. These results suggest that mixed rates have the potential to convey ITDs and to produce coherently-perceived azimuthal locations.

II. Introduction

In listeners with normal hearing (NH), binaural hearing allows individuals to localize sound sources in the horizontal plane and improves speech understanding in the presence of interfering sounds. Spatial cues result from differences in the time of arrival and intensity of sounds between the ears, and these cues change with the horizontal location of a sound relative to the listener's head. Two significant spatial cues are interaural level differences (ILDs), and interaural time differences (ITDs), both of which are frequency-dependent such that listeners are most sensitive to ILDs at high frequencies and ITDs at low frequencies (Macpherson and Middlebrooks, 2002; Middlebrooks et al., 1989; Mills, 1959; Wightman and Kistler, 1992). Humans are also sensitive to ITDs in high-frequency stimuli that are modulated by a low-frequency envelope (Henning, 1974; Middlebrooks and Green, 1990).

In contrast with NH listeners, patients with bilateral cochlear implants (BiCI) do not receive the same benefits of binaural hearing, and are thought to only rely on ILD cues when locating sound sources (Aronoff et al., 2010; Grantham et al., 2007). There are many reasons why these limitations exist. First, when listening through clinical processors, BiCIs do not have access to ITDs for low-frequency signals, known as temporal-fine-structure ITD cues. In several clinical devices currently used, the envelope-extraction process in cochlear implants and use of high-rate pulsatile stimulation (≥900 pulses per second), obliterates low-frequency ITDs (for review see van Hoesel and Tyler, 2003; Kan and Litovsky, 2015). Second, patients may have poor neural survival in one or both ears which can result in a binaural asymmetry, leading to poor encoding of ITDs (Ihlefeld et al., 2015). Third, there is a lack of surgical precision to ensure that electrode arrays in the two ears excite the same neural populations with the same frequency content. Although surgeons try to match the insertion depths in the two ears, small differences

across the ears are relatively common (Pearl et al., 2014). Insertion depth differences can lead to a mismatch in the place-of-stimulation across the ears which has been shown to decrease sensitivity to ITD and ILD cues (Goupell et al., 2013; Kan et al., 2013, 2015b). Finally, there is also a lack of interaural synchronization of the clinical processors in the two ears (Kan et al., 2018)

Because one of the primary device limitations is that clinical processors primarily use high-rate pulsatile stimulation, this creates little opportunity to capture ITDs in the temporal fine structure of the signal (Jones et al., 2014; Laback et al., 2004), reducing sensitivity to ITDs (Majdak et al., 2006). NH listeners, presented with pure tones can exhibit ITD thresholds ranging roughly from 10-75 μs (Bernstein and Trahiotis, 2002; Klumpp and Eady, 1956; Zwislocki and Feldman, 1956). ITD sensitivity for BiCI for patients with adult-onset of deafness ranges from 50-1000 μs when presented with very low rates of stimulation (~100-300 pulses per second, pps) through the research processors (van Hoesel, 2008; van Hoesel et al., 2009; Kan and Litovsky, 2015). Clinically-used strategies that relay fine structure information should attempt to relay ITD information, such as Med-El's FS4 strategy. However, this strategy has not shown meaningful improvements in ITD sensitivity in BiCI listeners (Hochmair et al., 2006). When compared to a constant high rate strategy (HDCIS), performance in the FS4 strategy yielded minimal improvements in ITD sensitivity (Zirn et al., 2016).

Previous work in our lab has sought to overcome the limitations of current clinical processors by selectively stimulating bilateral pairs of electrodes with ITDs (van Hoesel and Tyler, 2003; Kan and Litovsky, 2015; Laback et al., 2007, 2015; Litovsky et al., 2009). One such strategy, the "peak-derived timing" (PDT) strategy, (van Hoesel, 2007) used mixed rates of stimulation in order to encode fine-timed ITDs and better encode envelope ITDs. However, the

benefits of this approach in binaural tasks have not been shown yet (van Hoesel and Tyler, 2003). Churchill et al. (2014) implemented a "temporal fine structure strategy," or TFS, where BiCI listeners showed a significant improvement in ITD sensitivity with a mixed-rate strategy, compared to a high–rate only approach. Finally, Thakkar et al. (2018) presented low rates of stimulation to five binaural electrode pairs, along with high rates of stimulation at other electrodes pairs. This study suggested that presenting a single electrode with low rates while the remaining electrodes received high rates improved ITD sensitivity, comparable to having low rates only presented across the electrode array. Listeners with BiCIs were able to extract ITDs from the electrode pairs carrying low rates. Each listener's ITD discrimination thresholds were similar to the thresholds obtained when all five electrode pairs had only low rates.

Thakkar et al. (2018) suggested that multi-electrode, mixed-rate stimulation approaches could yield reasonable binaural sensitivity to ITDs in a discrimination task. Additionally, stimulation of low rates in the apical region of the array were the least effective region to stimulate with low rates. However, discrimination tasks only measure the smallest change in a cue needed to perceive a difference. Discrimination tasks do not provide information about a listeners' use of the cue to directly identify the perceived spatial location of a sound source. Here, we extended the investigation of multi-electrode, mixed-rate stimulation to a psychophysical task that focuses on the perception of auditory location (lateralization), which is more directly related to spatial hearing in real-world situations.

The novelty in this study is that it measures BiCI listeners' judgements about where the sound is perceived intracranially in the horizontal plane, rather than discriminating binaural cues in a mixed-rate stimulus. Perceived intracranial lateralization was used to study functional utility of the ITD cue, by observing how well the physical ITD cue is mapped to a perceived location in

the head. Previous studies in our lab have found this task to be effective for examining a range of lateralization across listeners (Kan et al., 2013, 2015b, 2016). Here, we measured intracranial judgments in location as a function of ITD. We conducted an experimental paradigm aimed at evaluating the extent of perceived laterality for each listener. The work in this study describes the impact of presenting a combination of low and high rates of stimulation across the electrode array on the extent of lateralization and mapping of perceived locations to an ITD cue.

Previous work in our lab using a lateralization task has only assessed listeners' ability to use multiple pairs of electrodes, with low-rate stimulation, not with mixed rates. Those studies found that BiCI listeners were able to detect and use ITD cues with a full range of lateralization and to map physical ITDs to left-right perceptual space (Kan et al., 2016). Appropriate mapping of ITDs is crucial because our goal is two-fold; listeners should be able to not only detect an ITD, but also identify the source's location accurately when multiple sources of speech are present in the environment. Due to the nature of the stimulus, it is unknown whether multi-electrode mixed rates may introduce distortions and ultimately cause the perception of multiple objects. The consequence of perceiving multiple objects is that this can undo the advantages of the multi-electrode mixed rate strategy. This type of distortion can hinder the ability of a listener to associate the ITD cue with its respective speech information and form the perception of a unitary object (McDonald and Alain, 2005).

Using a discrimination task to quantify whether listeners perceive a fused auditory object verses multiple objects can be challenging because BiCI listeners tend to use the information in the most dominant electrode pair, while ignoring information from other electrodes (Ihlefeld et al., 2014). In contrast, the lateralization task can capture the extent to which binaural cues result in a perceptually fused auditory image (Kan et al., 2013). Lateralization tasks also allow us to

capture the range of ITDs that a listener can perceive. Lateralization tasks can thus provide an estimate of whether mixed-rated stimulation is functionally relevant or interferes with auditory object formation.

The utility of an ITD cue is better understood when asking a listener to make more complex judgments regarding the identification of the sound source, such as determining its coherency or identifying its actual location. A key finding in Thakkar et al. (2018) was that sensitivity to a low-rate ITD in a mixed-rate stimulus is variable across the electrode array. Therefore, it is essential to determine the impact of variable sensitivity on fusion and lateralization of across-frequency components. Additional auditory objects perceived from multi-electrode stimulation have the potential to interfere with the ability to lateralize the ITD cue. The objective of the present study was to understand the functional utility of mixed-rate ITD cues presented at multiple places of stimulation along the electrode array. A large range of ITD laterality and presence of auditory object formation (i.e., the perception of single auditory objects) suggests a one-to-one mapping of the ITD cues to the auditory space, ultimately providing more evidence for the benefits of mixed rates of stimulation. Based on our previous data using mixed-rate ITDs, we hypothesized that the presence of at least one low-rate electrode will promote improved lateralization ranges and would not be detrimental to object formation.

III. Methods:

A. Subjects

Eight postlingually-deafened BiCI listeners with demonstrated sensitivity to ITDs from prior studies participated in this experiment. Listeners traveled to the University of Wisconsin-Madison for 3-5 days for testing and were paid a stipend for their participation. Listener demographics are displayed in Table I. All listeners had Cochlear Ltd (Sydney, Australia)

implants (CI24 and CI512 family of implants). These devices have 24-electrodes (22 intra-cochlear and two ground electrodes), with approximately 0.75 mm center-to-center inter-electrode spacing. Electrodes are numbered such that 22 is the apical-most electrode and 1 is the basal-most electrode. All experimental procedures followed the regulations set by the National Institutes of Health and were approved by the University of Wisconsin's Human Subject Institutional Review Board.

B. Stimuli

Stimuli were delivered using one of two research platforms: bilaterally-synchronized Lara34 research processors or an RF GeneratorXS interfaced with MATLAB (Mathworks, Natick, MA). Custom-written MATLAB software was used to generate the stimuli and communication with the research platform was through the Nucleus Implant Communicator (NIC) libraries (version 2 for Lara34s, version 3 for RF Generator). Stimuli were checked using an oscilloscope before beginning experiments. Listeners responded to stimuli on a touchscreen monitor connected to the same computer. All stimuli were 300-ms duration constant amplitude pulse trains presented via monopolar stimulation. Each pulse had a 25-μs phase duration (except for listener ICP who required a phase duration of 75 μs) and 8-μs phase gap. The study focused on presenting stimuli to five electrodes in each ear and varying the stimulation rates; see below for details.

Before testing with multi-electrode stimulation, each listener was tested to identify five pairs of electrodes across the ears that were pitch-matched. These five pairs of electrodes had also been selected in prior studies by the authors in order to measure ITD sensitivity (Kan et al., 2015a; Thakkar et al., 2018). Pitch matching is a proxy for frequency-matched inputs to the binaural system which can result in reasonably good ITD sensitivity (Kan et al., 2015b; Litovsky

et al., 2010). Other approaches such as the “binaural interaction component” may also be as successful for matching the place of stimulation across the ears (Haywood et al., 2015; Hu and Dietz, 2015). However, pitch-matching was selected in order to be consistent with our prior work.

Pitch matched electrodes were identified on an across-ear bilateral pair where on average, the same perceived pitch was selected by the listener in a left-ear electrode as the perceived pitch in a right-ear electrode. Generally, the left ear electrode was held constant and the right ear electrode was tested with the estimated pitch-matched electrode and neighboring electrodes (± 2 electrodes) in a two-interval, five-alternative forced choice task. Each of these pairs were presented with constant amplitude electrical pulse trains of equally-loud current levels at a stimulation rate of 100 pps with a duration of 300 ms across two intervals, where the left ear (i.e. the reference ear) was played first and the right ear (i.e. the test ear) stimulus was played second. On each trial, listeners were asked to compare the perceived pitch in the two ears directly. They responded by answering whether the sound in the second interval was “much higher,” “higher,” “same,” “lower,” or “much lower” in pitch compared to the first sound. The pair with the highest proportion of responses reported as “same” were selected as the pitch-matched pair. We selected five pairs of pitch matched electrodes distributed along most or all of the electrode arrays, at the following locations: base, mid-base, mid, mid-apex, and apex.

Using the five pitch-matched electrode pairs, we created seven multi-electrode, mixed rate configurations (see Figure 1). Two of these configurations had a uniform rate across all five electrodes; “High5” presented 1000 pps on all electrodes and “Low5” presented 100 pps on all electrodes. Three other configurations had 1000 pps on four electrode pairs, with the low-rate 100 pps presented at either the apex, middle, or base (configurations labeled “Apex1”, “Mid1,”

and “Base1,” respectively). Two other configurations had low rates at three electrode pairs, either the three apical-most or spread across the array (configurations labeled “Apex3,” and “Spread3,” respectively), with the remaining two electrode pairs at 1000 pps.

We created mixed-rate loudness maps to ensure that maps for all configurations elicited equal loudness and a centered image of the auditory percept. This was done by systematically introducing 100 pps stimulation on one electrode at a time, and balancing the loudness of the mixed-rate multi-electrode stimulus to match that of the “High5” multi-electrode stimulus. The loudness map defines the range of current units that generates an audible percept between threshold (T) and most comfortable (M) loudness levels at each electrode. Within this range, the experimenter measured a comfortable (C) level, which we defined as the stimulation level that the listener is willing to be tested at for an extended period. Electrodes were loudness-balanced in three steps. First, the experimenter stimulated the electrodes one at a time with an inter-stimulus interval of 100 ms, while the listener reported which stimuli were louder (only C-levels at the 100 pps electrodes were adjusted). Second, the experimenter balanced loudness bilaterally by presenting the C-level sequentially from left to right, then simultaneously on both left and right. The levels were then adjusted in either ear incrementally until listeners perceived a centered auditory image. Finally, we adjusted C-level across all configurations so that mixed-rate multi-electrode maps would have loudness perception matched to the loudness elicited with the “High5” multi-electrode stimulus. Note also that testing with five pairs of electrodes required temporal staggering of stimulation along each electrode array. Nucleus implants are unable to stimulate simultaneously when playing multiple electrodes at a time. Therefore, electrodes were stimulated sequentially in an apical-to-basal order.

C. Task

Listeners pointed to a perceived intracranial location on an image of a face on a computer monitor and used a visual icon in order to indicate the perceived location of the stimulus on each trial. If listeners perceived multiple auditory objects, listeners selected whether they perceived one, two, or sound sources and additional response bars on the image would appear corresponding to the source number. Listeners then indicated on each horizontal bar with a location for each sound source, ranking the source from most- to least-dominant. The term 'dominance' was selected to reflect the most robust, easily heard and localized auditory image. However, the number of perceived auditory objects was optional, if only one sound was perceived then only a single horizontal bar would appear. On each trial, listeners could repeat the sound as many times as they wished, but listeners typically only selected one or two repetitions. The task was a single-interval task, and a method of constant stimuli was used to test ITDs of 100, 200, 400, and 800 μs in all listeners. In some instances, we included larger ITDs to elicit a complete range of lateralization.

For each of the seven configurations described above, each ITD magnitude was repeated 40 times, with half the trials left-leading, and the other half right-leading. The different configuration types were pseudorandomized, and each configuration occurred in different blocks from the others. For example, block one could have five repetitions of all ITDs for the Low5 configuration and block two could have five repetitions of all ITDs for the Apex3 configuration. This method of pseudo-randomization continued until all seven configurations were tested at 40 repetitions for each ITD.

D. Data analysis

To quantify the range of perceived lateral locations from listeners' responses, we assigned values to the responses with 0 being the far left, 0.5 being the center, and 1 being the far right. We calculated lateralization functions using methods identical to Kan et al. (2016). Responses were fit with a three-parameter logistic function (see Eq. 1).

Equation (1):

$$p(ITD) = \frac{L_m}{1 + e^{-m(ITD-shift)}}$$

Where *m* represents the steepness of the function, the shift represents the bias, and L_m is the maximum value of the function, which is set to 1. The range is an estimate derived from Eq. 1 and provides an approximation of the perceptual range of the auditory object with each physiologically relevant ITD values. Overall, a narrower range of perceived lateralization indicates a weaker ability to map ITDs to lateralized positions.

IV. Results:

Lateralization functions for all listeners, for each stimulus configuration (High5, Low5, Apex1, Mid1, Base1, Spread3, and Apex3) are shown in Figure 2. In each panel, perceived intracranial lateral location is plotted for each ITD value. The gray line in each panel depicts the mean perceived location, and the solid colored line depicts the model fit. The right-most column shows perceived lateralization in response to a configuration with low rates only. Of the eight listeners, only one listener (IBK) perceived more than one auditory object in some of the conditions, primarily mixed-rate conditions. The predominance of the secondary auditory object

for listener IBK was typically low (percent reported as a secondary object in each configuration for listener IBK, Apex1: 10.5%; Apex3: 5.4%; Spread3: 1.3%; Low5: 13%). Results from five listeners (IBF, IBY, ICB, ICP, and IBK) exhibited a sigmoidal shape. A range of "full" left-to-right lateralization was achieved for listeners ICP, ICI, ICB, IBK, and IBF.

The High5 and Apex1 configurations both elicited the smallest lateralization ranges, while the remaining configurations elicited larger lateralization ranges. Figure 3 shows the ranges calculated from the logistic function (using Eq. 1) for each tested configuration. Range of lateralization was calculated using the upper and lower bounds of the estimated function in Eq. 1.

Using a Friedman's test with multiple comparisons and Bonferroni correction, lateralization ranges across all listeners yielded a significant difference, $\chi 2(6) = 22.43$, $p < 0.001$. However, effect sizes revealed that only the Base1 and Apex3 configuration proved to be significantly different from the High5 configuration. Effect sizes for all comparisons between groups are shown in Table 1. Using Cohen's scale for effect sizes, meaningful effect sizes were determined using the following scale: r= 0.10 (small effect, explains 1% of the total variance), r = .30 (medium effect, accounts for 9% of the total variance), and r = .50 (large effect, accounts for 25% of the variance).

Figure 4 shows a comparison of the normalized lateralization range of the High5 configuration on the x-axis, range of the remaining configurations are shown on the y-axis. The dotted red line illustrates the line of equivalence; if the data points fall on this line the extent of lateral range in both configurations are identical. This analysis aimed to determine whether, compared with the High5 condition, adding low-rate channels resulted in an increased lateralization range. Five of the six panels show that listeners exhibited an increased

lateralization range, specifically the Low5, Mid1, Base1, Apex3, and Spread3 configurations, all mean ranks in these conditions were significantly different from the High5 condition.

Posthoc Wilcoxon signed-rank tests revealed that means ranks of each condition, ordered from smallest to largest, were: 1.167 (High5), 2 (Low5), 4.5 (Spread3), 4.67 (Apex1), 4.83 (Mid1), 5.33 (Base1), 5.5 (Apex3). This effect suggests that mixed-rate configurations are sufficient for yielding generally broad perceived lateralization ranges for ITDs. In one configuration (Apex1) listeners did not show increased range of lateralization compared with High5. Listeners ICI and ICP showed little or no improvement in their lateralization ranges compared to High5. In comparing the medians, we see that the High5 configuration results in a range of 0.16, notably smaller than the Low5 range which is 0.71. This reduced range of lateralization is reflected in Table I, where the effect size comparing these two configurations was 0.492 (a medium to large effect). This effect is important to highlight because the remaining mixed-rate configurations, apart from Apex1 (r=0.445), yielded very little differences in lateralization ranges compared to the Low5 configuration (effect sizes when compared to the Low5 configuration were: Base1 (r= 0.023), Mid1 (r=0.352), Apex3 (r=0.211), Spread3 (r=0.352), resulting in small- to-medium effects.

V. Discussion:

Our results showed that the majority of subjects reported perceiving a single auditory object, and that, compared to stimulus configurations that had high-only rates, lateralization performance was better with configurations that had either mixed rates or low rates only. High stimulation rates are thought to be important for representing the speech envelope (Loizou et al., 2000; Vandali et al., 2000; Wilson and Dorman, 2008). Therefore the present study aimed to determine whether good lateralization could be achieved with mixed-rate stimulation compared

to high-rate only stimulation. We showed that object formation was sustained and that lateralization ranges increased when low-rate stimulation was introduced at either the basal electrode pair, middle electrode pair, or spread across the electrode array. Even though the configuration yielding the best performance for each listener may have been different, any one mixed-rate configuration did not lead to significantly different lateralization ranges from the Low5 configuration.

These results also suggest that coherent object formation can occur with a mixed-rate strategy despite having one or more electrodes with a sparse representation of the speech envelope. Strong auditory object formation is notable because it suggests that ITD information in the high rate channels, ideally representing the speech information, is allocated to the same perceptual object as the ITD information in the low rate channels. This means that for future studies investigating speech-in-noise with mixed rates, the speech signal and location cue have the potential to be associated together in a noisy environment.

Measurement of perceived lateralization is essential for understanding the utility of across-electrode ITDs, specifically for understanding whether the ITDs presented to multi-electrode mixed-rates would lead to a coherent auditory object and accurate lateralization. Due to poor neural health, across-channel stimulation of ITDs could have the potential to lead to conflicting cues (Jones et al., 2009), this is due to the fact that listeners exhibit individual differences regarding regions with poorer ITD sensitivity. Previous work in NH listeners has attempted to quantify the utility of across-frequency ITDs. These studies identified how listeners make decisions on the perceived location when different ITDs are combined across multiple frequency components of a fused auditory object (Woods and Colburn, 1992). Our results demonstrate that different rates of stimulation presented to five electrode pairs with ITDs, or

"mixed-rate ITDs," can be perceived as a single coherent object in a majority of listeners. This is somewhat surprising considering the considerable variability in ITD sensitivity at different places along the cochlea (van Hoesel and Clark, 1997; Litovsky et al., 2010).

We found that only listener IBK perceived a secondary object at most in 13% of their responses, but only in the Low5 configuration where there were no mixed rates present in the signal. This outcome suggests that this apparent lack of auditory object formation, or the inability to perceive a single sound source, was due to factors other than the presence of mixed rates, such as poor neural health. Further, the lateralization functions in all listeners appear to have a functional mapping of ITD to perceived laterality. A way to quantify this mapping is to observe the range of laterality across all mixed-rate configurations. Consistent with Thakkar et al. (2018), the High5 configuration yielded the worst performance across listeners and the mixed rates, apart from Apex1, yielded the best performance (see Figure 5). Additionally, we see that the apical region of the array is not the best place to present low rate information in a mixed-rate strategy.

Existing literature on the physiologically-based mechanisms of ITD processing particularly for broadband or complex sounds, shows that the response of neurons tuned to low frequencies respond to a larger range of interaural delays while neurons tuned to high frequencies respond to a small range of interaural delays (McAlpine et al., 1996). A major reason for this outcome is because the neural response to a low frequency or low rate tone is phase-locked, meaning the timing is monitored very well down to the relative phase information across the ears. Once a low frequency sound reaches the MSO, an interaural phase difference (IPD) could be used to lateralize the sound, this holds true for sounds that range multiple frequency channels. The low-rate electrical pulse train used in the current study, though does not resemble a low frequency pure tone, it does resemble a low-rate acoustic pulse train which has been shown

to relay good ITDs in NH listeners. The improved range of lateralization observed in the Base1 configuration is a clear example of how the binaural system exploits any low frequency information for extracting the ITD in the signal. Additional behavioral data also show that acuity for ITD perception further improves for broadband ITDs (Joris and Yin, 2007). The reasons for this are largely unknown, however, much of the literature suggests that when a low-frequency component, such as a pure tone or low-frequency envelope exists in a stimulus, the auditory system can exploit this so that the ITD is always accurately perceived. Taken together with the neurophysiological data, our data suggest that a multi-electrode, mixed-rate stimulus, in comparison to a high-rate only stimulus, has the potential to encode a broader range of ITDs at for BiCI listeners.

