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Mixed stimulation rates to improve sensitivity of interaural timing differences in bilateral cochlear implant listeners

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Normal hearing listeners extract small interaural time differences (ITDs) and interaural level differences (ILDs) 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 [\sim 1000 pulses per-second (pps)] for each electrode in order to provide good speech representation, but sensitivity to ITDs is best at low rates of stimulation (\sim 100–300 pps). Mixing rates of stimulation across the array is a potential solution. Here, 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 was examined. Results showed that ITD sensitivity in mixed-rate configurations when only one low rate electrode was included 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. © 2018 Acoustical Society of America. https://doi.org/10.1121/1.5026618

[MD] Pages: 1428-1440

I. INTRODUCTION

Patients fitted with bilateral cochlear implants (BiCIs) generally show improvements on measures of speech understanding in noise and sound localization when using two implants vs one (Kerber and Seeber, 2012; Litovsky et al., 2006, 2009). 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 highfrequencies, 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, 1992).

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 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 postlingually 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 intersubject 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., 2010), possible surgical trauma (Nadol and Eddington, 2006), and the placement of the electrode array within the cochlea (Stakhovskaya et al., 2007). To

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maximize the benefits of ITDs for BiCI listeners in the freefield, 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 better 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 finetiming 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 electrode arrays in both ears are stimulated at low rates (100 pps), ITD sensitivity can be comparable to a single pair of electrodes stimulated at low rates. In addition, sensitivity to ITDs was better when the set of ITD carrying electrodes was spaced across the electrode array than when all stimulation was 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, highdefinition continuous interleaved sampling (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 $700 \,\mu s$. 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 clock is 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. (2014) showed a much larger improvement in ITD sensitivity with a mixed-rate strategy compared to a strategy with only high rates. 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 \sim 135 μ s. Conversely, when all electrodes received high stimulation rates, speech understanding was good, but as expected, ITD discrimination was poor (average JND \sim 1430 μ s). With mixed stimulation rates, performance on ITD discrimination improved compared to performance where all-high rates were presented across the array (average JND \sim 278 μ s). 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 apicalmost 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.

II. 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 I. All listeners had Cochlear Ltd (Sydney, Australia) implants (CI24 and CI512 family of implants). These devices have 24-electrodes (22 intracochlear 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 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 in 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 μ s), 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 $70 \,\mu s$ 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 pitchmatching 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 pitchmatched 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 II. 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 Fig. 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.

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

Listener ID Age Sex		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	(CI24RE/CI24R (CA))	Hereditary		
			in the right ear after 3 years		•		
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 II. Pitch-matched electrode pairs. Summary of pitch-matched electrode pairs for all listeners. Also shown are comfortable (C) levels in CUs for each electrode and microamperes (see Cochlear Ltd., 2006, for details on how CUs are converted to microamperes). These are loudness-balanced CUs that were determined for all mixed rate multi-electrode configurations.

								Electrode Lo	ocation							
	Apical				Mid-Apex			Mid			Mid-Base			Basal		
ID	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 R5	,	150/ 262.7 152/ 272.3		•	•		206/ 722.3 205/ 709.3	•			•		•	167/ 357.1 175/ 412.6	
IBK		228/ 1012.8 220/ 930.1	. ,	L11	227/ 992.5	210/703.4	L14	227/ 992.5 215/ 849.7	213/747.4	L15	230/ 1054.7	212/732.4	L18	229/ 1033.5 205/ 709.3	212/732.4	
IBQ	L8 R1	223/ 981.8 220/ 861.3	185/ 494.3 196/ 529.7		215/ 849.7 212/ 732.4	,		207/ 735.4 210/ 703.4	•		•	•		213/ 819.6 212/ 732.4	•	
IBY	L4 R7	212/ 804.9 204/ 696.6	170/ 377 178/ 435.6	L8 R11	213/ 819.6 214/ 834.5	,		222/ 964.3 217/ 881	,		202/ 671.9 216/ 865.2	. ,		204/ 696.6 201/ 659.9	188/ 521.8 182/ 468.2	
ICB	L4 R4	222/ 964.3 221/ 878.9	172/ 390.8 190/ 469.1		•	,		237/ 1264.3 234/ 1143.7			•	,		230/ 1114.1 220/ 861.3	208/ 748.8 202/ 598.1	
ICD	L4 R2	179/ 443.5 193/ 498.5	161/320 177/360.5	L8 R6	•	•		189/ 531.3 201/ 586.1	•		•	. ,		198/ 625.1 194/ 508.7	176/ 420.1 194/ 508.7	
ICI	L2 R4	178/ 435.6 156/ 292.8	132/ 189.8 120/ 152.8		174/ 405.2 171/ 383.9	127/ 173.4 132/ 189.8		181/459.8 170/377			180/ 451.6 172/ 390.8	134/ 196.8 134/ 196.8		155/ 287.5 145/ 240	134/ 196.8 132/ 189.8	
ICJ	L4 R6	180/ 451.6 168/ 363.6	161/ 320.4 153/ 277.3		179/ 443.5 175/ 412.6	157/ 298.1 159/ 309.1		175/412.6 172/390.8			,	.,		174/ 405.2 142/ 227.3	142/ 227.3 143/ 231.5	
ICP	L4 R8	194/ 581.5 196/ 602.9	145/ 240 165/ 344.4	L7 R11	,	,		146/ 244.4 166/ 350.7	.,		140/ 219.3 156/ 292.8	-,		117/ 144.7 129/ 179.8	115/ 139.6 117/ 144.7	
ICS	L4 R5	187/ 512.5 186/ 432.6	173/ 398 165/ 282.7	L8 R7	•	•		175/412.6 197/540.5	•		•	•		•	167/ 357.1 180/ 383.1	