A number of behavioral studies using direct electrical stimulation have revealed two crucial pieces of information. First, BiCI listeners are sensitive to ITDs at lower rates of stimulation (100-300 pps; van Hoesel et al., 2009). Second, BiCI listeners are the least sensitive to ITDs at the apical region of the array (Kan et al., 2015a, 2016; Thakkar et al., 2018). Third, multi-electrode low-rate ITDs are sufficient to yield good lateralization while keeping object formation uninterrupted (Best et al., 2011; Egger et al., 2016; Francart et al., 2015; Kan et al., 2016). This is consistent with the results of Thakkar et al. (2018) and Kan et al. (2016), which showed that ITD sensitivity was also poorer when low-rate ITD information was confined to the apical end of the electrode array. Our work in the current study is consistent with the notion that multi-electrode stimulation keeps auditory object formation and lateralization and therefore, could have implications for good speech representation using mixed rates.

VI. Conclusions:

In this study we addressed whether using multi-electrode, mixed-rates ITD in a subjective lateralization task improves the ability to hear a full lateralized range when compared to a high-rate only ITD configuration. Our results suggest that mixed rates of stimulation yields improved lateralization and object formation when comparing a configuration with only high rates (High5) to any configuration with at least one electrode with low rate information, except for the Apex1 configuration. A comparison of these mixed-rate configurations showed that allocating the low rate ITD to the apical end of the electrode array reduces the lateral range of the auditory object. Overall, these data suggest that listeners achieved ITD lateralization with mixed rates comparable to, or better than, that of the Low5. These effects suggest that mixed rate ITDs offer a feasible way to improve ITD sensitivity for listeners without needing low rate stimulation to be presented to all electrodes.

VII. Tables and Figures

	High5	**Apex1**	**Mid1**	**Base1**	**Apex3**	**Spread3**	**Low5**
High5	0	0.3985	0.4922	0.4922	0.4922	0.4922	0.4922
Apex1	0	0	0.4922	0.4922	0.4922	0.4922	0.4454
Mid1	0	0	0	0.3516	0.1172	0.1172	0.0234
Base1	0	0	0	0	0.1641	0.0703	0.3516
Apex3	0	0	0	0	0	0.2578	0.211
Spread3	0	0	0	0	0	0	0.3516

Table I: Effect sizes for each pairwise comparison across High5, Low5, and all mixed rates configurations.

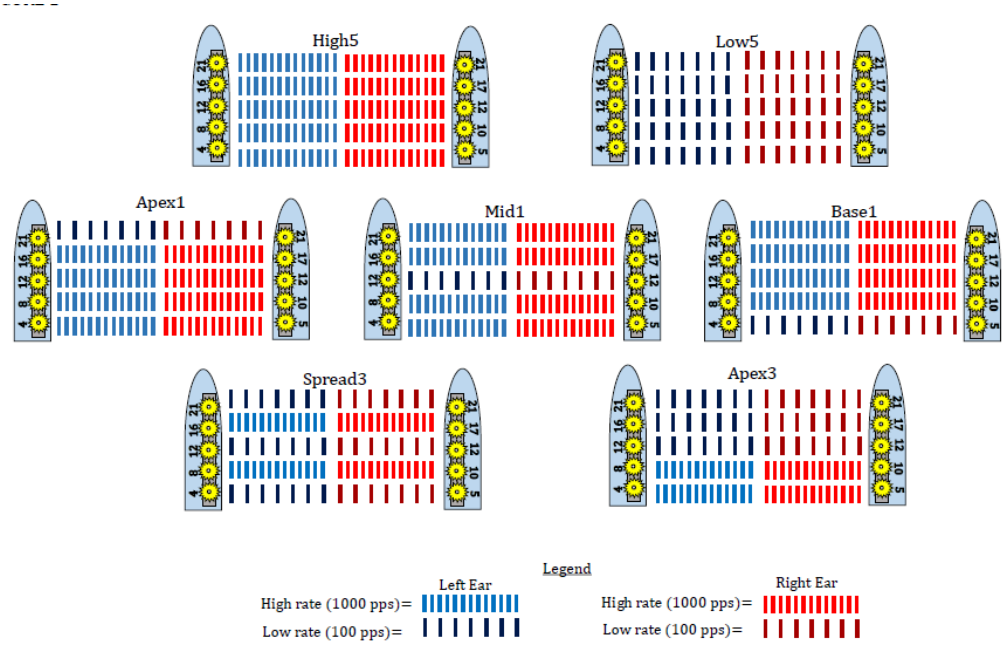

Figure 1: A schematic depicting the seven testing configurations used in the study. The multi-electrode configurations reflect their pitch-matched electrodes of a Cochlear array, where lower numbered electrodes (i.e. electrode 4) are basal and higher numbered electrodes (i.e. electrode 21) are apical. The label for each testing configuration is listed above each configuration. The legend below shows the light blue and light red pulse trains as the high rate stimulus (1000 pps) and the dark blue and dark red pulse trains as the low rate stimulus (100 pps).

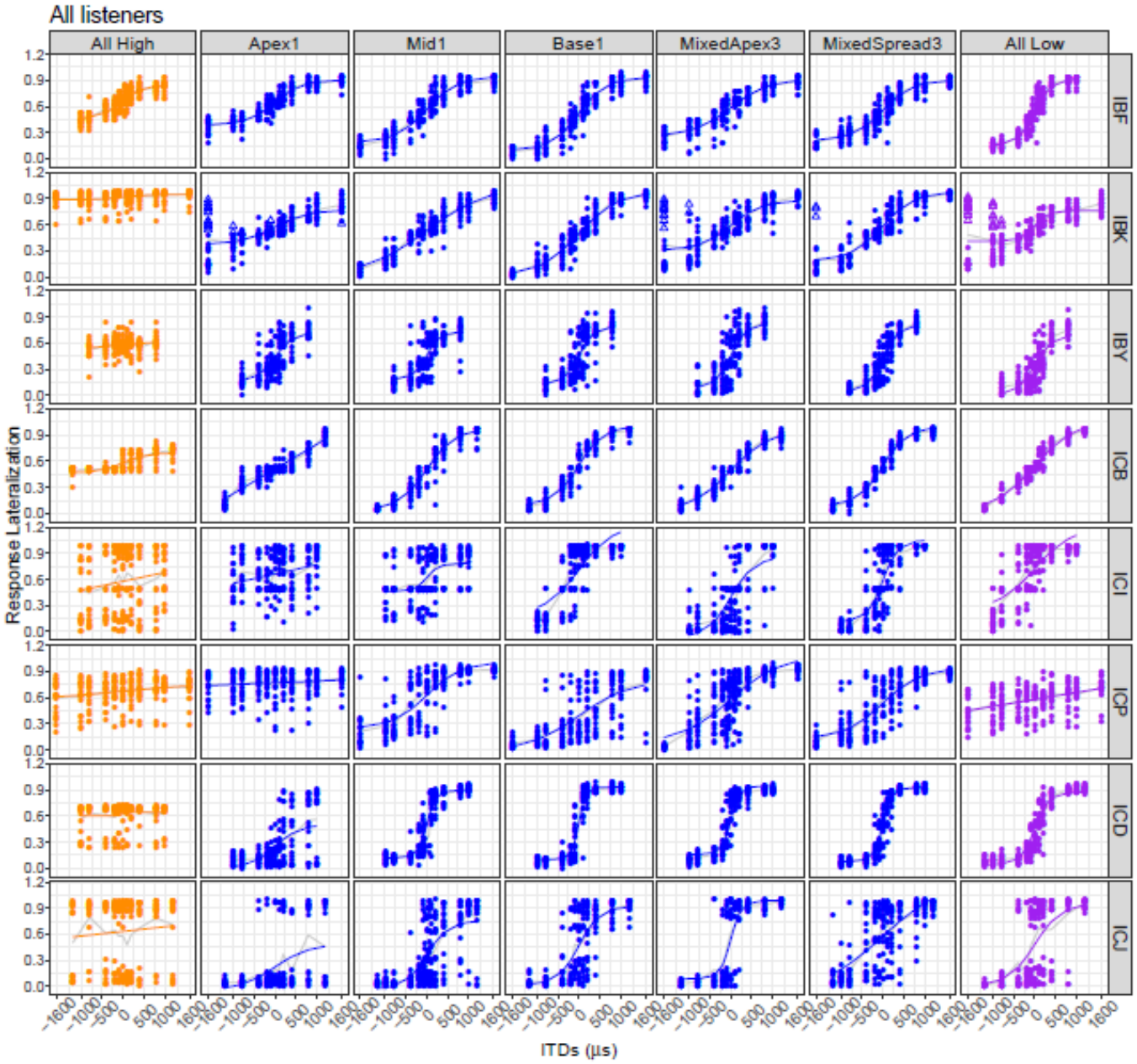

Figure 2: Response lateralization for all configurations and all listeners. Solid colored lines represent the model fit and the solid grey lines represent average lateralization response for each ITD. Responses are mapped to values 0 to 1, with 0 representing “far-left” and 1 representing “far-right.”

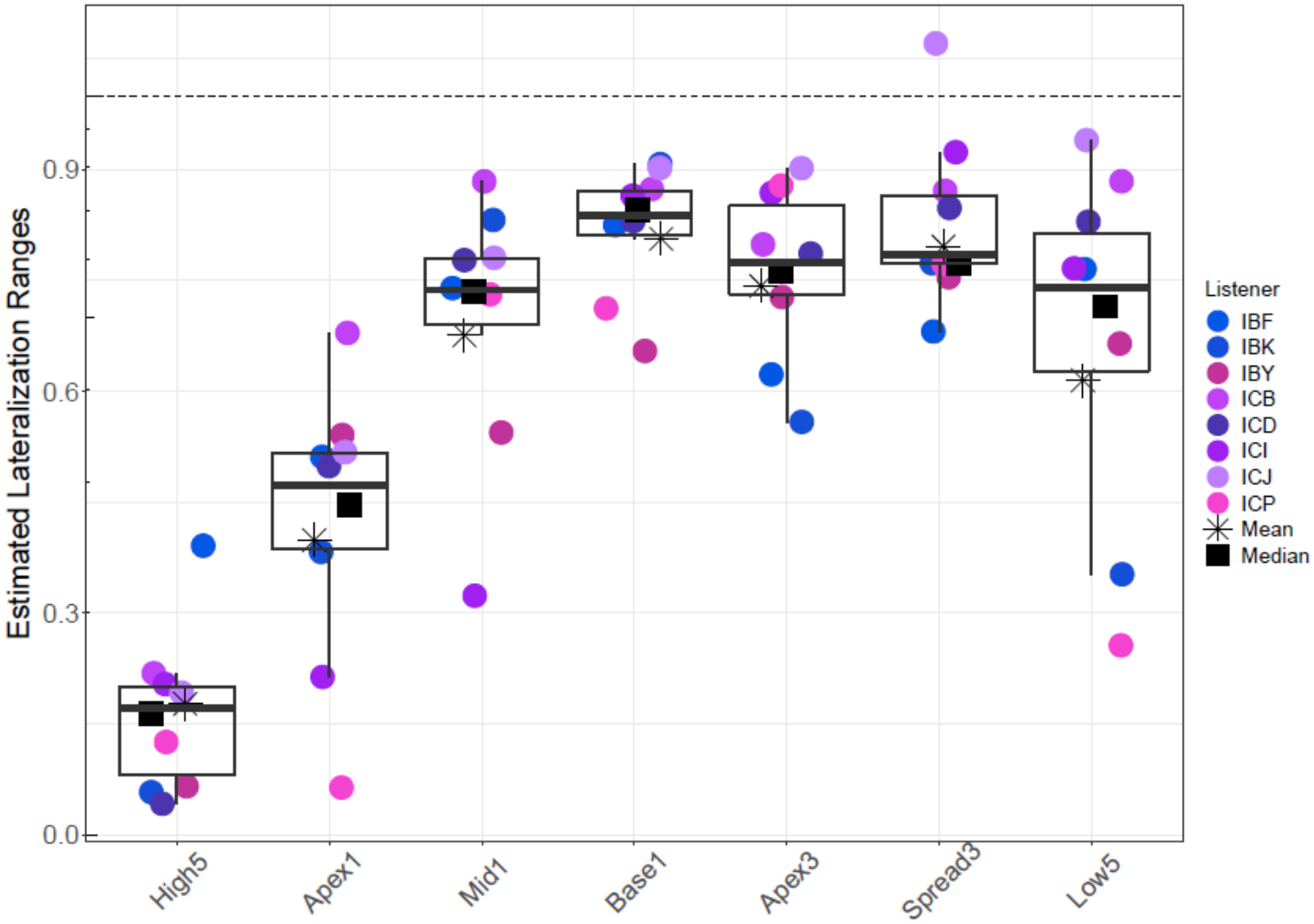

Figure 3: Lateralization ranges per listener and per condition; ranges are estimated from Equation 1. The five mixed-rate configurations are ordered from worst to best average lateralization range, while the High5 and Low5 configurations are placed at the left and right ends, respectively. A larger range is associated with a better mapping of ITD to perceived lateral location.

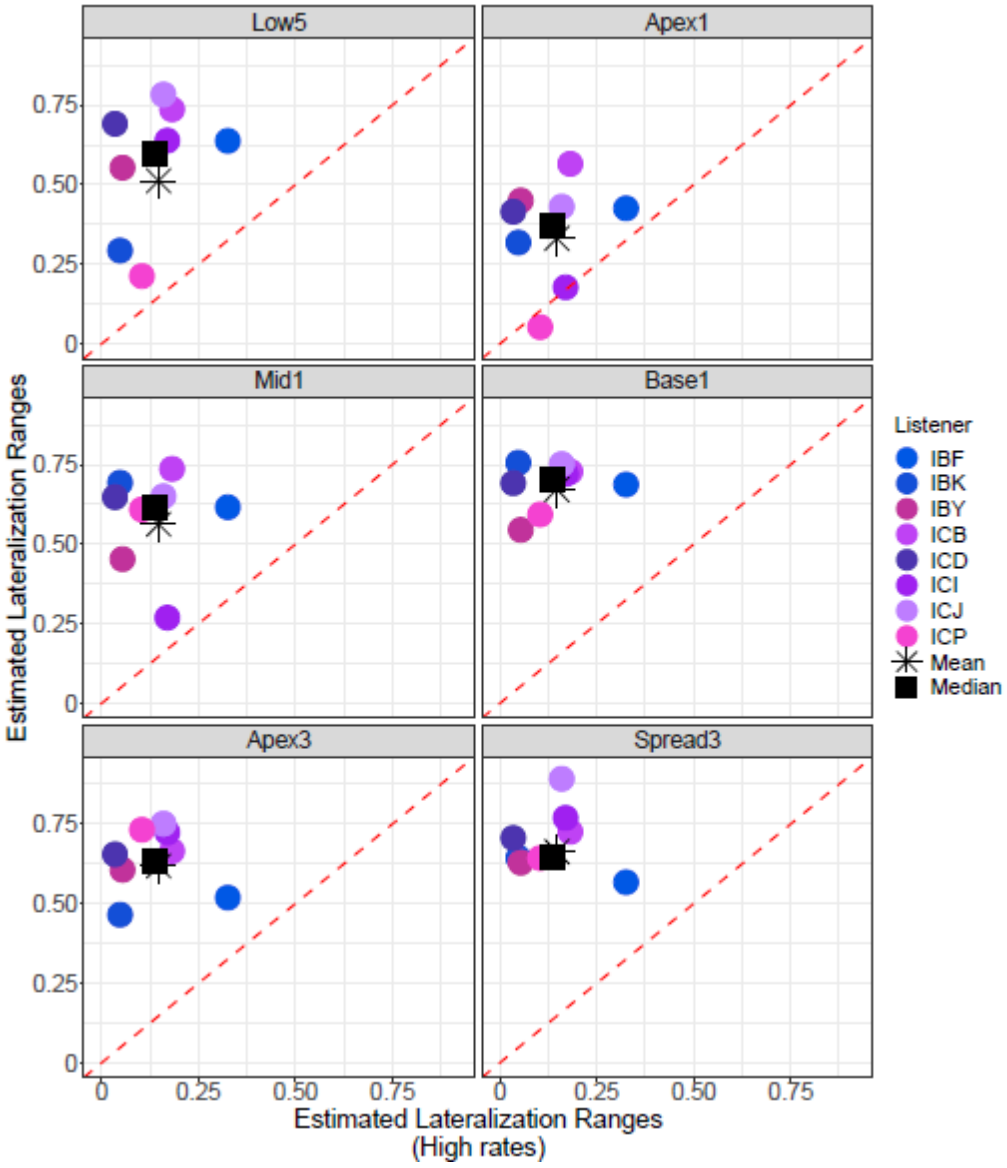

Figure 4: Lateralization comparison plots. Each mixed-rate range (y-axis) is plotted as a function of the High5 range (x-axis). The diagonal represents the line of unity, where ranges are identical in the two conditions plotted. Points that fall below the line depict ranges in the mixed-rate configuration that are equivalent or worse than the High5 configuration, and points that fall above the dotted line depict ranges that were better than the Low5 configuration.

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CHAPTER IV: The impact of interaural time differences with asymmetric rates on lateralization and auditory object formation in bilateral cochlear implant listeners

I. Abstract:

Binaural cues promote perceptual fusion of sound sources and auditory object formation (AOF). Good AOF is a prerequisite for spatial hearing in normal hearing (NH) listeners. Little is known about the role of AOF and its relation to binaural cues in bilateral cochlear implant (BiCI) listeners. With clinical devices, lack of synchronized across the ears can lead to non-synchronized timing of pulses across the two ears, which can result in an incoherent auditory object. Here, we introduced across-ear difference in stimulation rate (asymmetric rates) on stimuli that had an interaural time difference (ITD), to investigate how these cues are perceptually combined to produce a coherent lateralizable sound. We hypothesized that asymmetric rates would be more detrimental to AOF in NH listeners than BiCI listeners. Electrical stimulation with BiCIs is hypothesized to promote more tolerance for mismatched rates because BiCI users have shown to have poor sensitivity to across-ear temporal information. Listeners were asked to report *where* and *how many* sounds were heard. Stimuli for BiCI listeners were constant amplitude biphasic electrical pulse trains, stimulating one electrode in each ear. NH listeners were presented with acoustic pulsatile stimuli. One ear received a fixed rate of 100 pulses per second (pps), and the other ear received a variable rate (between 75-300 pps). Three ITDs were tested: 0 μs, -500 μs and +500 μs. Results showed that NH listeners report hearing two objects with asymmetric rates while BiCI listeners do not. Furthermore, we found that both NH and BiCI listeners rely on the ITD cue and not the rate asymmetry for accurate lateralization of a coherent auditory object, regardless of how asymmetric the rates were. These data suggest that though NH and BiCI listeners both relied more on the ITD cue, the fact that BiCI listeners were reporting greater proportion of AOF suggests that low rate ITDs, while good for relaying ITDs that have consistent timing, could lead to difficulties in detecting a

second sound source when presented in more complex auditory situation. Therefore, BiCI listeners may require temporally symmetric information in the ITD in order to distinguish a single object from two objects.

II. Introduction:

Patients fitted with bilateral cochlear implants (BiCIs) nonetheless struggle to locate sounds in noisy situations. For many years, only single cochlear implants were provided, as speech perception was the main goal. In recent decades, there has been an impetus to also provide BiCI users with auditory cues that are beneficial for accurate localization and understanding speech in noise, hence bilateral implantation has become routine in many clinics (Peters et al., 2007; Wilson et al., 1991).

Sound localization in the horizontal plane is mediated by an underlying network that processes differences between the ears in time of arrival via interaural time differences (ITDs) and interaural level differences (ILDs) (Stern and Colburn, 1978; Wallach, 1938). ITDs are caused by a difference in time of arrival between the two ears. The brain uses this time difference to compute sound location (Blauert, 1987; Mills, 1959; Stern and Colburn, 1978; Wallach, 1938). Studies to date suggest that receiving inputs through two implants improves BiCI listener's sound localization, compared to listening with only one cochlear implant (Grantham et al., 2007; Litovsky et al., 2012). However, BiCI listeners still struggle to achieve the same level of performance that normal hearing (NH) listeners perform at in spatial tasks (Jones et al., 2014; Kerber and Seeber, 2012; Litovsky et al., 2009, 2012; Loizou et al., 2009). Some studies suggest that this lower performance could be due to the fact that BiCI listeners may rely primarily on ILDs for sound localization (Aronoff et al., 2010, 2012), whereas it is known that

NH listeners use ITDs as their dominant cue for sound localization in the horizontal plane (Wightman and Kistler, 1992; Macpherson and Middlebrooks, 2002).

In normal hearing, utilizing ITDs during binaural hearing is critical for achieving accurate sound localization and sound source segregation (Arbogast et al., 2016; Hawley et al., 2004; Lutfi et al., 2013a; Stern and Colburn, 1978). However, ITDs are highly sensitive to across-ear and within-ear frequency differences, which can affect binaural processing in the auditory pathway. There is evidence that across-ear frequency information is kept intact as it reaches the cochlear nucleus, and subsequently arrives at the superior olivary complex (SOC). The SOC then processes binaural information as a function of frequency (Carr and Konishi, 1990; Yin and Chan, 1990). Further, the binaural system compares frequency information across auditory filters, also referred to as "within-ear" binaural processing, in other words listeners can make judgments in a psychophysical task simply by making comparisons across different auditory filters or electrode regions in a single ear . Localization of complex sounds often needs to be perceived as fused sound sources, whereby all the spectral components of a sounds are perceived as coming from the same source, or the same "auditory object." When different ITDs with inharmonic spectral components are presented within a complex tone, this can impede lateralization of the object (Best et al., 2007; Dye et al., 1996, 2005; Stellmack and Dye, 1993). These frequency-dependent rules highlight how ITD sensitivity can be impacted when not spectrally matched.

Auditory object formation (AOF) is a major contributor to localization/lateralization. AOF occurs when acoustic properties of the sound source in an ongoing acoustic event indicate to the listener that a source is a unified event and any properties associated with this source belong to that auditory object (Bregman, 1990). When sounds are spatially separated, a target

and masker are easily distinguished as separate auditory objects (Mi and Colburn, 2016; Woods and Colburn, 1992a). Further, in line with the finding that ITDs are highly sensitive to changes in frequency, separation of a target and masker as individual objects is also influenced by across-ear and within-ear frequency matching (Ihlefeld and Shinn-Cunningham, 2008). Additionally, perceiving independent objects can be influenced by ITDs (Stellmack and Dye, 1993; Woods and Colburn, 1992b). In many instances, perceptual fusion, or a perceived amalgamation of multiple sound sources, can occur when sounds don't have a strong ITD cue (Buell and Hafter, 1991), resulting in AOF. Furthermore, greater across-ear and within-ear matching of temporal information can enforce AOF and hence improve lateralization (Stellmack and Dye, 1993), and good AOF is likely a prerequisite for accurate spatial hearing in NH listeners (Shinn-Cunningham, 2005).

Identification of coherent sound objects is an essential aspect of auditory processing, because listeners are more likely to hear one vs. two auditory objects when a binaural cue is paired with a secondary cue such as an onset cue or pitch cue (Darwin and Hukin, 1999; Woods and Colburn, 1992b).

An objective measure of auditory object formation does not exist, however, studies have attempted to index AOF by introducing relative changes between acoustic cues. For example, the relative changes in a target or reference cue can help understand contribution of each cue to AOF (Lutfi et al., 2013b). Some studies have shown that changing certain frequency components trial-by-trial relative to a harmonically-complex target, indicates that the ability to identify the target depends on whether the sound is perceived as a single auditory object or not (Bregman, 1982; Lee and Shinn-Cunningham, 2008). In summary, the competition of auditory cue information can strongly influence AOF.

Listeners with BiCIs demonstrate poor sound localization and sound source segregation, in part because ITD cues and frequency-matched information are not always accessible to them. This happens for a variety of reasons, including: (1) poor neural survival in one or both ears, resulting in neural asymmetries between the ears; (2) surgical factors which can limit symmetrical placement of electrodes in the two ears; (3) lack of synchronized signal processing in the clinical processors in the two ears; (4) reduction of binaural sensitivity from the envelope-extraction process and use of high rate pulsatile stimulation (van Hoesel, 2008; van Hoesel and Tyler, 2003; Kan and Litovsky, 2015; Laback et al., 2004a). Prior studies have not addressed the important question of whether BiCI users perceive coherent auditory objects across the ears when ITDs are present. This is particularly important to consider when stimulating with idealized, well-controlled electrical stimulation stimuli that provide binaurally synchronized electrical pulse trains. Experiments which determine binaural benefits of ITDs and AOF using controlled electrical pulse trains have broader applications for performance in more complex environments.

Prior work has investigated the effect of presenting different ITDs to multiple electrode pairs on the effect of single vs. multiple electrode stimulation, and the perceptual integration of different ITDs (Best et al., 2011; Ihlefeld et al., 2014). Best et al. (2011) showed that BiCI listeners struggle to lateralize a sound when one electrode has a conflicting ITD. Similar results are observed for NH listeners (Dye et al., 1996). However, Best et al. (2011) measured their outcome as a *decrement in response lateralization* and not in *perceived coherence* or *fusion* of the sound. To address this shortcoming, Ihlefeld et al. (2014) showed that in multi-electrode stimulation BiCI listeners do not improve their ITD thresholds beyond that of a single bilateral pair stimulated with an ITD. As such, it is not clear if listeners are truly fusing or integrating

information across the electrode array. While important for understanding ITD lateralization and sensitivity, these studies do not directly measure the impact of conflicting ITD cues or conflicting frequency cues on auditory object formation, as they have not directly tested whether listeners perceived more than one sound source.

Previous studies have indicated that source segregation using onset time, but not rate, across the electrode array, is sufficient for segregating sound sources in BiCI listeners (Carlyon et al., 2007). While that finding is potentially relevant to the present study, only monaural fusion/segregation was considered. In earlier work, Carylon and Deeks (2002) showed that NH listeners are more sensitive to changes in stimulation rate than BiCI listeners (Carlyon and Deeks, 2002). Overall, there is a dearth of knowledge about the ability of BiCI listeners to perceptually fuse low rate signals (< 600 Hz). This is particularly true for cases when cochlear implant users are bilaterally implanted, where ITD cues are introduced.

In BiCI listeners, the research community lacks sufficient knowledge of the stimulus parameters that may be necessary to trigger both accurate sound localization and AOF. Here, we explored the extent to which AOF occurs in BiCI listeners when a single ITD cue is presented to a single electrode pair, at low stimulation rates (less than 600 Hz). Rather than varying the across-ear or across-electrode ITD, we varied the across-ear rate of stimulation to determine whether this would elicit the perception of separate objects. The reasoning behind using only low-rate stimulation is that BiCI listeners are known to be sensitive to ITDs at low rates (van Hoesel et al., 2009; van Hoesel, 2007). Further, if signal-processing strategies that preserve ITDs are implemented in CI speech processors, it is imperative to assess whether AOF can be promoted. The simplest case for investigating this issue is with a single target ITD at low rates of stimulation. However, a low-rate ITD presented to a single electrode pair is not sufficient to

understand AOF. Therefore, a stimulation rate asymmetry was imposed in different trials to induce the perception of separate auditory objects with a single fixed ITD cue. Creating across-ear symmetric rates or asymmetric rates allows us to indirectly influence AOF, and test whether listeners are still utilizing the ITD cue under these circumstances. The across-ear difference in rate was manipulated while the ITD was held constant in order to observe the extent of lateralization and auditory object formation in BiCI listeners. We investigated the impact of asymmetric rates combined with ITDs in both NH and BiCI adult listeners. As mentioned earlier, NH listeners require frequency-matched binaural information both within and across ears. Therefore, we also investigated whether an acoustic simulation of BiCI stimuli, using acoustic pulse trains, influenced ITD lateralization or AOF in NH listeners. We hypothesized that in NH listeners, if across-ear asymmetric rates strongly influence AOF with increasing asymmetry, listeners would report fewer single sound sources. BiCI listeners were hypothesized to show moderate AOF, because they generally have more difficulties detecting across-ear temporal differences. Thus, if the rate is a major component of lateralization and auditory object formation, then (a) asymmetric across-ear rates will weaken object formation and yield poor lateralization, and (b) symmetric across-ear rates will strengthen object formation and yield good lateralization.

Results from the current study have the potential to provide information that can improve engineering of CI processing strategies designed to capture binaural cues and improving spatial hearing in noisy environments.

III. Methods:

A. Listeners

Ten BiCI listeners who participated in prior studies on binaural sensitivity and have previously demonstrated sensitivity to ITDs participated in this study. All listeners had been exposed to acoustic hearing early in life and had onset of deafness after language acquisition (see Table I). All listeners had Cochlear Ltd (Sydney, Australia) implants (CI24 and CI512 family of implants). Stimuli were delivered via direct stimulation using bilaterally-synchronized Lara34 research processors, or an RF GeneratorXS interfaced with MATLAB (Mathworks, Natick, MA) via the Nucleus Implant Communicator (version 2 for Lara34s, version 3 for RF Generator). These devices have 24-electrodes (22 intra-cochlear and 2 ground electrodes), with approximately 0.75 mm center-to-center inter-electrode spacing. Electrodes are numbered such that 22 is the apical-most electrode, and 1 is the basal-most electrode. Twelve NH listeners participated in an identical task and were presented with acoustic pulse trains to simulate electrical stimulation via circumaural headphones (Sennheiser HD 650). All experimental procedures followed the regulations set by National Institutes of Health and were approved by the University of Wisconsin's Human Subject Institutional Review Board.

All testing was performed on a personal computer with custom-made software written in MATLAB. A touchscreen connected to the same computer was used to enter responses to their perception of the stimuli.

B. Stimuli & Mapping: BiCI listeners

Stimuli presented to BiCI listeners consisted of biphasic electric pulse trains at low rates of stimulation ranging from 75 to 300 pulses-per second (pps), delivered to a single pair of electrodes. All stimuli were 300-ms duration, 8-μs phase gap, and 25-μs phase duration (except

for listener ICP who was mapped with a phase duration of 75 μs) constant amplitude pulse trains. For each participant, a single bilateral pair of electrodes was selected based on previous testing. Interaural pitch-matching techniques were used as a proxy to identify pairs of electrodes that can lead to good ITD sensitivity (Kan et al., 2013, 2015b). The selected pair in the right and left ears was pitch-matched and had the best sensitivity to ITDs from all pairs of electrodes tested, in prior visits.

To determine a comfortable loudness level at each rate, BiCI listeners were first mapped at 100 pps and at 300 pps in each separate ear at single electrodes. The loudness map defines the range of current units (CUs) that generates an audible percept between threshold (T) and most comfortable (M) loudness levels at each electrode. Within this range, a comfortable (C) level was also measured, which we defined as the stimulation level that a listener is willing to be tested at for an extended period of time. C-levels were compared across electrodes within an ear to ensure the same loudness. We then stimulated the electrodes individually with an inter-stimulus interval of 100 ms, and listeners indicated which electrodes were louder than others, so that C-levels could be re-adjusted to yield equally loud perception for all electrodes.

Loudness typically increases with greater rate of stimulation, and as such loudness-balancing was required both across-ears and across-rates. Bilateral loudness balancing was determined by simultaneously stimulating paired electrodes in the two ears and asking listeners to indicate the intracranial horizontal location of the tone on the image of a face. This procedure was followed to ensure listeners heard a centered image. Subsequently, the experimenter made adjustments in 3 CU steps in the louder ear to find a perceptually centered auditory image. This bilateral loudness balancing technique was conducted for every across-ear set of rates.

During the experimental task, the across-ear rate was varied with each trial for stimuli presented to a single electrode pair. The left ear was always presented with 100 pps, while the right ear was presented with rates of different pulses per second in each trial: 75, 95, 99, 100, 101, 125, 150, 200 or 300 pps. Additionally, one ITD was presented to each pair of symmetric or asymmetric rates: a left-ward, center or right-ward ITD. The ITD cue presented to most BiCI listeners was either -500, 0 or +500 μs (adjusted to ±1000 μs and ±800 μs for listener IBZ and IAU, respectively). This ITD was applied to the entire stimulus in each trial and randomized in each block.

C. Stimuli: Normal hearing listeners

NH listeners were presented with acoustic pulse trains to simulate the electrical pulse trains delivered to BiCI listeners. The acoustic pulse trains had tonal carriers at a frequency of 4 kHz, and were modulated at a rate of 100 Hz by Gaussian envelopes (Goupell et al., 2010; Goupell et al., 2013b), referred to as Gaussian envelope tone (GET) stimuli. The spatial bandwidths of the GET stimuli along the cochlear arrays were calculated using Greenwood's cochlear place-to-frequency mapping function (Greenwood, 1990). Spatial bandwidths were calculated 0.75-mm above and below the 4-kHz carrier frequency resulting in a 1.5-mm bandwidth. These stimuli had either symmetric or asymmetric rates, and as was the case for BiCI listeners, were presented at different rates for the left and right ears (left: always at 100pps; right: varied across trials between 75, 85, 99, 100, 101, 125, 150, 200 and 300 pps). All acoustic stimuli were calibrated and presented at 65 dB SPL-A. During the task, ITDs were presented with a ± 700 μs (except for listener TMX who was presented with a ± 500 μs ITD). NH listeners experienced difficulties lateralizing to the far left and right with a ± 500 μs, therefore we exaggerated ITDs: There is some evidence that artificially enlarging ITDs that are played over

headphones is useful for increasing the range of ITD lateralization in NH listeners (Baumgärtel et al., 2017).

D. Task

The experimental task was designed to measure a combination of lateralization and AOF. Listeners were instructed to determine WHERE the sound was heard, and HOW MANY sounds were heard. A single-interval, six-alternative forced choice task was completed; listeners were shown six buttons on the screen. For each trial, listeners selected one of the following responses: “One-Left” (a single sound was heard on the left), “One-Center” (a single sound was heard in the center), “One-Right” a single sound was heard on the right), “Two-left dominant” (two sounds were heard, and the dominant one was on the left), “Two-center” (two sounds were heard in the center), “Two-right dominant” (two sounds were heard, and the dominant one was on the right) (Figure 1). Responses were binned according to the frequency of responses to each response button and then combined according to "correct responses" (i.e., selection of a location in the direction of the target ITD). Chance performance for location was considered to be at 33%, because all three ITDs (Left-ward, Center, and Right-ward) were presented and randomized in each block. Before beginning any testing, all listeners performed 2-3 practice runs with the condition that had matched rates across the ears to provide them with an example of a stimulus that promoted hearing only one sound. Following this familiarization phase, listeners heard a block of trials where all rate and ITD conditions were presented. In this block, listeners were expected to identify either more than one sound or only one sound in some trials.

During testing, blocks of trials for all asymmetric-rate conditions were randomized (20 trials per condition), and each listener heard 600 trials (3 ITDs, 10 across-ear combinations, 20

repetitions for condition). BiCI listeners were given the option to repeat responses, but only repeated responses one or two times. NH listeners were not given the option to repeat responses.

IV. Results:

A. Observed auditory object formation:

The stimulus conditions in the current study were set up to influence AOF. Therefore, due to the conflicting nature of the across-ear cues, only the conditions in which stimuli were perceived as a single sound are of interest, as they are either being driven by the direction of the ITD or the stimulation rate in the right ear (where stimulation rate was varied). Shown in Figure 2 is the average proportion of responses reported as "onse sound." These responses were collapsed across all reported directions (Left, Center, and Right) and only the responses for a single sound as a function of the stimulation in the right ear are illustrated. The results are displayed as a proportion of responses as a function of the stimulation rate in the right ear. Figures 3A and 4A show group averages of the proportion of *correct responses* reported as "one" sound source, for NH and BiCI listeners, respectively. Figures 3B and 4B show the proportion of correct responses reported as "two" sounds, for NH and BiCI listeners, respectively. Data for each individual are shown in Figures 5 and 6. The condition with symmetric rates (100 pps both ears) is denoted by the shaded gray area; this area denotes where the ITD is not dynamically changing and thus provides the most salient ITD cues. Thus, we should expect to see a peak in all three ITDs (left, center, and right) in this shaded region. The proportion of trials were determined according to the number of trials for each reported location (left, center or right); Equation 1 shows how this proportion is calculated.

Eq. (1):

$$The\ proportion\ of\ trials = \frac{Number\ of\ trials\ in\ the\ direction\ of\ the\ ITD\ (reported\ as\ a\ single\ sound)}{Total\ number\ of\ trials\ in\ the\ direction\ of\ the\ ITD\ (20\ per\ ITD)}$$

Additionally, a logistic regression was fit for each individual's "single sound" for all correctly reported directions. The outcome variable in this model was the number of correctly reported responses, while the predictor variables were either the direction of the ITD (left, center, or right) or the value of the stimulation rate in the right ear (75, 85, 95 pps etc.). Correct responses were coded as a "1" and incorrect responses were coded as "0". This model was aimed at capturing the contribution of ITD and/or the rate of stimulation in the right ear to proportion correct. The ITD variable was separated into two predictors, "Left" and "Right." For either the "Left" or "Right" predictor, a trial was coded as "1" to signify a correct response and coded as a "0" otherwise. The effect of the "Center" condition was considered a reference condition and captured in the intercept of the model.

The variable describing the stimulation rates was also separated into two predictors: "RateHigher" for the magnitude of difference *greater than* the reference condition and "RateLower" for stimulus rates presented below 100 pps. The effect of the 100 pps condition (the symmetric rate condition) was captured in the intercept of the model. The logistic regression is shown in Eq. 2.

Equation (2):

$$\begin{aligned} logit(correct\ responses\ reported\ as\ a\ single\ source) \\ = X + \beta_1 Left + \beta_3 Right + \beta_4 RateLower + \beta_5 RateHigher + \beta_6(Left \\ * RateHigher) + \beta_7(Right * RateHigher) + \beta_8(Left * RateLower) \\ + \beta_9(Right * RateLower) \end{aligned}$$

In Eq.2, X describes the intercept; β_1 through β_9 describe the coefficients for each of the previously described predictors and their interactions.

i. *NH Listeners:*

For NH listeners, Figure 3A shows proportion of responses where listeners reported hearing a single object in the direction of the ITD. The grey region (the symmetric rate condition) represents the area where performance should be best if listeners are using only the ITD cue during the task. NH listeners demonstrated strong AOF for a narrow range of asymmetric rates across the ears, as indicated by Figure 3A. The proportion of responses for the symmetric-rate conditions were 0.44, 0.38, and 0.78 for the left, right, and center ITDs, respectively. NH listeners showed weak lateralization when rates were symmetric, even in the presence of AOF, as indicated by the low proportion correct. More importantly, NH listeners poorly lateralized ITDs when the difference in rates across the ears was very large, resulting in poor AOF. Conversely, when the rate in the right ear was ≤ 85 pps or ≥ 125 pps, AOF was diminished (a lower proportion of "one" sound was perceived). In addition, less than 20% of the responses were reported in the correct direction. However, NH listeners always reported hearing two sounds when the right-ear rate was outside of 85 to 125 pps range, particularly when the rates were ≥ 125 pps and the response was to either the left or to the right (shown by the cyan and pink symbols in Figure 3B).

ii. *BiCI Listeners:*

For BiCI listeners, we hypothesized that listeners would only show good AOF and good lateralization (i.e., higher proportion reported in the correct direction) when symmetric rates were presented across the ears, because these listeners have demonstrated binaural sensitivity in prior experiments (see Table II). Instead, BiCI listeners showed poor lateralization and poor

AOF (greater perceptual "fusion") regardless of whether rates were symmetric or asymmetric across the ears (see Figures 4A). For the symmetric-rate conditions (100 pps in each ear), proportions of correct lateralization responses when listeners heard “one sound” were 0.67, 0.78, and 0.5, for responses to the Left, Center, and Right, respectively. Notably, these proportions are higher than those of the NH listeners. However, when rates were asymmetric, BiCI listeners had lower proportion correct than NH listeners. The proportion correct for “one sound” responses for rates < 100 pps were 0.41, 0.15, and 0.14 for Left, Center, and Right, respectively. For rates >100 pps, proportions correct were 0.29, 0.18, and 0.31 for Left, Center, and Right, respectively. For some conditions, the proportions of responses were above chance (chance = 33%), and therefore, responses reported in the correct direction may have been unrelated to the degree of rate asymmetry for BiCI listeners. For example, in Figure 4, listeners IBZ, ICD, ICJ, ICP, IBQ, and IAU did not have a peak in the proportion of correct responses when the across-ear rates were symmetric. This is the opposite of what was observed in NH listeners where correct responses reported as a single sound were only reported when rates were symmetric across the ears.

B. Results of logistic regression (NH and BiCI):

For the logistic regression, Tables III-A and III-B show model coefficients for BiCI and NH listeners, respectively. For each listener, the values of each predictor (“Left”, “Right”, “RateLower”, or “RateHigher”) can be interpreted as follows: for an individual’s responses, predictors which have values deviating far from zero and from the intercept value implies that a certain predictor holds more weight than one that is closer to zero. Figures 7 and 8 show the coefficients for each of these predictors for NH and BiCI listeners, respectively (interactions are not included). For example, listener IBQ had an intercept of -15.78 and the predictor for

“RateHigher” was 1.214l; this positive shift in the value indicates that their responses were heavily influenced by having the rate higher in the right ear. We found for a majority of BiCI and NH listeners, the values for the rate predictor, regardless of whether the rate was higher or lower, did not deviate far from the intercept, indicating a small impact of rate. However, we found that responses were only slightly weighted by the ITD predictor for both BiCI listeners. This is in contrast to NH listeners who have values of coefficients deviating far from the intercept values, regardless of the sign, indicated that listeners either heavily up-weighted or down-weighted the ITD cue Figure 7A and 7B (smaller y-axis) show that NH listeners appear to rely heavily on the ITD cue, while a change in stimulation rate has a relatively small contribution (coefficients are within -0.2 and 0.2, with more negative values). Figure 8A and 8B (smaller y-axis) show that BiCI listeners have a similar pattern to NH listeners. However, the coefficients corresponding to the ITD direction appear to be more variable in NH listeners, indicating that some listeners may have b utilized the ITD cue in the task while other listeners did not use the ITD cue.

A principal components analysis (PCA) was conducted in order to better interpret the group effect, to understand whether model coefficients reveal a relationship between NH and BiCI groups. Further, PCA can help interpret whether NH and BiCI listeners relied on different cues when completing the experimental task. PCA uses an orthogonal transformation to convert a set of variables into latent variables that represent linearly-correlated values. In a PCA eigenvalues correspond to the variance explained by each principal component. The largest eigenvalues correspond to the principal component that explains most of the covariance in the data. Both the BiCI and NH coefficients were analyzed in the same PCA. The largest eigenvalues in the PCA (18.4 and 3.5 for the first and second principal components, respectively) indicated that the first two components explained 83.65% and 16.35% of the variance,

respectively. The remainder of the components had eigenvalues less than 1. These values are generally discarded because they do not explain a significant portion of the variance.

The component matrix shown in Table IV indicates that, for eight BiCI participants, principal component (PC) 1 was positively associated with performance while PC 2 was negatively associated with performance. When comparing these values to their individual performances in Figure 4, seven listeners (IAU, ICP, IBQ, ICB, ICD, ICI and ICJ) showed an increase in the proportion of correct responses outside of the grey shaded region, meaning the proportion correct of their responses could not have been related to the ITD. This is because the ITD for all asymmetric rates were dynamically changing, resulting in an unreliable cue. Additionally, all model coefficients for the ITD predictor were relatively small (see Figure 8A and 8B) for all BiCI listeners (apart from listeners IBQ and IBK), this could mean that that PC 1 describes some reliance on internal noise or biases to perform the task. Only listeners IBZ and IBF showed a small or negative value for PC 1 and a large value for PC 2; both of these listeners had relatively good performance in the grey region and poorer performance outside of that region The only exception to this categorization was listener IBK, who had a high proportion correct in the shaded region, but had value of 0.998 for PC 1, similar to the other BiCI listeners. It follows now that PC 2 represents the reliance on the ITD cue, this is because the biggest PC values in PC2 were for listener IBF and IBZ, the best performers in the task who had the most correct responses in the shaded grey region (i.e. where the rate was symmetric)

For the NH listeners, the importance of PC 1 and PC 2 was the opposite of the PC allocation for the BiCI listeners. Assuming that PC 1 represents internal noise and PC 2 represents the ITD cue, then negative values of PC 1 and positive values of PC 2 for NH listeners TFV, TMP, TMU, and TMY, indicate that at least some listeners used the ITD cue to choose the

correct location of the tone. This can be confirmed by observing their responses in Figure 5. Listeners TFV, TMP, TMU, and TMY show the highest proportion correct in the shaded region and reduced correct responses when the rate difference was greater than 1 Hz across the ears. Surprisingly, according to the PCA, the remainder of the NH listeners showed the same pattern as the BiCI listeners did, this could also be attributed to internal noise because the logistic regression showed very little influence of the rate cue

V. Discussion:

The present study was designed to investigate how BiCI listeners may perform in complex environments, and how their performance compares with that of NH listeners. More specifically, we tested the influence of asymmetric rates on AOF whilst varying ITD cues in both BiCI and NH listeners. This allowed us to assess how well BiCI listeners can determine whether they hear a single sound, and how well they can lateralize that sound. The unique six-alternative task and the novel stimuli used in this study captured the degree of across-ear integration in a manner that is not captured in previously used left-right discrimination tasks. The current study implemented a task that measured both AOF and intracranial sound source lateralization. In the field of psychoacoustics, the "real-world" equivalent of AOF and lateralization are "sound-source segregation" and "sound localization," respectively (Arbogast et al., 2016; Freyman et al., 2005; Lutfi et al., 2013b; Moore, 2013).