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.

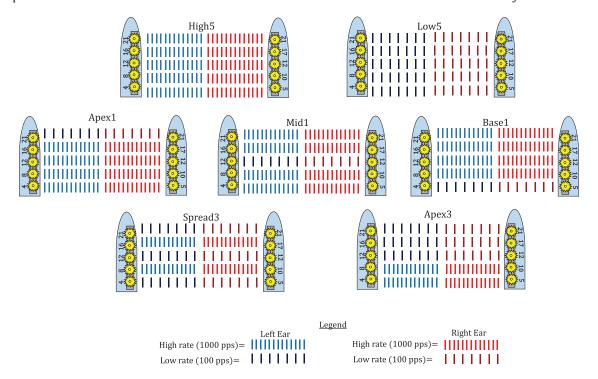


FIG. 1. A schematic depicting the seven testing configurations used in the study. Using listener IBF as an example, the multi-electrode configurations reflect their pitch-matched electrodes of a Cochlear array, where lower numbered electrodes (i.e., electrode 4) are basal and higher numbered electrodes (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 (1000 pps).

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), hence 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 was 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.

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 = $\sim 146 \,\mu\text{As}$), Right = $\sim 146 \,\mu\text{As}$; Mid-Apex, Left = \sim 247 μ As, Right = \sim 253 μ As); Mid, Left $= \sim 250 \,\mu\text{As}$, Right $= \sim 260 \,\mu\text{As}$; Mid-Base, Left $= \sim 109 \,\mu\text{As}$, Right = \sim 71 μ As; Basal, Left = \sim 86 μ As, Right = \sim 60 μ As. These values were determined by averaging the microamperes across listeners in Table II, 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 two-interval, twoalternative forced-choice paradigm with a 300 ms interstimulus 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 μ s 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 was 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 leftleading and 20-right leading trials. The experiment was conducted in blocks, where each block consisted of ten trials at each ITD (five left-leading and five 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 Fig. 1. JNDs were first measured in the Low5 and High5 configurations to establish the range of performance.

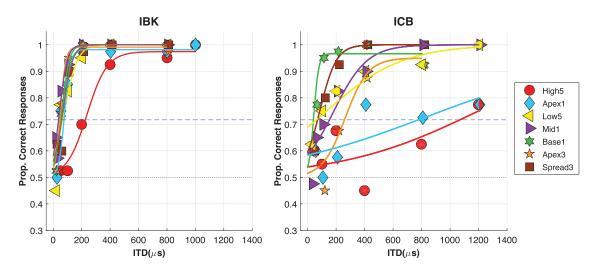


FIG. 2. Psychometric functions for two listeners (IBK and ICB) in all tested configurations. Proportion correct is plotted as a function of ITD (μ s) and the model fits for each tested configuration are shown in different colors. The dashed horizontal line denotes the 70.7% mark and the dotted horizontal line denotes the 50% mark.

TABLE III. 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-fitted model are different. For some conditions, the deviance was not estimated because a threshold was not measured. This is indicated by a dash.

	Estimated bias(c) and goodness-of-fit (D)													
	High5		Apex1		Mid1		Base1		Apex3		Spread3		Low5	
Listener ID	С	D	С	D	С	D	С	D	С	D	С	D	С	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

Subsequently, performance was measured for Apex1, Mid1, Base1, Spread3, and Apex3 in a pseudo-random manner.

III. 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 III). 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 loglikelihood 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 ($\alpha = 0.05$). Additionally, biases in all psychometric functions were calculated, values with biases are considered to be greater or less than zero (Macmillan, 2002). Bias values are reported as c in Table V, and were typically small. Hence, it can be concluded that our psychometric functions fit the data well, with listeners showing very little bias.

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 $\sim 700 \, \mu s$, 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 IV) 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 V. Using Cohen's scale for interpreting the

TABLE IV. ITD JNDs for all listeners under all seven configurations. Missing values indicate JNDs that could not be determined.