Experimental paradigms aimed at understanding both sound-source segregation and sound localization in BiCI listeners are lacking, because so far, the field as a whole has focused on improving sensitivity to fine structure location cues, namely ITD cues (Buechel et al., 2018; Chung et al., 2014; Francart et al., 2015; Hancock et al., 2011; Kan et al., 2015a; Laback et al., 2004b; Thakkar et al., 2018). A limitation in prior approaches was the lack of a holistic

understanding of the extent to which BiCI listeners can integrate or fuse sounds across the ears. A number of factors contribute to asymmetries between the two ears of BiCI users: surgical placement of the electrodes in the two ears can create asymmetries in depth of insertion, asymmetric neural preservation, and clinical programming of the devices may not be ideally suited for symmetrical hearing (for recent reviews see Kan and Litovsky, 2015; Laback et al., 2015). Another issue is that more patients are fitted with Cochlear's Nucleus system are programmed with the ACE speech processing strategy. These listeners may receive differences in pulse-timing due to peak-picking resulting in simultaneous stimulation of different sounds presented to the right and left ears. Cochlear's ACE strategy is adaptive, whereby the strategy continuously estimates the outputs of the 22 electrode filters and selects the eight with the largest amplitude. Only those eight electrodes are stimulated. Finally, clinical mapping decisions which assign different pulse rates for each ear could lead to temporal asymmetries that may further interrupt spatial hearing abilities and AOF. The extent to which a signal, both within- and across-ears, needs to be integrated for sufficient fusion of ITDs is not well-understood for the BiCI population. Therefore, this study aimed to take one step towards assessing the usefulness of location cues (ITDs) in the presence of asymmetrically presented sounds (i.e. across-ear differences in stimulation rate), a task which ultimately forces the listener to segregate the across-ear signal.

Studies in NH listeners can be informative. For example, sound-source segregation studies which manipulated the across-frequency ITDs have shown the impact of conflicting ITDs that belong to a single sound. Specifically, NH listeners can exhibit poorer sensitivity to a target ITD in a certain frequency band when (1) the other frequency bands have a closer spectral spacing, when (2) there are smaller differences between the across-frequency onset times, or

when (3) there are smaller differences in across-frequency inharmonicity (Stellmack and Dye, 1993). A key point highlighted in the present study is that fusion or object formation, based on ITD alone, is not sufficient. Similarly, we found that NH listeners reported hearing two auditory objects when the across-ear rates were greater than 1 Hz apart, resulting in segregation, regardless of the ITD (see Figure 2B). This suggests that the ITD cue was not sufficient to produce the percept of a single object. However, our BiCI listeners, who typically show excellent sensitivity to ITDs (Table II) were unable to segregate the asymmetric signal into two objects when the rates were asymmetric across ears (Figure 3B). They were also unable to report the location based on the ITD accurately. This suggests that the target ITD is susceptible to misinformation about the location of the sound when the asymmetric rates are reported as single auditory objects. The lack of segregation of the across-ear rates renders the ITD cue unusable.

Results from the present study are consistent with the idea that listeners operate like "ideal observers." An ideal observer accurately judges a stimulus' features by optimally integrating the information in each presentation of the sound (Berg, 1989). Most studies generally determine whether listeners deviate from the "ideal observer" using a measure of relative weights where the weights are based on the extent to which the listener's trial-by-trial responses are related to a trial-by-trial variation in the individual acoustic cues (Dye et al., 2005; Lentz and Leek, 2002; Lutfi et al., 2013a). A weight is given to each acoustic feature, whereby a set of arbitrary weights is a function of d-prime (an index of sensitivity). Typically, an ideal observer would have performance that leads to a d-prime of 1 (Berg, 1989; Lutfi and Jesteadt, 2006). Studies which measure the extent to which listeners integrate information across multiple cues have suggested listeners' decision-making tends to be consequence of the statistical properties of the individual acoustic cues. Listeners typically do not integrate information

optimally in a multiple observation task, but rather they deviate from the ideal-observer model (Berg, 1989; Lutfi and Jesteadt, 2016). BiCI listeners do not behave as ideal observers when combining ITD information across the electrode array, instead sensitivity appears to be influenced by the electrodes that are the most sensitive to the ITD (Ihlefeld et al., 2014). Unlike the study by Ihlefeld et al. (2014), the present study assessed whether listeners optimally integrate ITD information across the ears, as opposed to across the electrode array. However, the fundamental concept is very similar: In the Ihlefeld (2014) study, BiCI listeners were unable to integrate the ITD information across electrodes, meaning listeners were instead relying on the information in one electrode. We found that BiCI listeners are unable to perceive that there are multiple rates being presented to them, resulting in greater proportion of fused sounds.

In a prior NH study, Lutfi et al. (2013) designed an experiment where random perturbations were introduced within a trial for a set of acoustic parameters. The decision weights of these perturbations were derived through a linear combination of the various components present in the signal. Individual responses to these perturbations help in the interpretation of the target acoustic cue. In the present study, we have attempted to understand whether BiCI listeners are selecting just one feature of the sound, either the change in stimulation rate or the ITD cue, in order to report the lateral location and the number of auditory objects. The coefficients determined from the logistic regression in the current study represent "weights" of each acoustic feature in the stimulus. The response patterns within each population (NH and BiCI) were not homogenous: different listeners weight the ITD predictor differently. Figure 6B and 7B illustrate the large variability in the coefficients determined for the “Left” and “Right” ITD predictors for each group of listeners (NH and BiCI, respectively).

The principal components analysis, though a descriptive measure, illuminated the degree of importance to either the ITD cue or the rate cue. Overall, the principal components analysis suggests that two components heavily influence BiCI listeners' responses. When the values of the component matrix (see Table IV) are compared to those of the individual data plots (Figures 4 and 5), it suggests that PC 1 and PC 2 reflect the rate cue and the ITD cue, respectively. We further observe that BiCI listeners are strongly influenced by a stimulation rate change, as shown by the values for PC 1, which are close to 1. This is counterintuitive, because a rate change across the ears does not have a stable location cue. For NH listeners PC 2, which appears to reflect the ITD cue, is heavily weighted for four of the listeners but not the remaining eight. The reason for this outcome is not well-understood, however, unlike the BiCI listeners, NH listeners did not have a "repeat" button available to them during testing. Therefore, it is possible that the inability to repeat a trial reduced the saliency of the ITD cue. Another caveat is that the ITD presented to NH listeners was much larger than that to BiCI listeners. Therefore, the ITD could have been too large to perceive as a coherent sound with the addition of the across-ear asymmetric rates. Overall, these results suggest that temporal rate asymmetries across the ears appear to drive decision-making, even when ITDs are present in the signal, at least for BiCI listeners.

Low rate ITD discrimination and detection in BiCI listeners is well-studied phenomenon, additionally, BiCI listeners are sensitive to ITD cues and temporal pitch cues through pulse-based rather than envelope-based cues, when controlled through research processors. It is important to highlight that BiCI listener's sensitivity to temporal information deteriorates very quickly at stimulation rates above 300 pps (Shannon 1983; Townshend et al., 1987; Kong et al., 2009; van Hoesel, 2008; van Hoesel et al., 2009; Venter and Hanekom 2014). This rate

limitation has been observed both in rate discrimination tasks where both unilateral and bilateral CI listeners made discrimination judgments with one ear (Shannon 1983; Townshend et al.,1987; Zeng, 2002; Baumann and Nobbe, 2004; Kong et al., 2009; Bahmer and Baumann, 2013, Carlyon, 2007), and also for the detection of ITDs in BiCI listeners (van Hoesel et al.,2002; van Hoesel and Tyler 2003; Laback et al., 2007; van Hoesel, 2007; van Hoesel et al., 2009). This implies that if low stimulation rates are ultimately used to convey ITDs in clinical devices, any asymmetries in the temporal relationship across the ears could skew the perceived location and result in strong AOF (i.e. the increased propensity to report hearing a single sound source), even if two sources are present.

VI. Conclusions

In the current study, we found that BiCI listeners have a higher propensity to fusing sounds into a single auditory object regardless of how different the information across the ears may be (i.e., asymmetric rates). Conversely, NH listeners report hearing "one" sound and correctly lateralize only when across-ear rates are symmetric. BiCI listeners also exhibit incorrect lateralization, which is contrary to the outcome seen in NH listeners. These data suggest that perceptual fusion of across-ear asymmetric temporal information has a substantial impact on a listener's decision-making in a lateralization and auditory object formation task. Further, it suggests that BiCI listeners who have previously demonstrated sensitivity to ITDs may still exhibit poor AOF in lateralization tasks when interrupted by asymmetric temporal information.

VII. Figures and Tables

Listener ID	Age	Sex	Years of CI experience (left/right)	Implant Type (left/right)	Etiology
IAU	67	M	(17/10)	(CI24M/CI24RE)	Hereditary
IBF	64	F	(8/9)	(CI24RE/ CI24RE)	Hereditary
IBK	75	M	(12/6)	(CI24R (CS)/ CI24RE)	Hereditary, noise exposure
IBQ	84	F	(10/13)	(CI24RE/ CI24R (CS))	Meniere's
IBZ	49	F	(9/10)	(CI24RE(CI24RE)	Normal hearing until 33 years old; sudden hearing loss (unknown)
ICB	66	F	(12/12-15) *listener was reimplanted in the right ear after 3 years	(CI24RE/ CI24R (CA))	Hereditary
ICD	58	F	(7/13)	(CI24RE/ CI24R (CS))	Hearing loss at 3 years old
ICI	57	F	(7/6)	(CI24RE/ CI24RE)	Hearing loss at 31 years, etiology unknown
ICJ	6	F	(6/6)	(CI512/CI512)	Hearing loss at 13 years, perhaps due to illness
ICP	54	M	(7/4)	(CI24RE/ CI24RE)	Hearing loss at 3 years old

Table I: Listener demographics and etiology for all BiCI listeners. Table lists age at testing, sex, years of experience with a CI, and etiology.

Listener ID	Electrode	Left	Right	JND (μs)
IBF	Mid	12	12	62
IBQ	Mid	14	7	264.53
IBZ	Mid	12	12	670.45
ICB	Mid	12	12	192.88
ICD	Base	4	2	57.9
ICI	Base	4	6	140.95
ICJ	Apex	20	16	203.37
ICP	Mid	12	14	203.25
IBK	Base	6	6	57.6
IAU	Base	1	1	638

Table II: ITD Just-noticeable differences (JNDs) for all BiCI listeners. JNDs represent sensitivity to ITDs of a *symmetric* low-rate (100 pulses per second) constant amplitude electric pulse train. Normal hearing listeners typically have JNDs as small as 10-20 (μs) (McFadden and Pasanen, 1976)

ID	Intercept	Left	Right	RateHigher	RateLower	Left: RateLower	Left: RateHigher	Right: RateLower	Right: RateHigher
IBF	1.620	1.193	-0.807*	-0.020*	-0.306*	-0.257	0.137	NA	0.014*
IBK	-0.122	17.688	2.022*	-0.005	-0.046	0.046	-0.346	NA	-0.008
IBZ	-0.062	0.436	0.605	-0.007	-0.235	0.224	0.003	15.257	0.037
IAU	-0.590*	-0.128	0.359	-0.021	0.024	-0.015	0.021	-0.151	-0.014
ICP	-0.694*	0.193	0.443	0.001	-0.002	-0.015	0.003	-0.093	-0.003
IBQ	-15.780	14.826	15.291	1.214	0.000	0.017	-1.215	NA	-1.216
ICB	-0.618*	0.781*	0.787*	-0.001	-0.040	-0.060	-0.009	-2.706	0.001
ICD	-0.526*	0.842*	0.245	-0.005	-0.002	0.014	-0.001	0.023	0.040*
ICI	-0.589*	0.343	0.511	0.001	0.004	0.019	0.000	NA	0.001
ICJ	-0.690	0.396	0.467	0.000	0.000	0.008	0.006	0.026	0.002

Table III-A: Model coefficients for all BiCI listeners. Asterisks next to values represent coefficients which were significant in the model.

ID	Intercept	Left	Right	RateHigher	RateLower	Left: RateLower	Left: RateHigher	Right: RateLower	Right: RateHigher
TFV	0.004961	1.930105*	0.854208	-0.00874	-0.20453	-0.17429	0.012124	15.91143	0.008441
TJV	-0.29105	0.856717*	2.280145*	-0.14585	-0.2183	0.10798	0.268496	14.79528	0.12321
TKU	-0.57148*	16.25026	1.264625	-0.11272	-0.17837	NA	NA	-0.51478	0.518178
TMP	2.197225*	-1.28093	-0.40547	-0.11778	-0.49248	0.3234	0.06649	16.26679	-0.1699
TMQ	-0.43803	NA	NA	-0.07281	-0.15553	NA	NA	NA	NA
TMS	-0.09077*	2.322727*	1.311313	-0.10168	0.011178	-0.44019	14.94052	-0.27019	0.094125
TMU	1.443978*	-1.01847	-0.1731	-0.01831	-0.14981	-0.07654*	0.062808	0.025541	-0.03682
TMW	-0.63374*	16.19981	1.86575*	-0.00327	0.019149	-31.1513	NA	-0.55801	-0.02678
TMX	-0.59278*	1.797774*	0.977286	0.004993	0.005066	-0.17816*	0.033413	-0.21998*	-0.01276
TMY	0.217413	1.241235*	18.34866	0.188052	-0.01589	-0.25796	0.550524	0.015889	-0.18805
TNA	-0.53456*	15.10062	1.082908*	0.004744	-0.06936	-29.0628	NA	-0.10463	-0.01199
TNB	0.794997*	1.16464*	0.823528	-0.02198	0.13596	-0.39312*	0.026789	-0.26027	-0.00978

Table III-B: Model coefficients for all NH listeners. Asterisks next to values represent coefficients which were significant in the model

Component Matrix for PC 1 and PC 2		
	Component	
	1	2
IBF	-.908	.418
IBK	.998	.057
IBZ	.001	1.000
IAU	.937	-.351
ICP	.958	-.285
IBQ	.974	-.227
ICB	.972	-.234
ICD	.956	-.293
ICI	.956	-.293
ICJ	.957	-.289
TFV	-.285	.959
TJV	.974	.227
TKU	.987	-.160
TMP	-.912	.410
TMQ	.997	-.075
TMS	.142	-.990
TMU	-.933	.359
TMW	.948	-.318
TMX	.957	-.289
TMY	-.339	.941
TNA	.986	-.165
TNB	-.994	.110

Table IV: Component matrix for principal component (PC) 1 and PC 2. Values in table represent the "weight" for each component across individuals. PC represent two variables from the PCA which explain the most variance.

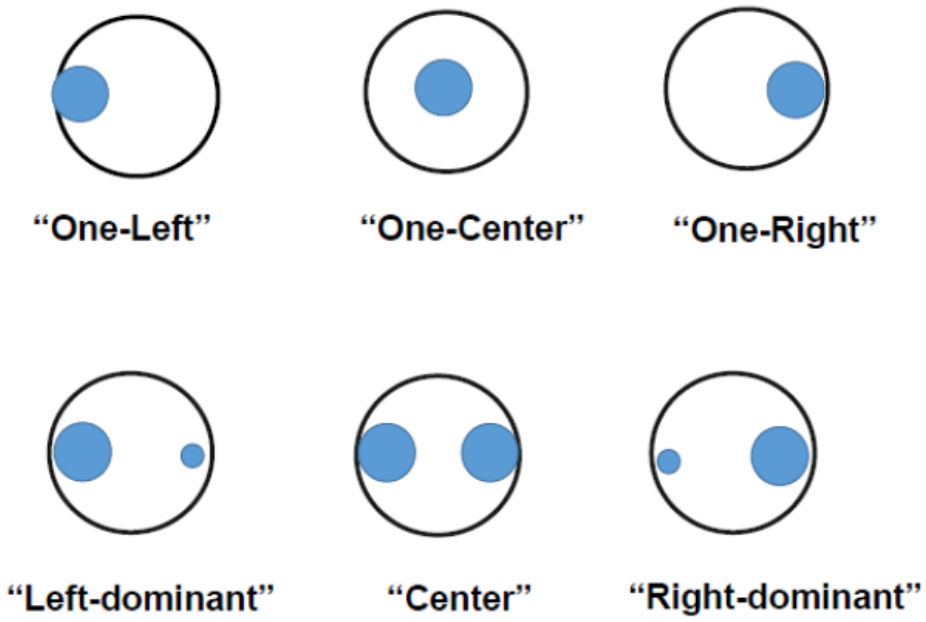

Figure 1: Response options for the lateralization and auditory object formation task. The task was a single-interval six-alternative forced choice task.

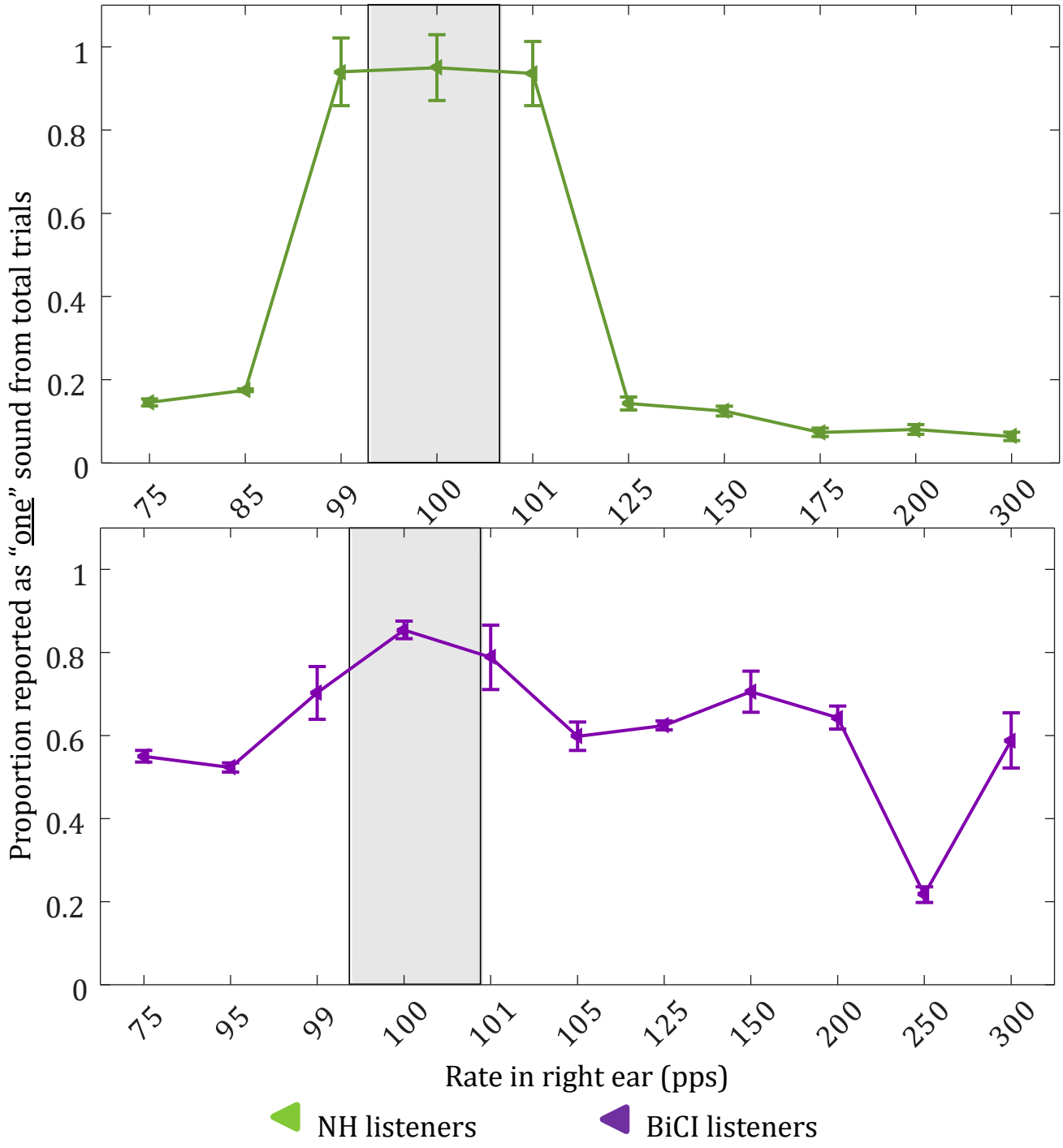

Figure 2: Proportion of responses reported as "one sound" as a function of the rate played in the right ear. Top panel shows the average proportion for all NH listeners while the bottom panel shows the average proportion of all BiCI listeners. Error bars represent standard error. The grey region depicts where the rates were symmetric across the ears.

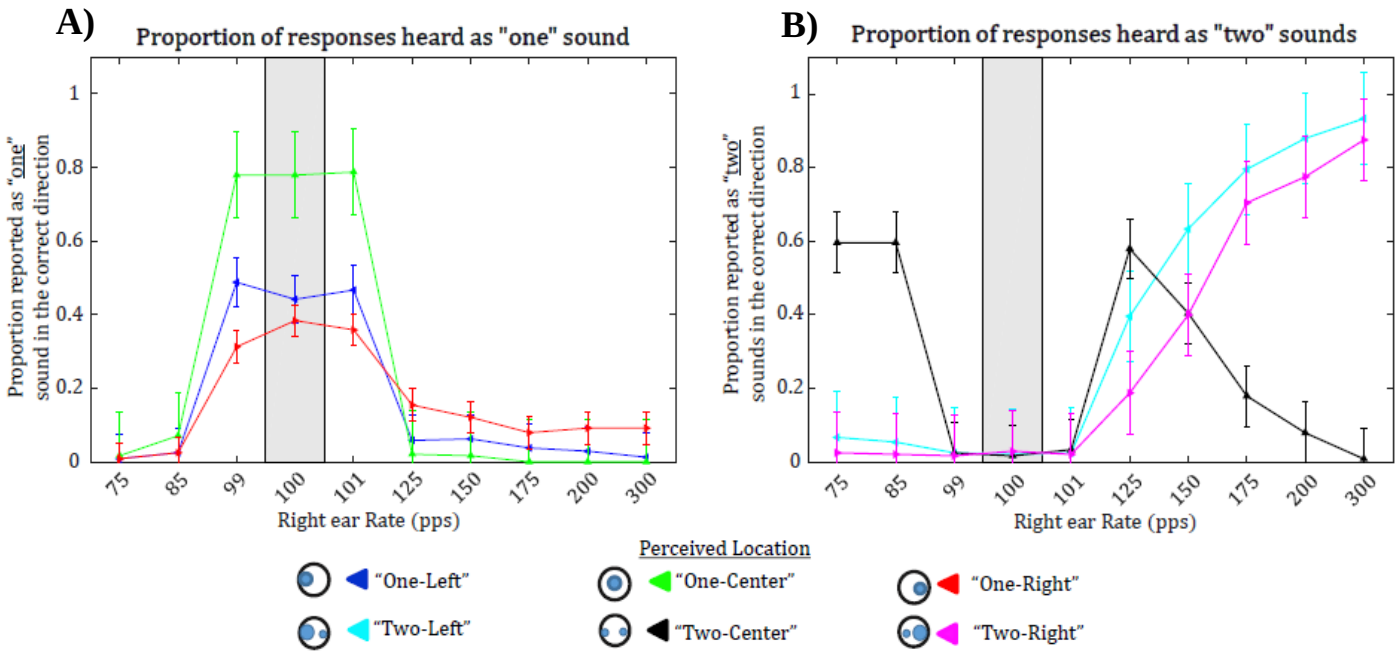

Figure 3: Proportion of responses per target ITD presented (i.e. reported in the correct direction), averaged across the group of NH listeners. Error bars represent standard error. Panel A shows proportion of sounds reported as a single course, panel B shows proportion of responses heard as two sounds. The grey region depicts where the rates were symmetric across the ears.

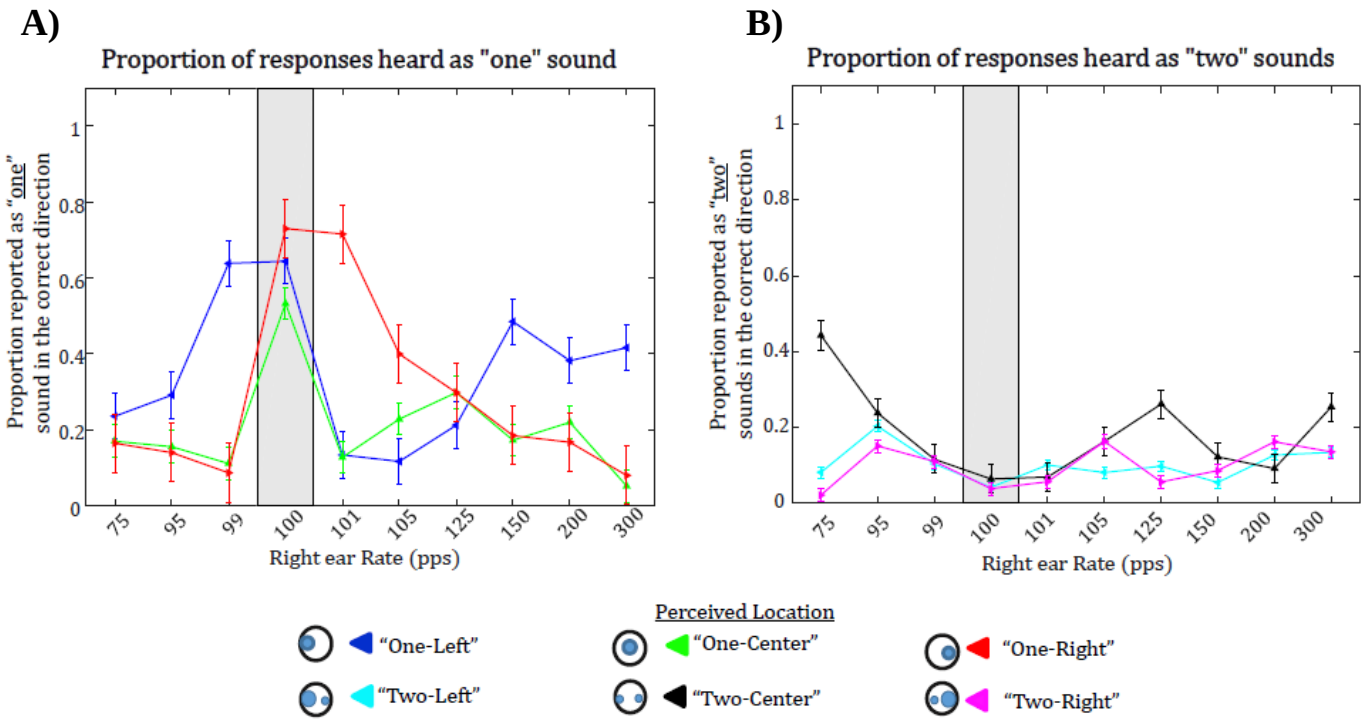

Figure 4: Proportion of correctly lateralized responses per target ITD presented, averaged across the group of BiCI listeners. Error bars represent standard error. Panel A shows proportion of sounds reported as a single course, panel B shows proportion of responses heard as two sounds. The grey region depicts where the rates were symmetric across the ears.

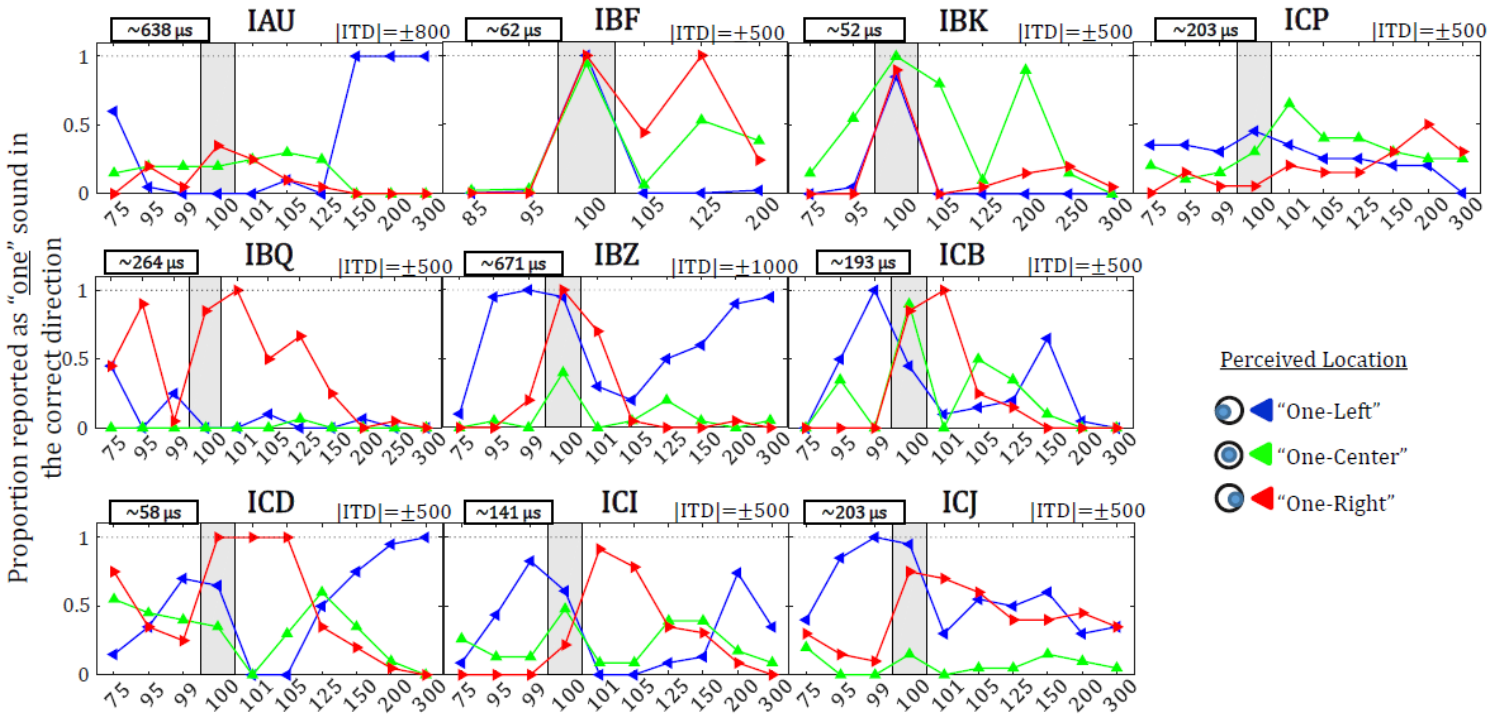

Figure 5: Proportion of lateralized responses reported as "one" sound per target ITD for each individual BiCI listener; ITDs tested shown in top right of each panel; each BiCI listener's threshold sensitivity to ITDs to a 100pp pulse train with symmetric rates is shown in top left.

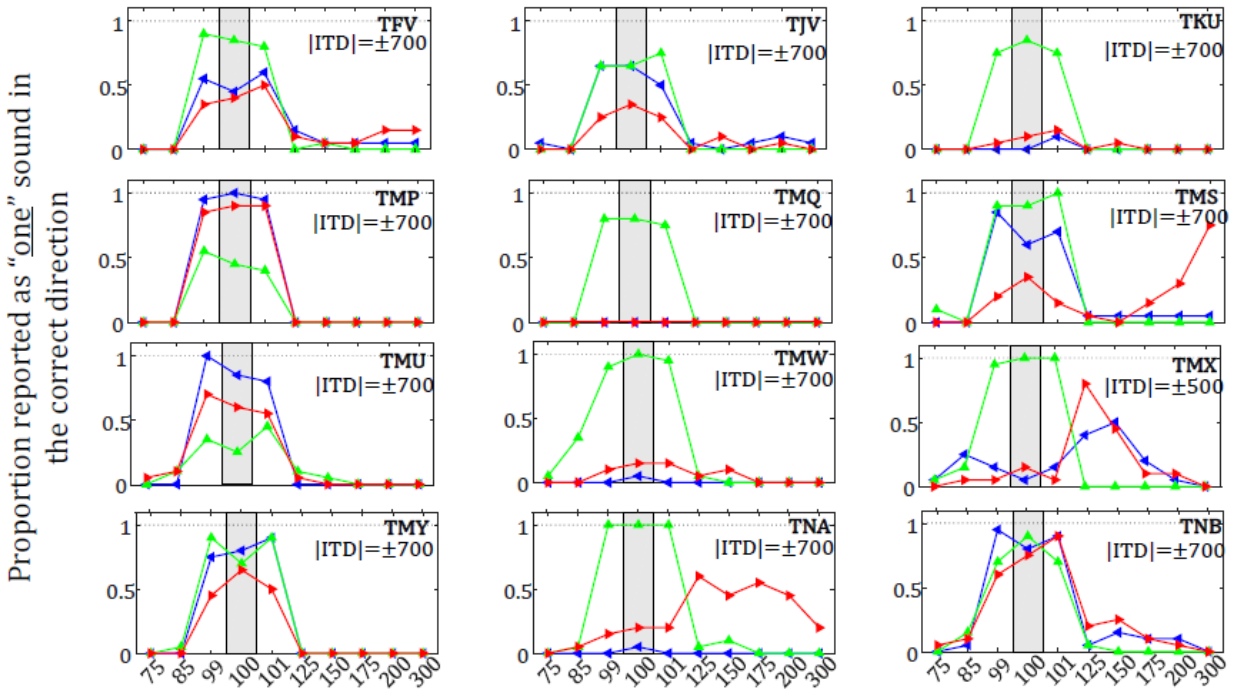

Figure 6: Proportion of lateralized responses reported as "one" sound per target ITD for each individual NH listener; ITDs tested shown in top right of each panel. Only one listener was presented with a ± 500 µs ITD while the remainder of individuals were presented with a ± 700 µs ITD.

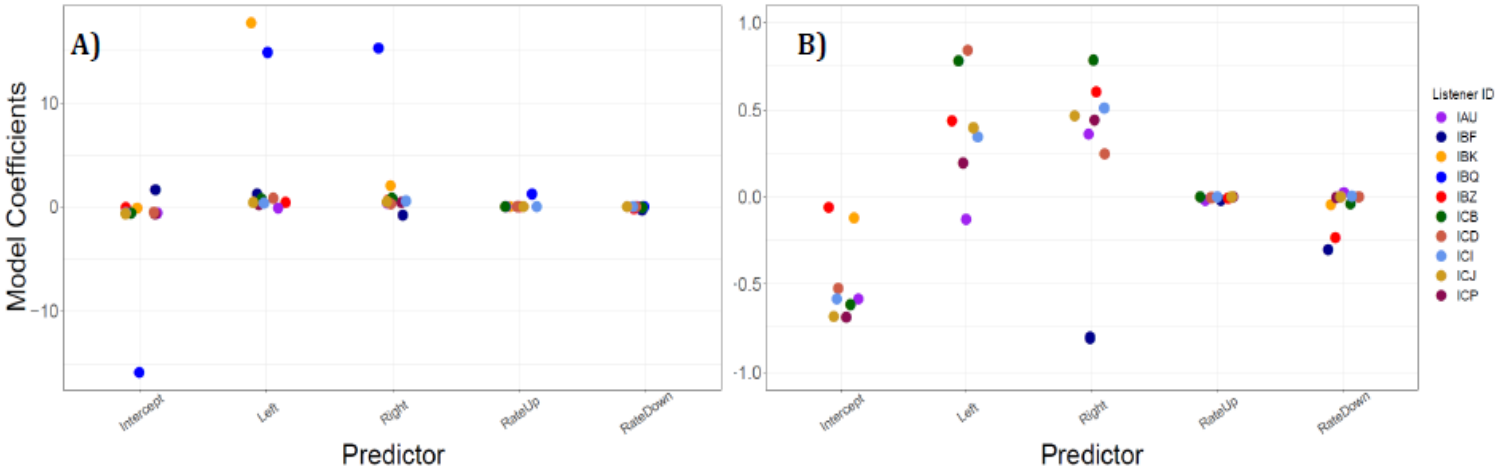

Figure 7: Model coefficients (for NH listeners) determined using a logistic regression for the intercept, left responses (Left), right responses (Right), rate asymmetries greater than 100 pps (RateUp), and rate asymmetries less than 100 pps (RateDown). Panel A shows all coefficients while panel B shows a smaller range on the y-axis to illustrate the small differences between values across each predictor. Each colored symbol represents a different NH listener.

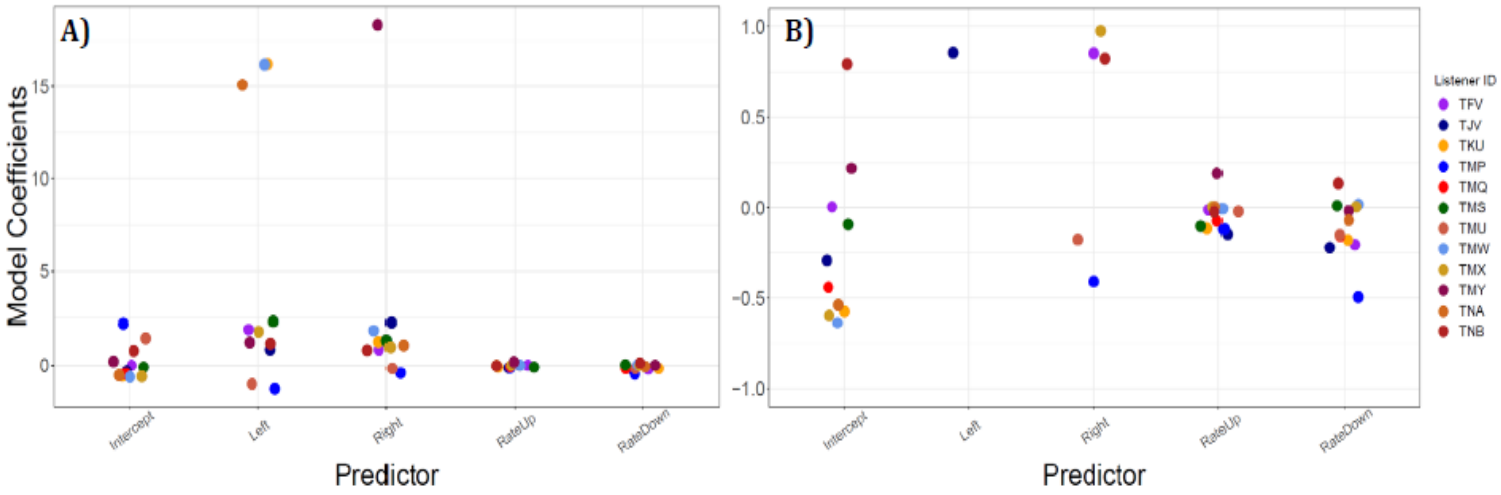

Figure 8: Model coefficients (for BiCI listeners) determined using a logistic regression for the intercept, left responses (Left), right responses (Right), rate asymmetries greater than 100 pps (RateUp), and rate asymmetries less than 100 pps (RateDown). Panel A shows all coefficients while panel B shows a smaller range on the y-axis to illustrate the small differences between values across each predictor. Each colored symbol represents a different BiCI listener.

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CHAPTER V: The importance of consistent onset cues for enhancing low-rate ITDs and establishing good sound lateralization and object formation.

I. Abstract

Noisy environments cause localization cues such as interaural time differences (ITDs) to vary in time dynamically, which can degrade localization abilities. Normal hearing (NH) listeners can overcome dynamic ITDs and correctly lateralize an auditory object in complex environments by weighting onset ITDs more heavily than the ongoing ITD. Bilateral cochlear implant (BiCI) listeners localize sounds in noisy and complex environments more poorly than NH listeners. Here, we aimed to understand whether consistent vs. dynamic ITDs in a pulsatile stimulus would impact lateralization and auditory object formation in BiCI listeners. Using synchronized research processors, trains of biphasic electrical pulses (100 pulses-per-second, 300-millisecond duration) were presented to a pair of interaural electrodes. The number of onset pulses that carried the same ITD was varied. Remaining pulses had a dynamically-changing ITD that originated in at an ITD either in the same or opposite hemifield as the onset, and the ITD was jittered by ±40 μs. Listeners identified the number of objects perceived and the intracranial lateralization. Results showed that when consistent and dynamic ITDs originated in opposite hemifields, BiCI listeners required five or more pulses with consistent ITDs for correct lateralization of an auditory object. However, when consistent and dynamic ITDs pointed in the same hemifield, listeners more often correctly lateralized the primary auditory object, regardless of the number of consistent ITDs. These findings suggest that BiCI listeners may benefit from a sound coding strategy having consistent ITDs in a few pulses in order to correctly lateralize a sound object in a complex auditory environment.

II. Introduction

As bilateral cochlear implantation becomes the standard-of-care for patients with severe-to-profound bilateral hearing loss, there is growing evidence for improved performance with bilateral hearing compared with unilateral hearing (Litovsky, 2011; Litovsky et al., 2012; Nopp et al., 2004). An impetus for providing bilateral cochlear implants (BiCIs) is to give patients access to binaural cues. Normal hearing (NH) listeners utilize binaural cues for localizing sounds in the horizontal plane and separating speech from noise in complex environments (Blauert, 1996; Feddersen et al., 1957; Freyman et al., 2006; Hawley et al., 2004; Macpherson and Middlebrooks, 2002; Middlebrooks et al., 1989). However, BiCI listeners still struggle to achieve the same level of performance on spatial hearing tasks that NH listeners can perform with high accuracy (Aronoff et al., 2010; Dorman et al., 2016; van Hoesel and Tyler, 2003; Litovsky et al., 2012; Schoen et al., 2005; Seeber and Fastl, 2008). Sound localization in the horizontal plane is driven by a binaural network that processes interaural time differences (ITDs) and interaural level differences (ILDs) (Feddersen et al., 1957; Hershkowitz and Durlach, 2005; Klumpp and Eady, 1956; Mills, 1959; Wightman and Kistler, 1992). Object formation, an extension of sound-source segregation (Bregman, 1990), results in the ability to perceive separate auditory objects. However, when those separate objects possess different spatial locations or are incoherent, binaural cues are helpful to accurately detect a target sound in the presence of masking sounds (Freyman et al., 2005; Rakerd and Hartmann, 2010).

Perceiving independent objects is known to enhance sensitivity to ITDs and facilitate spatial separation of a target from competing sounds (Bremen and Middlebrooks, 2013; Dye et al., 1996; Woods and Colburn, 1992). Therefore, this study aimed to understand which stimulus features are important for shaping both sound localization and object formation in listeners with

BiCIs. In the laboratory setting, sound localization and sound-source segregation can be tested in isolated tasks whereby a limited number of cues are manipulated. When ITD and/or ILD cues are controlled and presented over headphones, perceived location in the head, referred to as "lateralization" and fusion or segregation of sounds is referred to as “object identification” or “auditory object formation” (Darwin and Hukin, 1999; Goossens et al., 2009; Woods and Colburn, 1992). Understanding which stimulus features impact both lateralization and auditory object formation (AOF) in BiCI listeners can be beneficial for determining strategies that will facilitate improved outcomes in noisy and complex environments. Additionally, BiCI listeners with adult-onset of deafness typically show sensitivity to ITDs in controlled laboratory settings (van Hoesel et al., 2009; van Hoesel and Clark, 1997; van Hoesel, 2007). Thus, if –regarding AOF – BiCI listeners with adult-onset of deafness show similar effects of onset cues as NH listeners, binaural mechanisms involved in onset dominance are preserved in electrical hearing.

To date, research on binaural hearing in the BiCI population has concluded that both patient factors and device factors can limit performance in spatial hearing tasks. One of the major device limitations is that clinical processors primarily use high-rate pulsatile stimulation; this creates little opportunity to capture ITDs in the temporal fine structure of the signal (van Hoesel et al., 2009; Hu et al., 2017). Limitations from the clinical processors can be bypassed in a laboratory setting such that coordinated stimulation of electrodes can be presented to the two ears at lower rates of stimulation (van Hoesel et al., 2009; van Hoesel and Clark, 1997; van Hoesel, 2007). Even still, BiCI listeners drastically vary in their performance on tasks that measure ITD sensitivity, and are far from achieving the same sensitivity as NH listeners. With research cochlear implant processors, BiCI listeners who had acoustic hearing prior in life and experienced adult-onset of deafness, have demonstrated ITD sensitivity with thresholds ranging

from 50-1000 μs at low rates of stimulation (~100-300 pulses per second, pps) (van Hoesel et al., 2009; van Hoesel and Clark, 1997; van Hoesel, 2007).

Prior work from our lab has explored binaural sensitivity in BiCI users with electrical stimuli. In those studies, some multiple electrode pairs are stimulated, and some electrodes receive high rates while other electrodes receive low rates. Our work demonstrated that mixed rates of stimulation can improve sensitivity to ITDs and increase the range of lateralization compared to a condition with only high rates of stimulation. We also found that presenting a low-rate pulsatile stimulus to a single bilateral pair of electrodes in a multi-electrode stimulus allows for better discrimination of ITDs (Thakkar et al., 2018). However, this approach did not consider how sound lateralization is related to an important aspect of hearing in realistic situations. In other words, how do BiCI listeners experience auditory object formation? The relation between lateralization and AOF is key to the potential success of novel signal processing strategies, which represent low-rate binaural cues with fidelity in BiCI listeners. Novel strategies will maximize performance of BiCI listeners if they can promote not only better localization of sounds, but also enable listeners to parse out multiple sound objects. To our knowledge, previous studies with BiCI users have not investigated the ability to detect single vs. multiple sound objects with low rate ITDs.

The relationship between lateralization of ITDs and auditory object formation has been investigated in NH listeners. When different ITDs are imposed on different frequency bands in a complex tone, the resulting lateralization of the tone is either inaccurate, or the listener segregates the frequency components into separate objects to overcome conflicting information (Dye et al., 2005; Stellmack and Dye, 1993). Lutfi et al. (2013) explored sound-source segregation with a novel approach using the "information divergence hypothesis:" this technique

measures performance where the statistical difference between the acoustic properties of a target and masker is measured as an index for a listener's performance in the task. A trial-by-trial measurement of the acoustic variation of the target and masker is used to generate probability density functions (PDFs) of each acoustic parameter. The hypothesis is that with additional trials, the listener's response depends on the relative difference between those PDFs. This is contrary to other studies, where measurements of performance are made in relation to a change of a single arbitrary acoustic parameter, such as signal-to-noise ratio (SNR), ILD, ITD, etc. Lutfi et al. (2013) found that varying the location of a target sound and masker sound in their relative azimuthal positions in the free field, results in a strong correlation of listeners' performance with the information-divergence metric (Simpson–Fitter's d_a). The relative changes made between the two sources was the degree of similarity in frequency content, how close in space they were, or the degree of masker uncertainty (an increase in standard deviation of the masker location). Therefore, the ability of a listener to localize a target object was directly impacted by the relative conflicting positions of primary (target) and secondary (masker) objects. In summary, listeners' performance related well to the relative changes in physical locations between two objects, rather than to the absolute change in the target object or masker object alone. This indicates that lateralization of a target object is dependent on the relative properties of a perceived secondary object.

For NH listeners, the binaural cue provided in the initial onset of a sound is a major contributor to ITD lateralization and AOF. Onset cues have strong salience, which can enhance localization abilities (Freyman, 1997; Stecker and Hafter, 2002). When presented with an acoustic pulse train, the NH auditory system processes ITDs in a periodic, time-locked manner. As such, the timing of each pulse (or modulation phase) is directly related to the auditory

system's ability to phase lock to the signal (Hancock and Delgutte, 2004; Joris et al., 1994; Rose et al., 1967; Yin and Chan, 1990). The listener's ability to lateralize ITDs in onset of the stimulus can be affected by the duration of the inter-pulse intervals, a change in the overall rate, the overall duration, or a random change in the ITD in each pair of pulses over time (Balakrishnan and Freyman, 2002; Freyman et al., 2010). Therefore, the listener's ability to lateralize the sound is based on a relative perceptual weight assigned to each pulse in the signal. It has been shown that the relative effectiveness of each pulse declines monotonically as a function of the pulse number following the onset pulse (Hafter et al., 1983; Hafter and Buell, 1990; Stecker, 2014; Stecker and Hafter, 2002). In those experiments, individual listeners' lateralization responses are used to estimate the relative binaural information available in each pulse. The number of "informative pulses" is a compressive power function directly relating to the total number of acoustic pulses. For pulse trains with inter-pulse intervals shorter than 12 ms, informative clicks exist only in a few pulses towards the onset of a signal (Stecker and Hafter, 2002). Furthermore, when acoustic pulses in a pulse train are consistent over time, meaning each cycle has the same ITD and inter-pulse interval, accurate lateralization of the stimulus is optimized (Brown and Stecker, 2011; Goupell et al., 2009). That is, consistent ITDs have the potential to drive the perception of a salient auditory object. In short, having the same inter-pulse interval and ITD in each pulse could be ideal for sound localization and AOF. This is even more important at very low rates where temporal changes in the ongoing portion could potentially degrade spatial hearing, a point of strong relevance to BiCI listeners, as there is no guarantee that the pulse timing will be the consistent over time (Kan et al., 2018)

Regarding AOF, earlier studies presenting NH listeners with sounds containing multiple frequency bands that have onset asynchronies of 60 ms (with either sharp or gradual onsets)

caused listeners to have a harder time indicating the order of presentation with sharper onsets than gradual onsets (Bregman et al., 1994). The implication is that listeners have a clearer perception of the pitch pattern formed by a gradual onset sound. Therefore, perceiving independent onsets of multiple frequency bands can reinforce the perception of a single unitary object in the presence of other sound sources. Furthermore, there is evidence to suggest that the similarity of across-ear and within-ear spectral and onset cues in the normal hearing system is a prerequisite for object formation (Bregman, 1982; Steiger & Bregman, 1982).

Conversely, in BiCI listeners, there is little existing evidence for the influence of onsets on ITD lateralization. However, some key findings regarding onset dominance have shown that BiCI listeners can accurately discriminate ITDs in part by the dominance of the first pulse of the signal when the remainder of the signal has a random ITD (van Hoesel, 2008). However, these prior studies did not measure how or if listeners can distinguish ITDs and identify them as coherent objects. Furthermore, there are very few studies on BiCI listeners that have suggested a role of onsets on object formation. A pivotal study by Carlyon et al. (2007) showed that CI listeners could utilize the differences in onset times across electrodes in order to perceptually segregate sound sources; however, this study only investigated monaural conditions and did not test the utility of onset times across the two ears. Another key study found that assessing pulse rate discrimination both within and across ears (upper limit: ~ 600 pps) improved sensitivity to across-ear differences in rate, with the addition of a binaural cue such as an ITD at higher rates – at least in NH listeners. By contrast, for BiCI listeners, improvement in detection of an across-ear rate difference with the addition of a binaural cue was not observed (Carlyon et al., 2008). The inability to benefit from the binaural cue could be due to the fact that rate discrimination for BiCI listeners in discrimination does not improve beyond 300 pps, compared to around 600 pps in NH

listeners. However, the underlying causes for this outcome are still unknown. Findings from these two studies suggest that across-ear temporal differences, smaller than the period of a 300 pps pulse train, can be difficult to discriminate across ears for BiCI listeners. However, it may instead be possible for BiCI listeners to make use of onset information to perceptually fuse or segregate sound sources.

By using tasks that measure both AOF and lateralization, here we aimed to investigate whether BiCI listeners, similar to NH listeners, benefit from dependency on consistency in onset timing as a necessary cue for both lateralization and AOF. We hypothesized that when the relative locations of a consistent onset ITD and dynamically-changing ITDs are on opposite sides of the head, BiCI and NH listeners would be able to lateralize the onset ITD and perceive it as a separate object from the dynamic ITD. We predicted that when the relative locations of the onset and dynamic ITD are closer, both groups of listeners would be unable to dissociate the two ITD locations, leading to inaccurate lateralization of the onset ITD. Additionally, we hypothesized that BiCI listeners might require greater consistency in the onset ITD than NH listeners in order to lateralize and form separate auditory objects between the onset and dynamic ITD. This hypothesis is rooted in evidence from prior work demonstrating that BiCI listeners have more difficulty discriminating across-ear temporal differences than NH listeners (Carlyon et al., 2008). Such a finding would imply that binaural processes in the NH and BiCI systems share common features and mechanisms, yet effects are weaker in BiCI users, due to the differences in the nature of acoustic vs. electrical stimulation, or differences in neural health between the two populations, or both.

III. Methods

Eight postlingually-deafened BiCI listeners with previously-determined sensitivity to ITDs participated in the present study. All listeners were implanted with the Cochlear Ltd (Sydney, Australia) cochlear implants (CI24 and CI512 family of implants). Stimuli were delivered via direct stimulation using bilaterally-synchronized Lara34 research processors, or an RF GeneratorXS interfaced with MATLAB (Mathworks, Natick, MA) via the Nucleus Implant Communicator (version 2 for Lara34s, version 3 for RF Generator). All testing was performed using a personal computer with custom-made software written in MATLAB. Responses to stimuli were made on a touchscreen connected to the same computer. Four NH listeners participated in an identical task and all had normal audiometric hearing.

Testing with BiCI listeners was conducted using pairs of electrodes across the ears that had, in previous experiments (Kan et al., 2015), been determined to be matched in pitch and to have the best sensitivity to ITDs of all possible pairs of electrodes tested (see Table I). The criteria used to select pairs of electrodes were based on findings that interaural pitch-matching techniques can be used to approximate frequency-matched regions of the cochleae in the two ears, stimulating pairs of electrodes that produce relatively good ITD sensitivity (van Hoesel and Clark, 1997; van Hoesel, 2007; Kan et al., 2015; Litovsky et al., 2010; Long et al., 2003; Poon et al., 2009).

A. Mapping

The selected pitch-matched electrode pair was mapped for each BiCI listener by obtaining threshold (T), comfortable (C), and maximum comfortable (M) levels at each electrode separately determined for the selected pair. During the mapping session, the listener reported the perceived loudness of a 100 pps constant amplitude pulse train. The T-level is the level (in

current units, CUs) which the listener hears approximately 50% of the time; the C-level is the level which the listener reported to be comfortably loud and which the listener is willing to listen to all day. Finally, the M-level is defined as the highest current level which the listener could listen to without being uncomfortably loud. Once C-levels were determined for each ear, the same pulse trains were played sequentially from left to right, and then simultaneously until the listener perceived the tones as equally loud and coming from the center of the head.

B. Stimulus

For BiCI listeners, all stimuli were 300-ms duration, 8-μs phase gap, and 25-μs phase duration, constant amplitude pulse trains presented at 100 pps biphasic electric pulse train. Therefore, a total of 30 biphasic pulses were present in the stimulus. The goal was to introduce ITDs that were either consistent or dynamically changing during the train of pulses. The experiment was designed such that the number of pulses from the onset of the pulse train that carried consistent ITDs was systematically manipulated (see Figure 1). In the condition with consistent ITDs for the duration of a trial, the same ITD occurred on every pair of pulses, with large values favoring the left or right side of the head (these values were either -800 μs for left-ward ITDs, and +800 μs for right-ward ITDs). The 800-μs values were relevant for all listeners but two, who needed ITDs of 900 μs to hear the fully lateralized stimulus. The location of the consistent ITD is abbreviated as 'OnsetLoc.' The number of consistent ITDs is abbreviated as 'NumOnsets' – this number ranged from 1 to a maximum of 30 (if 30 then spanning the entire stimulus) - the remaining pulses were instead given a dynamically-changing ITD.

Equation (1):

$$30 - NumOnsets$$

The dynamically-changing ITDs originated on average from a location either on the same side of the head or on the opposite side of the head as the OnsetLoc. Calculation for the number of dynamically-changing ITD is shown in Eq. 1. ITD values for the dynamically-changing pulses were randomly sampled from a uniform distribution, using the function 'unifrnd' in MATLAB. The center of the distribution had an ITD that was abbreviated as 'DynamicLoc,' and corresponded to one of the following: -200, +200, -800, or +800 μs. Some listeners received a larger OnsetLoc of ±900 μs, whereby the DyanmicLoc were -225, +225, -855, +855 μs[1] . The upper and lower bounds of the continuous uniform distribution were approximately -40 μs and + 40 μs for all dynamically-changing ITDs. All parameters are shown in Table II. Stimuli were generated in real-time for each electrode in each ear.

NH listeners heard acoustic pulse trains to simulate electrical stimulation, presented through circumaural Sennheiser HD 650 headphones. The acoustic pulse trains had tones (carrier frequency of 4 kHz) modulated by Gaussian envelopes (Goupell et al., 2010, 2013) at 100 Hz. The spatial bandwidths for the GET pulse trains were calculated using Greenwood's cochlear place-to-frequency mapping function (Greenwood, 1990). Spatial bandwidths were calculated 0.75-mm above and below the carrier frequency resulting in a spatial bandwidth of 1.5-mm. OnsetLoc, DynamicLoc, and NumOnsets parameters were different from the values used for BiCI listeners and are shown in Table II. Because NH listener have better sensitivity to ITDs, the

[1]. Stimuli that had an OnsetLoc of ± 900 μs did not have a DynamicLoc condition that fully corresponded to 900 μs because the constraints of the Cochlear devices are that each frame of the stimulus must be 10,000 μs and each sub-frame must be no shorter than 70 μs. In a 100 pps stimulus, each frame has only a single pulse with a specified current amplitude based on their individual maps, the duration of this pulse was 70 μs for all participants.
To introduce random perturbations of the ITD in each frame, the amount of time in each sub-frame was traded such that the entire frame added up to 10,000 μs (corresponds to a 10 ms period). Random perturbations of ITDs larger than 900 μs resulted in sub-frames in smaller than 70 μs. Since Cochlear devices are unable to stimulate with a sub-frame this small, the location of two of the dynamic ITDs (DynamicLoc) for listeners with an OnsetLoc of 900 μs was adjusted to -855 and + 855 μs.

values used for NH stimuli were +/- 600 μs for the OnsetLoc ITD. The DynamicLoc was presented at either +450 or –450 μs, to test whether or not the second source listeners were perceiving would be lateralized in a different location than the OnsetLoc. Finally, NumOnsets range from 1 to 30.

The aforementioned stimulus parameters resulted in four conditions for both BiCI and NH listeners: *Same-side Right, Same-side Left, Opposite-side Right, and Opposite-side Left*. Figure 1A illustrates the conditions, and Figure 1B illustrates the example stimulus parameters; solid lines depict the location of the OnsetLoc ITD and shaded triangles depict the location of the DynamicLoc ITDs.

C. Task

i. Preliminary Task

BiCI Listeners completed a preliminary lateralization task without any randomized ITDs. They were asked to use a visual pointer on a computer monitor to identify the perceived intracranial location of a 300 ms, 100 pps electric pulse train. ITD values were the same for each pulse and ranged from 0 to 1000 μs in each trial. Each ITD presented was repeated 40 times. Half of the ITDs were left-leading, and the other half were right-leading. After lateralization functions were measured for each listener, an ITD value was selected for the ‘OnsetLoc’ for the experimental task. The selected ITD represented a value on the lateralization function for which listeners consistently reported hearing a sound on the extreme left or extreme right of the visual pointer. The OnsetLoc value was approximately ±800 μs for all listeners, except for listener IDH who had an OnsetLoc of ±900 μs (see Table II).

ii. Experimental Task

During the experimental task, all listeners used the same interface as described in the preliminary task but were given different instructions. Listeners first completed two blocks of 20 trials where no ITD-perturbations were imposed on the stimulus and only the OnsetLoc was presented (i.e., all 30 pulses had the same ITD). In the first two blocks, listeners were told to report the intracranial location, and that they should only expect to hear one sound at one location. This was done in order to familiarize them with what it would mean to report hearing only one sound. In the following blocks, listeners were given instructions for a two-fold task. For each stimulus, listeners first reported the number of locations as an indicator of the number of objects perceived (one sound or two sounds). Second, listeners reported the location for each sound source[2]. Because conditions were randomized, listeners were told to expect hearing one sound on some trials and two sounds on other trials. Sources are referred to as the "primary source location" and "secondary source location" in the analysis described below.

Within a block of the experimental task, each trial had a different NumOnset and different OnsetLoc, however, DynamicLoc was varied across blocks. For example, block #1 could have the OnsetLoc set to either -800 or +800 μs (adjusted to 900 μs for listener IDH) with a DynamicLoc centered at -200 μs; in the following block, the OnsetLoc could be set to set to -800 or +800 μs with a DynamicLoc centered at + 200 μs. With a total of four conditions (See Figure 1), eight types of stimuli corresponding to the number of consistent pulses, and two onset

[2] All listeners were given the following instructions: "During this portion of the experiment you will be asked to make judgments about the virtual locations of brief sounds. On each trial, your task will be twofold. First, if you hear a single sound, or if you hear two sounds that appear to come from exactly the same location, you are to select the 'I hear one location' button; if you hear two sounds that appear to come from two different locations or more than two, you can press the 'I hear one locations' button. Your second task, simultaneous with the first, is to touch where you feel best corresponds to the location of the sound you heard. For example, if you hear a sound at one location far to the right, choose a location on the horizontal bar at its right edge. If you hear two locations, touch the 'I hear two locations' button, and then choose their locations with the most dominant one in the first bar and the next dominant one in the second bar."

ITDs (+800 and -800 μs), tested at 20 repetitions for each, this gave a total of 1280 trials per listener.

IV. Results

A. Auditory Object Formation

AOF was indexed using the proportion of “primary sound sources” reported out of the total number of responses on each condition. Figures 2A and 2B display combined data for the "Same-side" and "Opposite-side" conditions, for both NH and BiCI listeners, respectively. These figures show the mean and standard deviation for the proportion of sounds reported as the “primary sound location;" a higher value on this figure would mean that listeners reported very few secondary sound locations. A two-way repeated measures ANOVA was conducted to examine the effect of Condition (Same-side vs. Opposite-side condition) and the NumOnsets (number of consistent ITDs) in the stimulus. For NH listeners, Mauchly’s test indicated that the assumption of sphericity had been violated for the main effects of NumOnsets, but not for Condition. Generally, at least three conditions are needed for sphericity to be violated, therefore when using a variable that has only two levels, sphericity is already met. Using the corrected Greenhouse-Geisser estimates of sphericity (ε=0.33 and 1.0, respectively), we found a significant main effect of NumOnsets on the proportion of “primary” locations reported [$F(1.99, 5.97) = 98.69$, $p<0.05$]. There was also a significant main effect of Condition [$F(1, 3) = 57.23$, $p<0.05$] and an interaction of (NumOnsets)*(Condition), [$F(1.17, 3.5) = 13.37$, $p<0.05$]. Pairwise comparisons for NumOnsets revealed that with 1, 25, 29, or 30 consistent ITDs, the proportion of “primary” sound locations was not significantly different from each other. However, the proportion observed at those values (1, 25, 29, or 30) was significantly different from the proportion of primary sources observed with 5, 10, and 15 consistent ITDs. Therefore, having

either an entire stimulus or just one pulse with a consistent ITD did not produce a difference in the perceived number of auditory objects. This result suggests that NH listeners exhibited a change in the proportion of primary sound sources as a function of the NumOnsets, and this was dependent on whether the OnsetLoc was on the same or opposite side of the head as DynamicLoc.

For BiCI listeners, Mauchly's indicated that the assumption of sphericity was violated for both main effects. When using the corrected Greenhouse-Geisser estimates of sphericity (ε= 0.27 for NumOnsets and 1.0 for Condition), all effects are reported with an alpha of 0.05. There was a significant main effect of NumOnsets, [$F(1.8, 12.6) = 11.57$, $p<0.05$] and Condition, [$F(1, 7) = 20.75$, $p<0.05$]. Finally, there was a significant interaction of Condition and NumOnsets [$F(2, 14.05) = 10.5$, $p<0.05$]. Pairwise comparisons for the NumOnsets revealed that, when NumOnsets was just 1, the proportion of “primary” sound locations reported was not significantly different from the proportion at any other value (5, 10, 15, 20, 25, 29, and 30). The results regarding the proportion of “primary” sound locations reported in BiCI listeners suggest that regardless of whether ITD cues were consistent or dynamic, and regardless of whether the relationship of the consistent vs. dynamic ITDs was on the same or opposite side of the head, listeners had a propensity to report more “primary” sound locations.

B. Lateralization

Average lateralization responses for NH and BiCI listeners are shown in Figures 3A and 3B, respectively; each figure depicts the average lateralization responses of the primary and secondary sound sources reported. Individual BiCI and NH data are shown in Figures 4A and 4B, illustrating the considerable variability observed across each group of the listeners. In the remainder of this section, analyses of lateralization responses are described only with respect to

the primary sound source. Secondary sources responses will be disregarded in the remainder of the analyses. A logistic regression was used to interpret the impact of three stimulus factors (OnsetLoc, DynamicLoc, and NumOnsets) on lateralization responses of the primary sound source. These factors served as predictors in the model. Because NH and BiCI listeners exhibited large variability, a subject-specific model was carried out for each listener. Considering that lateralization responses were bounded to arbitrary units from 0 to 1, a logit transform was applied to all lateralization responses (Eq. 2). This transformation allows the variable to be unbounded such that parameter estimates determined from the model can be accounted for if they fall outside the 0-to-1 range.

Equation (2):

$$logitacc = (Rightward\ OnsetLoc) * Ln(Response/(1 - Response)) + (Leftward\ OnsetLoc) * Ln((1 - Response)/(Response)).$$

Table III-A shows all effects for all predictors for each BiCI listener. All eight BiCI listeners exhibited a significant effect of NumOnsets. Of the eight listeners, five also exhibited a significant effect of DynamicLoc, while three listeners (IAJ, IBF, and IDH) did not show an effect of DynamicLoc. Finally, all but one listener (IBY) exhibited a significant effect of OnsetLoc. Interestingly, an interaction for OnsetLoc*NumOnsets was non-significant for four out of eight listeners (IDH, ICI, ICJ, and IBK); this result seemed to be unrelated to observations of the individual predictors alone. These results suggest that consistency in the ITD, revealed by the NumOnsets predictor, is important for accurate lateralization. Unsurprisingly, the OnsetLoc predictor also influenced accurate lateralization. Conversely, accurate lateralization was directly related to the impact of the DynamicLoc predictor for only five out of eight listeners and not for three of the eight listeners. The large significance determined for the DynamicLoc was an odd

finding, however, one possible explanation is that BiCI listeners achieved accurate lateralization by ignoring the DynamicLoc interpreting it as noise.

Although only four NH listeners were tested, they each showed a significant effect of NumOnsets. Three out of four listeners showed a significant effect of the OnsetLoc, and two out of four listeners showed a significant effect of the DynamicLoc. Model effects and p-values for all NH listeners are shown in Table III-B. This result implies that the number of consistent ITDs plays a dominant role accurate lateralization when there are consistent vs. dynamic ITDs in a signal, regardless of the origin of sources.

A secondary aim in this study was to investigate the effect of the number of consistent ITDs on lateralization responses. Parameter estimates (shown in Figure 5A for BiCI listeners) determined for each listener and each predictor are informed by the intercept value, which correspond to the reference condition (see Table IV-A). In this model, the reference conditions were: OnsetLoc= +800 µs, DynamicLoc= +800 µs, and NumOnsets= 30. For example, listener IBK had an intercept of -2.72. Therefore, all lateralization responses corresponding to the reference condition have a value of -2.72 on the unbounded lateralization scale. However, comparing the intercept value to an estimate for a condition where OnsetLoc= -800 µs, DynamicLoc= +800 µs, and NumOnsets= 30. The estimate was 0.666, indicating a change in lateralization responses in the opposite direction, which implies that the OnsetLoc (i.e., direction of the consistent ITDs) was perceived to the left. All other listeners similarly had a negative intercept with a corresponding OnsetLoc estimate (representing the Left ITD) that shifted in the positive direction, except for listener IDH. Listener IDH, though not significant, exhibited a greater negative estimate (-2.68) for the OnsetLoc predictor than to their intercept value (-1.73), indicating that responses to the left-ward ITDs were incorrectly lateralized towards the right.

To understand how many consistent ITDs are required for accurate lateralization of the onset ITD, individual parameter estimates for each level of the NumOnsets variable were examined. Figure 5 shows the number of consistent pulses that each listener required before accurate lateralization of the primary sound source worsened, meaning that responses were no longer lateralized in the direction of the ITD. Again, the intercept value represents a condition where the OnsetLoc is a right-ward ITD; however, the estimate for the OnsetLoc value in the model represents the estimate when the consistent ITD was to the far left. Therefore, if listeners correctly lateralize sounds based on the NumOnsets, the large positive estimates indicate that lateralization responses deviated from what would be accurate responses as a function of the number of consistent ITDs. Table IV-A shows estimates for each level of the NumOnsets predictor for each BiCI listener; red highlights show estimates where $p>0.05$. Here we see that, on average, worse estimates (indicated by a large positive value) occur when NumOnsets equals 1, 5, or 10, suggesting that BiCI listeners require more than a single pulse for accurate lateralization of the consistent onset ITD (OnsetLoc). This contrasts with the parameter estimates observed for NH listeners (Table IV-B and Figure 5B). On average, conditions where NumOnsets equaled only 1 or 5 were sufficient to cause a deviation from accurate lateralization. For all remainder of the NumOnsets conditions, estimates were not significant.

V. Discussion

Results from the present study showed that BiCI listeners heavily rely on the number of consistent ITDs in a low rate pulse train for accurate lateralization and object formation. Specifically, BiCI listeners require at least five or more consistent ITDs from the onset of the stimulus. The present study implemented conditions which in NH listeners result in a binaural phenomenon known as ITD onset dominance (Hafter and Buell, 1990; Rakerd and Hartmann,

2005; Stecker and Brown, 2010; Stecker and Hafter, 2002). Here, a similar paradigm was used to determine the extent to which listeners with BiCIs also utilize ITD onset cues. Further, this study was designed to investigate whether lateralization and AOF in BiCI users are either facilitated or interrupted by, a salient, consistent onset ITD in a low-rate stimulus. We tested NH listeners to be able to gauge the extent to which performance with electric hearing deviates from, or resembles that with acoustic hearing. Results will fill a gap in our understanding of why BiCI users perform significantly worse than NH listeners in noisy environments, because the stimuli used here were designed to resemble temporal variations of auditory signals in noisy environments.

The results from the present study on AOF suggest that, for BiCI listeners, regardless of where the dynamic ITDs originated, the proportion of primary sources reported by listeners remained very high. This result is unlike that observed in NH listeners where the proportion of primary sources in relation to secondary sources decreased as a function of the consistent number of pulses (Figures 2A and 2B). Though AOF has not been extensively studied with respect to ITD cues, there is some behavioral and electrophysiological evidence in NH listeners which suggests that listeners can segregate sounds based on harmonicity or location cues alone. One study investigated NH listeners' ability to detect a target vowel in the presence of the same or different ITDs. This study found that small relative ITD differences (±45 us) were effective at segregating a harmonic from a vowel (Darwin and Hukin, 1999); however, large relative ITD differences were ineffective. Our findings are consistent with that observation, NH listeners could perceive more than one sound source based on a dynamically-changing ITDs while BiCI listeners could not. Furthermore, this effect was specifically related to the number of consistent

ITDs in the signal. This suggests that any variation in the timing of the clinical devices across the ears can go undetected if they are not consistent and salient over time.

Recent studies have identified a new ERP component referred to as the object-related negativity (ORN); the amplitude of the ORN correlates with listeners' likelihood of reporting two simultaneous auditory objects (Alain et al., 2001; Alain and Izenberg, 2003). Using these ERP measures, one study found that when mistuned harmonics were played to listeners in different locations, a significant ORN was observed in cases where sounds were segregated based on the location alone (McDonald and Alain, 2005). The behavioral data showed that listeners reported perceiving more than one concurrent sound only when there was mistuning in the harmonics, regardless of the spatial separation. ERP data suggest that segregation based on sound location cues still plays a role in detecting concurrent sources, but only during active listening. In the context of our findings, we determined that BiCI listeners, unlike NH listeners, rarely report secondary sources. This outcome was due to a lack of segregation in the dynamically-changing vs. consistent, ITD-based signal. While the ERP study postulated that NH listeners tend to benefit in a source segregation task when location cues are present during active listening, it would be reasonable to assume that when BiCI listeners wear their clinical devices a low-rate signal will still impair their ability to detect different source locations if they are not actively listening. Furthermore, this impairment would be especially apparent if the ITD is varying over time. Therefore, in addition to any spectral information, consistency in the ITD of a low rate signal could potentially provide information about differences between two sources.

Lateralization results from the present study were found to be heavily weighted by the number of consistent ITDs. BiCI listeners required at least five or more consistent ITDs from the onset of the stimulus to lateralize the onset ITD (OnsetLoc). There is some evidence that onset

dominance in BiCI listeners operates in a similar fashion to that observed in NH listeners. Work from van Hoesel (2008) showed that, when electrical pulse trains presented to BiCI listeners at 100 pps had varying ITD cues on every pulse, each pulse made a substantial contribution to overall lateralization performance. When the rate was increased to 300 and 600 pps the onset was weighted much more heavily than the later pulses. Furthermore, the relative weighting of an ILD cue showed less onset dominance than an ITD cue. In the context of the current study, we have shown that BiCI listeners' lateralization performance is impacted by information in each electric or acoustic pulse beginning from the onset of the signal. However, in addition to finding an effect of the number of consistent ITDs, we determined that where the consistent ITD originates, played a role in accurate lateralization. This result suggests that when wearing clinical processors, an electric pulsatile stimulus needs to have both consistency and a salient onset ITD for accurate lateralization, whereas the location of the dynamic ITD may not be important. In the context of a processing strategy, a combination of high rates (to relay speech) and low rates (to relay ITDs) could theoretically be used to relay ITD information, however, the data shown here would suggest that ITD needs to be stable enough to lead to good lateralization.

Dominance of onset ITDs have not been extensively studied in listeners with BiCI, and the observed effect of onset dominance with electric hearing could be explained by some evidence that shows that with only a single pair of pulsatile stimuli BiCI listeners, also are able to prioritize the ITD in the first pulse over ITD in the second pulse (Brown et al., 2015). Studies performed in NH listeners have suggested that ability of the auditory system to prioritize onset ITDs is related to the phenomenon of "binaural adaptation," whereby temporal relationships of later-arriving ITDs in pulsatile are similarly suppressed or disregarded (Hafter and Buell, 1990; Kawashima and Sato, 2012; Stecker and Hafter, 2002). In fact, as mentioned

earlier, there is some evidence that BiCI listeners weight ITDs more in first pulse than in the remainder of the signal (van Hoesel, 2008). Taken together, the findings from this study add more evidence to the notion that BiCI listeners integrate low rate ITDs similar to NH listeners, suggesting that the underlying binaural mechanisms for onset dominance still exist for this population.

One caveat in the current study design is that the onset ITDs used to assess the impact of consistent vs. dynamic ITDs (±800 for BiCI listeners and ±600 for NH listeners) were fairly large. In fact, these ITD values were much greater that the ITDs at which each listener could discriminate stimuli presented to the left vs. right (i.e., just-noticeable difference thresholds). Real-world sounds may not have ITDs this large, therefore the effects we see might diminish with smaller ITDs that do not perceptually extend to the far left or far right. We chose to use supra-threshold ITDs because they are informative about the effective range of ITDs that can be impacted by varying temporal information in the signal. Future studies could be aimed at determining the impact of onset ITDs that span the entire range of the head, and across the electrode array.

VI. Conclusions

Results from the present study have revealed that when a low-rate pulsatile stimulus, imposed with an ITD, has both consistent ITDs and dynamic ITDs, more consistency in the signal yields a more salient onset cue and better lateralization and object formation. While NH listeners need a minimum of five consistent pulses for accurate lateralization, BiCI listeners require *at least* five pulses for accurate lateralization. Object formation appeared to be dependent on the number of consistent pulses, but only for NH and not BiCI listeners. These results have important implications for low rate strategies aimed at restoring ITD sensitivity to BiCI listeners.

VII. Tables and Figures

Listener ID	Left Electrode No.	Right Electrode No	JND (μs)	Left CUs	Right CUs
IBK	14	13		240	230
ICB	4	4	199.22	203	204
ICI	4	6	140.95	181	162
ICJ	12	12	160.1	171	159
IBF	12	12	38.0	218	219
IBY	4	7	96.71	195	204
IDH	12	12	N/A	199	197
IAJ	16	19	268.7	179	209

Table I: Table of eight post-lingually deafened adult BiCI listeners. Shown are the electrode number tested in each ear and the sensitivity, or just-noticeable-difference (JND), of that electrode pair to ITDs (in microseconds). The two right-most show the loudness-balanced current units (CUs) played in the left and right ears. Listener IDH was never tested in a discrimination task and therefore did not have a JND threshold.

	Normal-hearing Listeners		**Bilateral cochlear implant listeners**	
Stimulus Type	Gaussian envelope tone, carrier frequency 4 kHz		Electrical pulse train delivered to an interaural pitch-matched pair.	
Rate	100 pulses per second		100 pulses per second	
Duration	300 ms		300 ms	
NumOnsets	1, 5, 10, 15, 25, 29, or 30		1, 5, 10, 15, 20, 25, 29, or 30	
Direction of OnsetLoc	-600 µs	+600 µs	-800 µs	+800 µs
Location of DynamicLoc	Same-side: -450	Same-side:+450	Same-side:-800	Same-side:+800
	Opposite side:+450	Opposite-side:-450	Opposite-side:+800	Opposite-side:-800

Table II: Stimulus parameters used for each group of listeners.

Model Effects (BiCI listeners)						
ID	Condition	df	Mean Square	F	Sig	Model R-squared
	OnsetLoc	1	214.603	139.757	<<0.05	
	DynamicLoc	1	0.533	0.36	0.549	
IAJ	NumOnsets	7	17.698	11.526	<<0.05	0.196
	OnsetLoc	1	7.786	7.723	0.006	
	DynamicLoc	1	7.942	7.878	0.005	
IBK	NumOnsets	7	51.6	51.86	<<0.05	0.306
	OnsetLoc	1	42.324	105.546	<<0.05	
	DynamicLoc	1	1.135	2.831	0.093	
IBF	NumOnsets	7	17.862	44.542	<<0.05	0.346
	OnsetLoc	1	2.296	3.115	<<0.05	
	DynamicLoc	1	2.057	2.791	0.015	
IBY	NumOnsets	7	13.588	18.432	0.002	0.143
	OnsetLoc	1	5.64	6.765	<<0.05	
	DynamicLoc	1	5.027	6.03	<<0.05	
ICB	NumOnsets	7	34.416	41.277	0.02	0.353
	OnsetLoc	1	15.07	3.95	0.047	
	DynamicLoc	1	18.865	4.945	0.027	
ICJ	NumOnsets	7	27.03	7.085	<<0.05	0.105
	OnsetLoc	1	19.427	14.01	<<0.05	
	DynamicLoc	1	17.217	12.417	<<0.05	
ICI	NumOnsets	7	93.488	67.422	<<0.05	0.334
	OnsetLoc	1	152.752	141.161	<<0.05	
	DynamicLoc	1	2.803	2.591	0.052	
IDH	NumOnsets	7	34.074	31.489	<<0.05	0.306

Table III-A: Effects for predictors in the logistic model shown for each BiCI listener. All effects were significant; those that were not significant are shown in red text.

Model Effects (NH listeners)						
ID	Condition	df	Mean Square	F	Sig	Model R-squared
	OnsetLoc	1	1308.613	139.757	<<0.05	
	DynamicLoc	1	46.832	0.36	0.082	
TGQ	NumOnsets	6	1.279	11.526	<<0.05	0.573
	OnsetLoc	1	80.642	33.375	<<0.05	
	DynamicLoc	1	31.058	12.816	<<0.05	
TRC	NumOnsets	6	83.036	34.263	<<0.05	0.398
	OnsetLoc	1	3.36	3.19	0.075	
	DynamicLoc	1	0.772	0.732	0.392	
TTC	NumOnsets	6	78.555	74.574	<<0.05	0.511
	OnsetLoc	1	183.292	348.843	<<0.05	
	DynamicLoc	1	37.781	71.863	<<0.05	
TVU	NumOnsets	6	38.368	72.98	<<0.05	0.621

Table III-B: Effects for predictors in the logistic model shown for each NH listener. All effects were significant; those that were not significant are shown in red text.

Model Estimates for BiCI Listeners								
Predictor	**IAJ**	**IBF**	**IBK**	**IBY**	**ICB**	**ICI**	**ICJ**	**IDH**
OnsetLoc=RightITD (Intercept)	-0.917	-2.078	-2.721	-1.547	-2.769	-2.951	-2.337	-1.734
OnsetLoc=LeftITD	-0.937	0.617	0.66	0.448	0.416	0.787	-0.028	-2.68
NumOnsets=1	1.678	1.042	2.007	1.414	2.404	2.169	2.104	1.13
NumOnsets=5	0.661	0.717	1.929	1.109	1.513	0.81	1.133	0.727
NumOnsets=10	0.521	0.601	1.835	1.059	0.895	0.44	1.142	0.317
NumOnsets=15	0.401	0.574	1.769	0.99	0.611	0.186	1.532	0.217
NumOnsets=20	0.182	0.432	1.711	0.887	0.302	0.211	1.6	0.147
NumOnsets=25	0.228	0.395	1.335	0.702	0.281	0.067	0.323	-0.172
NumOnsets=29	-0.182	0.329	0.518	0.147	0.045	-0.083	0.9	-0.005
NumOnsets=30	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table IV-A: Logistic regression model estimates for predictors of OnsetLoc and NumOnsets for all BiCI listeners. Estimates in red denote values that had a p-value greater than 0.05.

Predictor	**TTC**	**TVU**	**TRC**	**TGQ**
OnsetLoc=RightITD (Intercept)	-3.025	-0.947	-3.637	-1.918
OnsetLoc=LeftITD	0.728	-1.364	0.746	-0.101
NumOnsets=1	2.709	2.188	2.612	1.882
NumOnsets=5	0.403	0.137	1.733	0.373
NumOnsets=10	0.036	0.027	1.024	0.241
NumOnsets=15	0.081	-0.15	0.747	0.06
NumOnsets=25	-0.002	-0.092	0.501	0.155
NumOnsets=29	0.002	-0.232	-0.032	0.058
NumOnsets=30	N/A	N/A	N/A	N/A

Table IV-B: Logistic regression model estimates for predictors of OnsetLoc and NumOnsets for all NH listeners. Estimates in red denote values that had a p-value greater than 0.05.

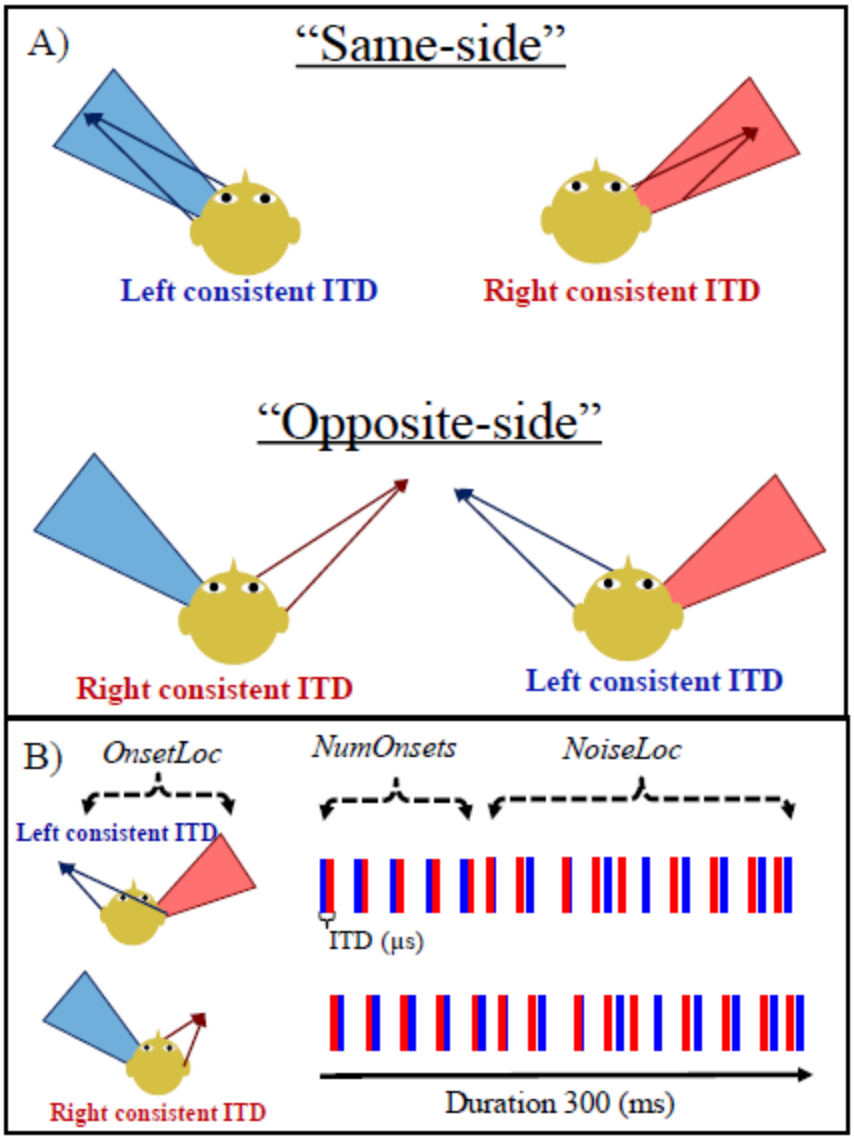

Figure 1: Panel A illustrates the four conditions tested for each combination of the OnsetLoc and DynamicLoc. Solid lines depict the OnsetLoc direction fand the shaded triangle depicts the DynamicLoc direction. Panel B shows example stimuli for the two "Opposite side" conditions. Vertical red and blue lines depict a biphasic pulse in an electrical pulse train; red lines depict the right-ear stimulus, and blue line depicts the left-ear stimulus.

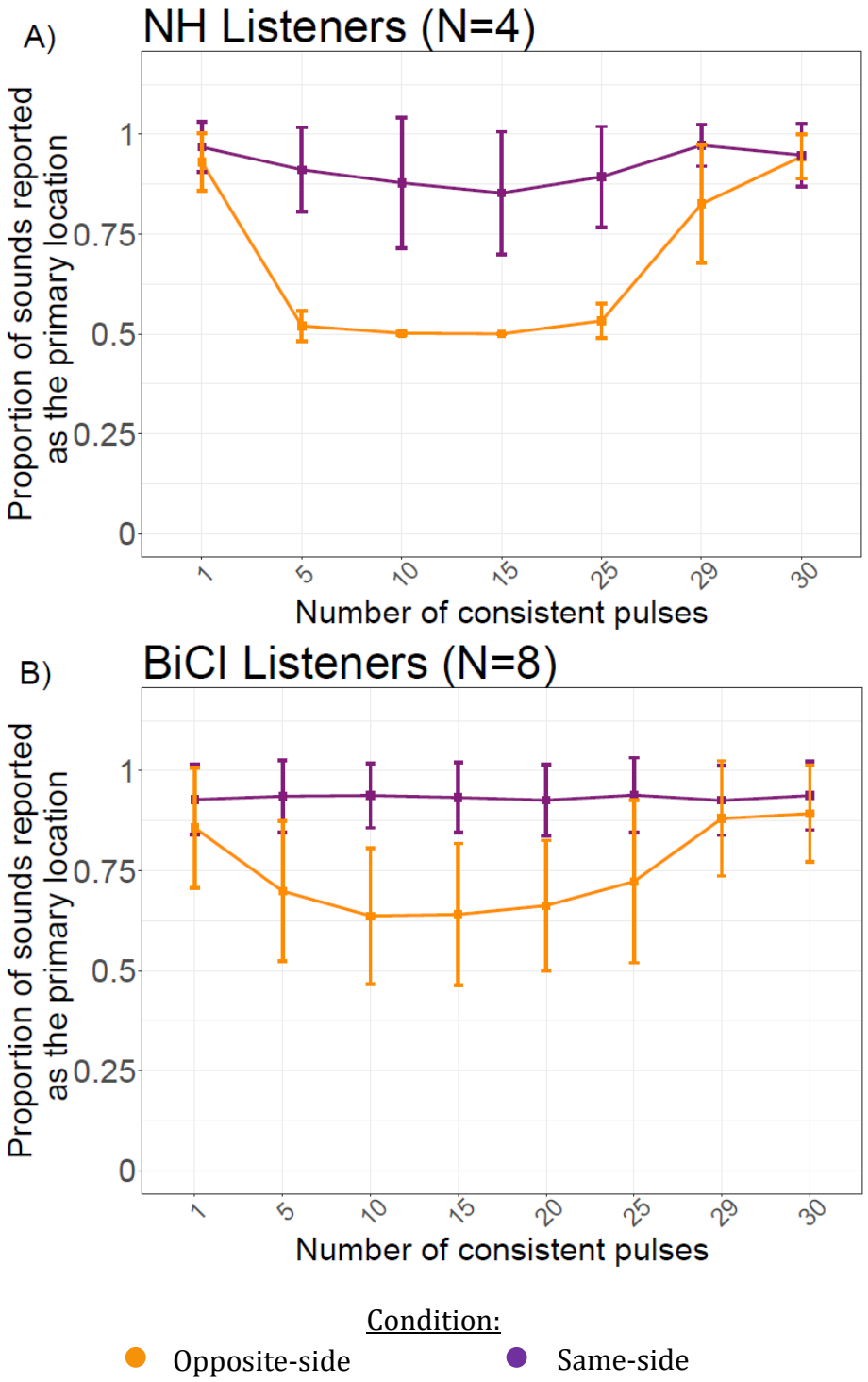

Figure 2: Proportion of responses reported as the primary sound source for both NH (panel A) and BiCI (panel B) listeners. Orange symbols denote the Opposite-side condition and Same-side condition.

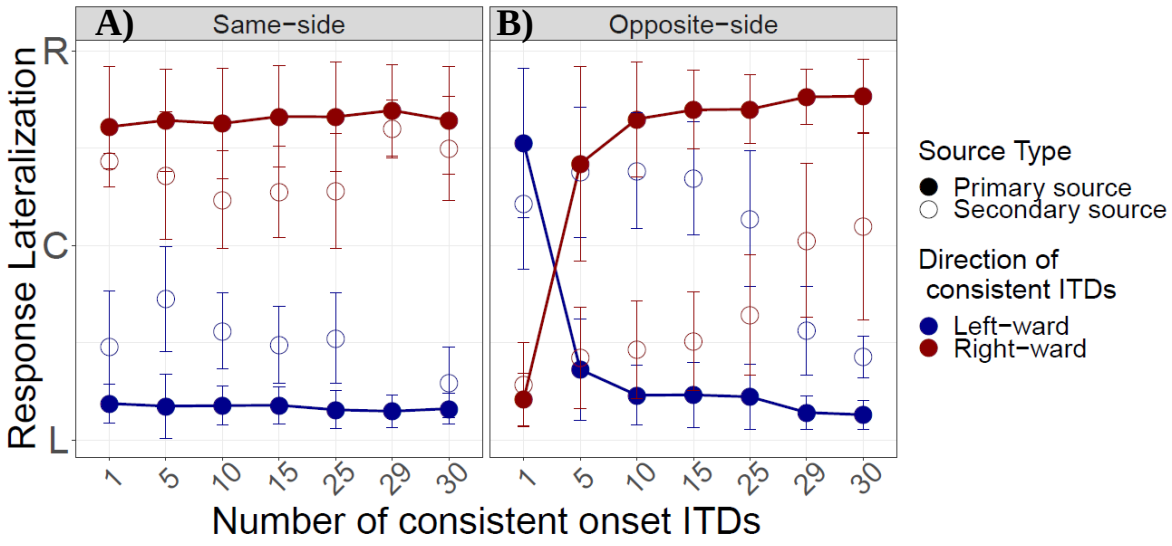

Figure 3A: Average response lateralization for NH listeners when the OnsetLoc and DynamicLoc were on the same side of the head (panel A) and when the OnsetLoc and DynamicLoc were on opposite sides of the head (panel B). ‘R', ‘C', and ‘L' correspond to the range of lateralization on the image of the face with ‘R’ representing the far right edge of the face, ‘C’ as the midline, and ‘L’ representing the far left edge. Solid symbols denote the location of the primary sound source, and open symbols denote the secondary sound source. Blue symbols depict responses when the OnsetLoc was to the left, and red symbols depict responses when the OnsetLoc was to the right.

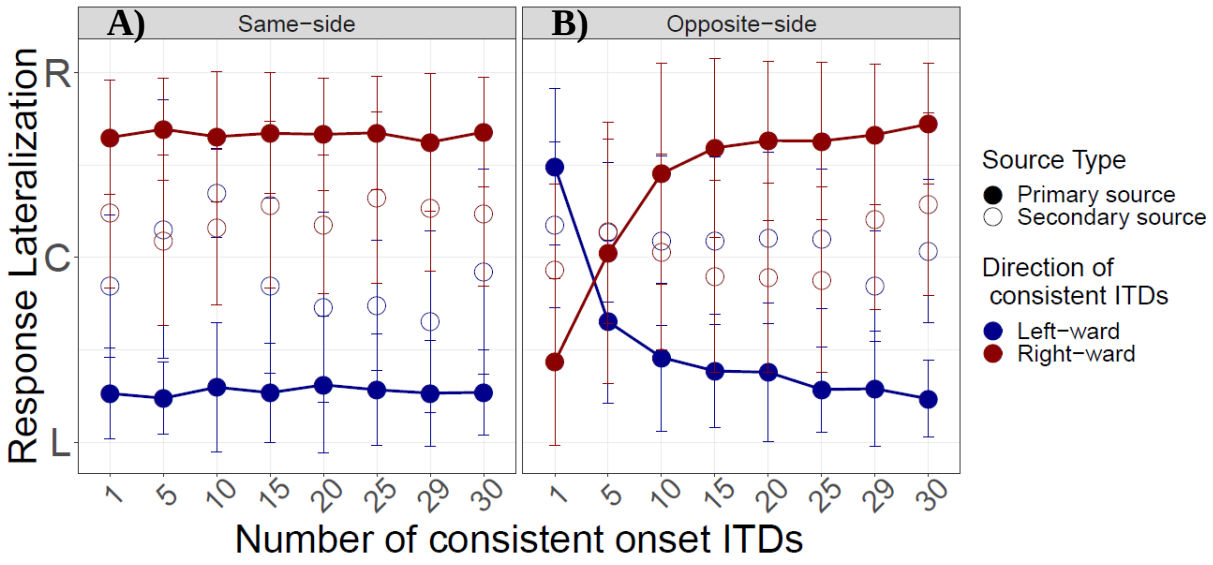

Figure 3B: Average response lateralization for BiCI listeners when the OnsetLoc and DynamicLoc were on the same side of the head (panel A) and when the OnsetLoc and DynamicLoc were on opposite sides of the head (panel B). ‘R,' ‘C,' and ‘L' correspond to the range of lateralization on the image of the face with ‘R' representing the far right edge of the face, ‘C' as the midline, and ‘L' representing the far left edge. Solid symbols denote the location of the primary sound source, and open symbols denote the secondary sound source. Blue symbols depict responses for when the OnsetLoc was to the left, and red symbols depict responses when the OnsetLoc was to the right.

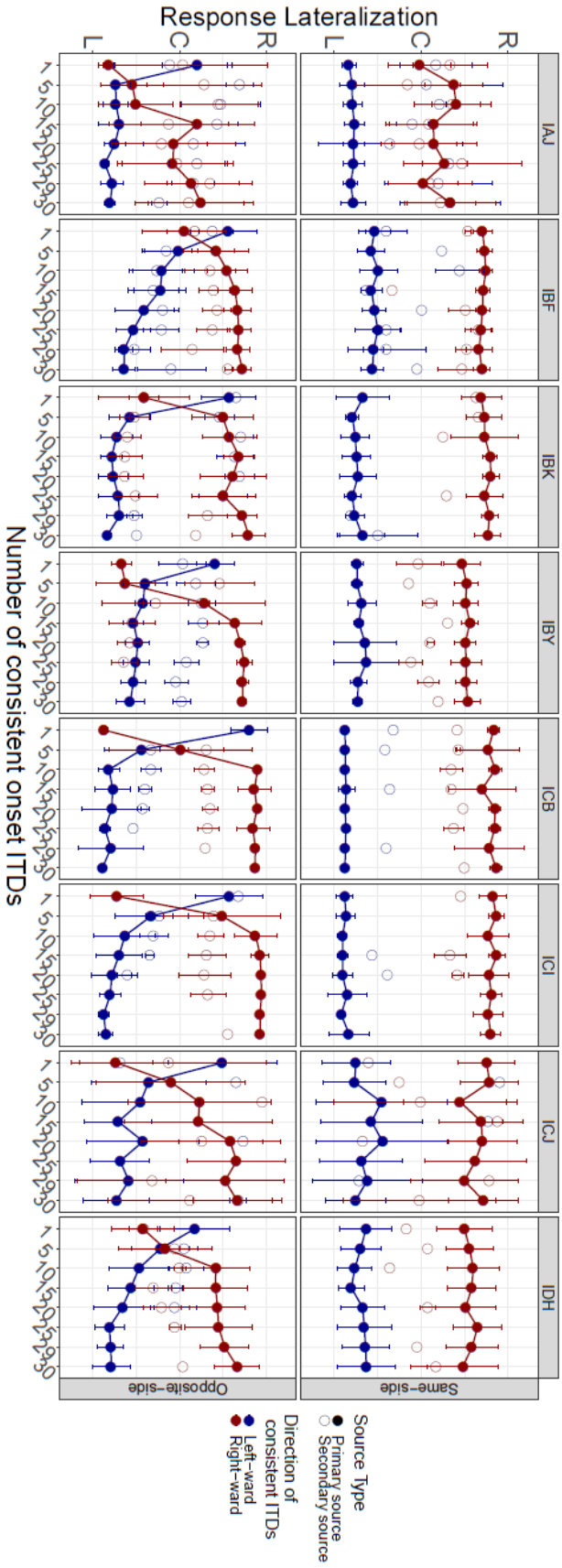

Figure 4A: Individual lateralization responses for all eight BiCI listeners.

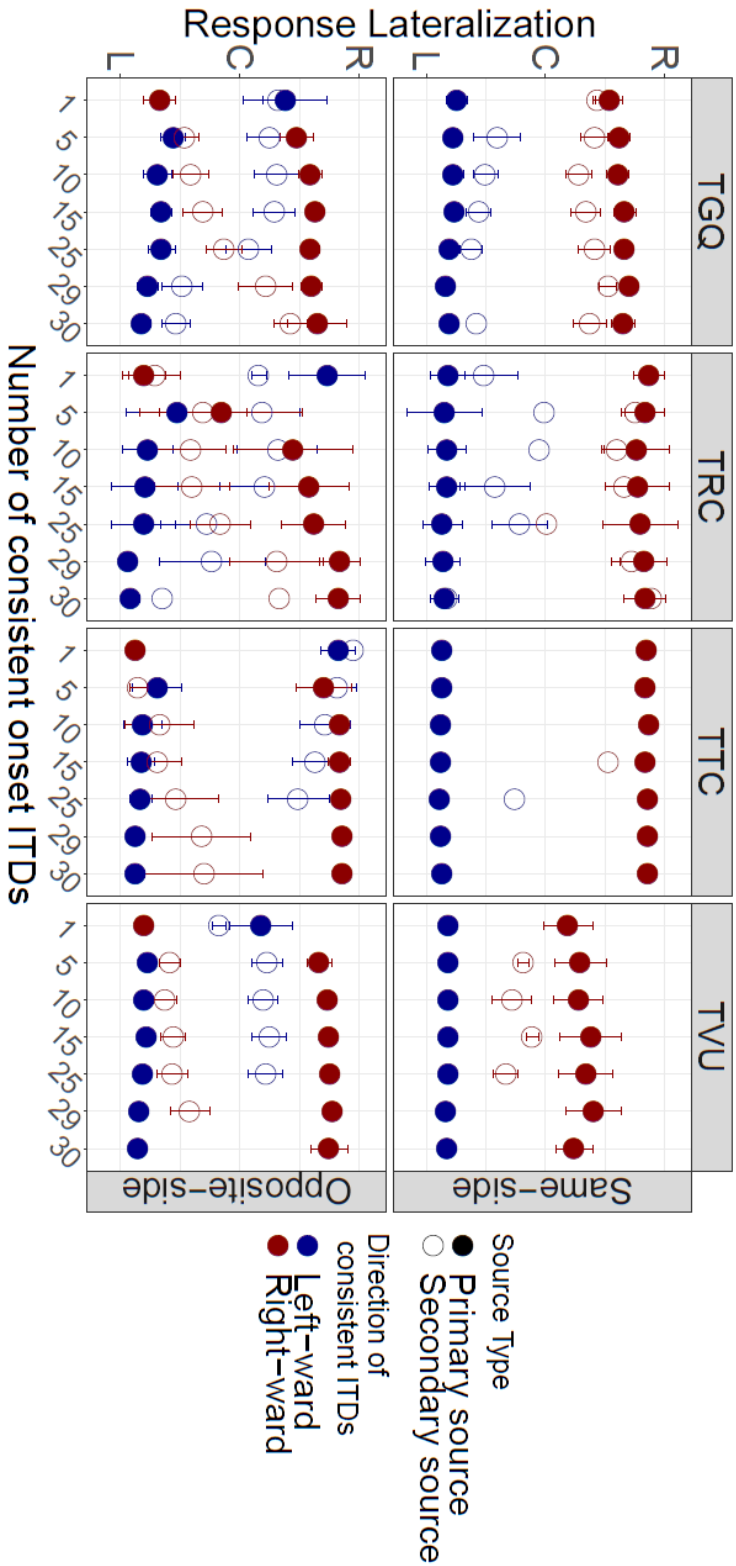

Figure 4B: Individual lateralization responses for all four NH listeners.

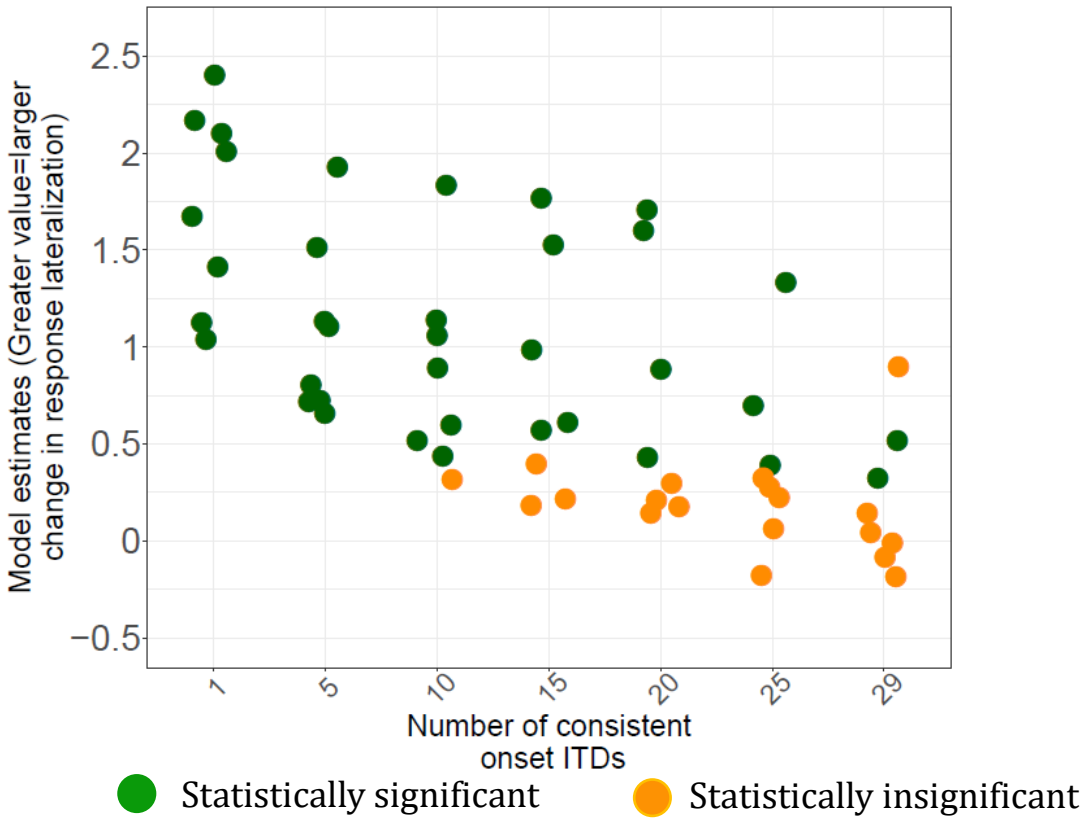

Figure 5A: Parameter estimates plotted as a function of the number of consistent onset ITDs for all BiCI listeners. Values plotted correspond to values shown in Table IV-A. Each data point for every x-axis value represents a single listener. Green symbols depict estimates which were significant and orange depict estimates that were insignificant. A greater estimate value indicates a greater change in the lateralization response from the reference condition (i.e. NumOnsets=30).

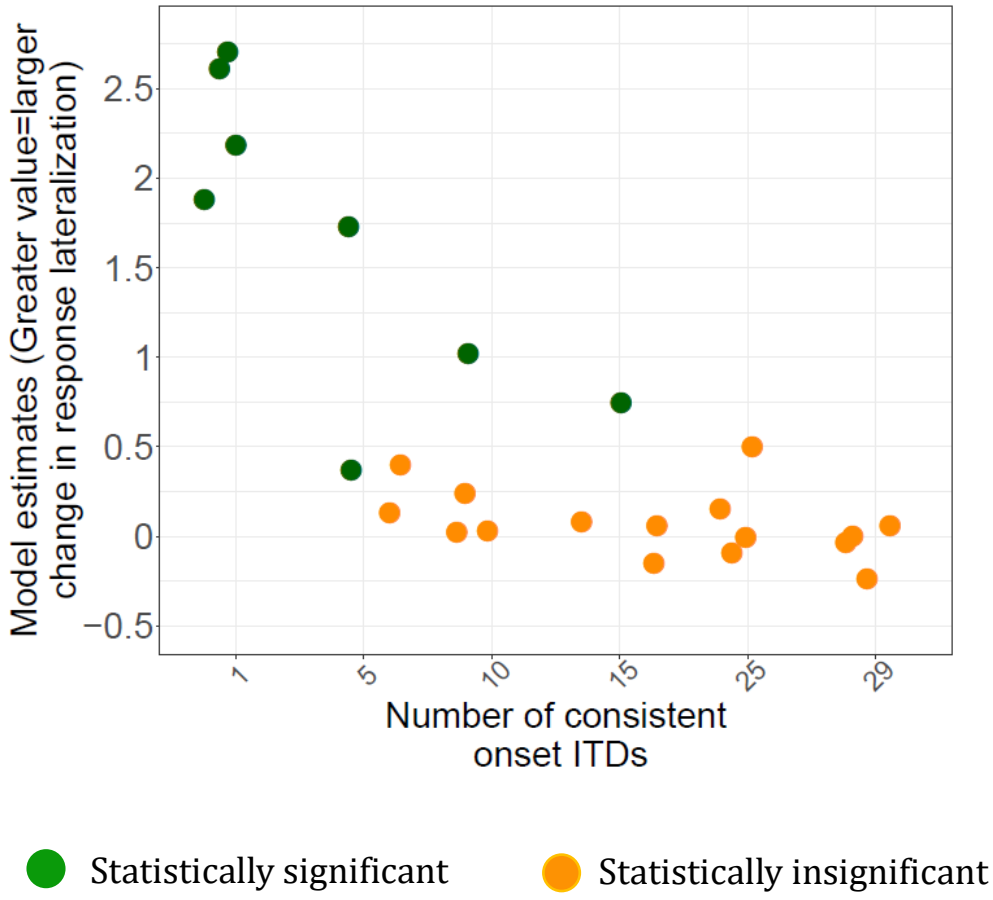

Figure 5B: Parameter estimates plotted as a function of the number of consistent onset ITDs for all NH listeners. Values plotted correspond to values shown in Table IV-A. Each data point for every x-axis value represents a single listener. Green symbols depict estimates which were significant and orange depict estimates that were insignificant. A greater estimate value indicates a greater change in the lateralization response from the reference condition (i.e. NumOnsets=30).

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CHAPTER VI: Summary & Conclusions

The aim of this dissertation was to investigate binaural sensitivity, lateralization, and auditory object formation (AOF) when interaural time differences (ITDs) are preserved with fidelity and presented through research processors to listeners with bilateral cochlear implants (BiCIs). We selected to study BiCI listeners with adult-onset of deafness because these listeners have had exposure to acoustic hearing prior to becoming deaf, and have the highest likelihood of benefitting from ITD cues. While previous work has determined that BiCI listeners with adult-onset of deafness show binaural sensitivity to constant amplitude, low rate stimulation (~100 Hz) with consistent ITDs, these stimulus conditions are not representative of real-life stimuli which are typically more spectrally complex, dynamic, and varying in time. The stimuli created for the studies described in this dissertation take a step towards a more a more realistic representation of the complex signals that BiCI listeners may face in everyday listening situations.

The main objectives of this dissertation were to understand (1) the extent to which ITDs provide a salient cue for lateralization while high rates of stimulation are also provided to represent speech envelope cues (Chapters II and III); (2) whether across-ear conflicting information could interfere with auditory object formation and lateralization (Chapter IV); and (3) whether controlling timing of the onset in a low-rate electrical signal needs to be enhanced in order to increase the saliency of the ITD cue (Chapter V).

In chapter II we investigated whether various mixed-rate configurations, designed to preserve high-rate stimulation for speech understanding and preserve low-rate stimulation for spatial hearing, would result in good ITD sensitivity. We found that ITD thresholds in the mixed rate configurations were comparable to a configuration with low rates only. This finding illustrated the fact that low-rate ITDs have the potential to be usable when high rates are present in a multi-electrode stimulus. The observation that mixed-rate ITDs yield performance

comparable to having only low-rate ITDs suggests that the binaural system of BiCI listeners can extract pertinent cues to achieve ITD sensitivity even when high rate ITD information is presented at the majority of the cochlear locations.

In chapter III, we measured the perceived intracranial lateralization of the same mixed-rate configurations used in chapter II and measured the range of lateralization as an index of appropriate ITD-to-azimuth mapping. The largest ranges were seen in low-rate-only conditions, but, we also found that the mixed-rate configurations yielded improved lateralization ranges when compared to the configuration with only high rates. This finding helps to understand that low-rate stimulation in a mixture of high-rate stimulation does not compromise the ability to hear a coherent sound source in the correct location.

In chapter IV, we combined differences in the interaural rate (i.e. asymmetric rate) with an ITD in order to investigate how well listeners accurately group these two types of cues across the ears into a coherent auditory object. Prior work has demonstrated that BiCI listeners generally have poorer sensitivity to across-ear temporal information than NH listeners. Due to the inability of BiCI listeners to detect across-ear differences in rate and poorer thresholds for ITD sensitivity, we hypothesized that asymmetric rates would be less detrimental to the ability of NH listeners to form objects compared with BiCI listeners, but more detrimental to the BiCI listeners in terms of lateralization performance. We found that when presented with interaural asymmetries in rate, BiCI listeners report hearing “one sound” often responses, this may have contributed to the detrimental performance observed in their lateralization responses. This was opposite of the result observed in NH listeners, where having asymmetric rates produced a perception of “two sounds” more often than for BiCI listeners. These findings imply that future design of signal processing strategies should be aimed at improving binaural hearing in BiCI

users. Specifically, these novel strategies may need to incorporate temporally symmetric across-ear pulsatile stimuli to promote optimal object formation and lateralization in complex auditory environments.

In chapter V, we aimed to understand how varying consistent and dynamic ITDs in a pulsatile stimulus would impact lateralization and auditory object formation in BiCI listeners. Results showed that when consistent and dynamic ITDs originated in opposite hemifields, at least five pulses with consistent ITDs were required for correct lateralization of an auditory object for both NH and BiCI listeners. However, when consistent and dynamic ITDs originated in the same hemifield, listeners more often correctly lateralized the primary auditory object, regardless of the number of consistent ITDs. These findings suggest that BiCI listeners rely on consistent ITDs in a low rate stimulus, just as NH listeners do. Thus, it is possible that BiCI users who became deaf as adults, and had acoustic hearing earlier in life, were able to preserve binaural circuits in a manner similar to those of NH listeners. When electrical stimuli are presented to CI users in a manner that controls ITD cues, BiCI listeners might possess similar binaural mechanisms as NH adults for weighting of onset ITDs. Additionally, because BiCI listeners are only sensitive to ITDs at low rates, a sound coding strategy aimed at relaying binaural cues may need to incorporate consistent ITDs at low rates, in five or more onset pulses, to ensure accurate lateralization and AOF.

The four studies described here were intended to provide proof of concept for how BiCI patients can benefit from an ITD cue that is embedded in more realistic and complex stimulus structures. The majority of prior studies have only revealed that low-rate ITDs presented to a single bilateral pair of electrodes are substantial cues for discrimination and lateralization of ITDs. The studies here have found that a) ITDs in with combined low and high rates across the

electrode array can be sufficient for accurate discrimination and lateralization of ITDs, b) conflicting across-ear temporal information, such as having asymmetric rates, can result in "over-fusing" of auditory objects and result in poor lateralization of ITD, and c) consistent, periodic timing of the ITD is a large contributor in increasing the "saliency" of ITDs such that a coherent object is perceived. The objective of these four studies was to provide important knowledge for the future of cochlear implant research. However, a secondary objective was to uncover whether the binaural system of BiCI users with adult-onset of deafness process ITDs under the same rules for localization and sound source segregation as NH listeners do.

The studies described here have clear limitations. CIs have been remarkable at enabling people with profound hearing loss to understand speech perception, especially in quiet situations. However, speech perception in noisy and complex acoustic environments is highly challenging for CI users, even those with bilateral devices. The stimuli constructed in the present studies did not address questions about speech perception. Restoring ITDs is a just one solution to improving binaural hearing in listeners with BiCIs, such that these listeners can perceive the intended target talker in noisy environments. Therefore, future studies will examine the impact of these stimulus manipulations on speech understanding in noise.