	ITD thresholds (μ s)											
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 V. Effect sizes for pairwise comparisons of all configurations.

	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

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 for 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), indicating that these effects were relatively consistent across listeners.

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 $1000 \,\mu\text{s}$, to listener IBF who could discriminate ITDs at approximately $50 \,\mu\text{s}$. JNDs that were "Not Determined" (ND) are represented with a diamond symbol. When comparing across configurations, there was no particular configuration yielding the best JNDs for all subjects (see Table IV). To further illustrate this, Fig. 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 diagonal 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 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 Fig. 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 Fig. 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 Fig. 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 (Fig. 5, panel B).

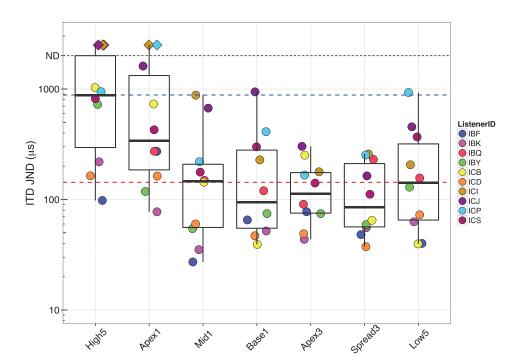


FIG. 3. ITD JNDs (in microseconds) per listener and per condition. The five mixed-rate configurations are ordered from worst to best average ITD sensitivity, while the High5 and Low5 configurations are placed at the left and right ends, respectively. Each symbol color depicts a different listener. Box 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.

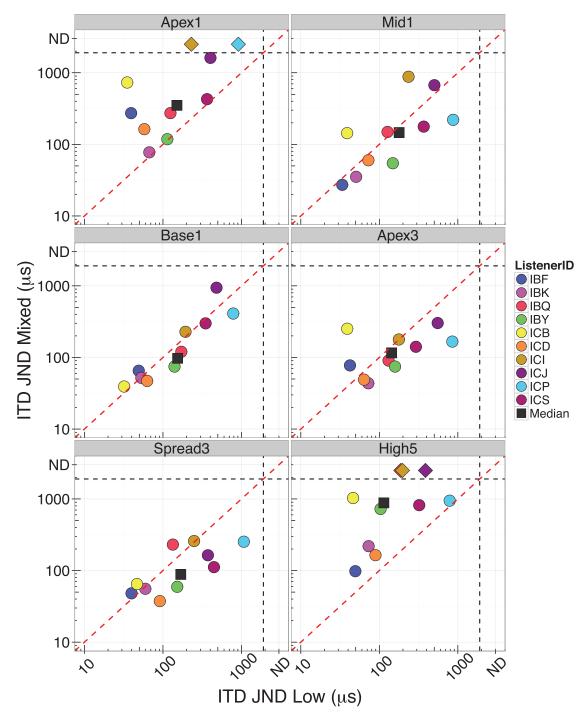


FIG. 4. ITD JND comparison plots. Each mixed-rate JND (y-axis) is plotted as a function of the Low5 JND (x-axis). The diagonal represents the line of unity, where JNDs are identical in the two conditions plotted. Points that fall below the line depict JNDs in the mixed-rate configuration were better 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. Diamond symbols refer to listeners whose JNDs could not be determined (ND).

IV. 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 242 and 228 μ s (Mid1 and Base1, respectively), which was significantly better than the configuration with only high rates (High5) (see Table IV). Notably, the mixed-rate configurations and the Low5 configuration

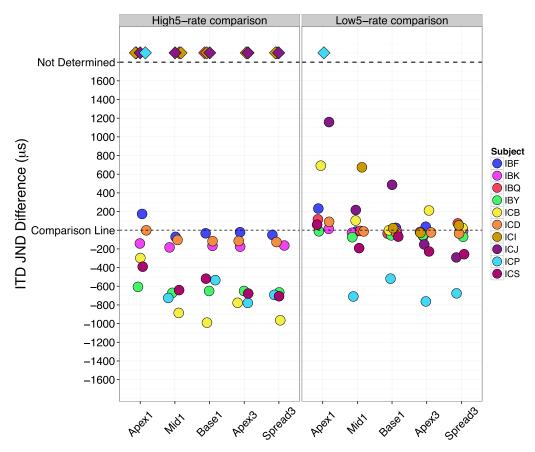


FIG. 5. (Color online) ITD JND difference values on a linear scale. Panel (a) shows a comparison of each of the mixed-rate JNDs to the High5 JND, and panel (b) shows a comparison of each of the mixed-rate JNDs to the Low5 JND. The dashed horizontal line is the line of unity, or point of comparison, whereby 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.

(average: 246 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 tonotopically-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, we have here 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. That 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 (Fig. 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 impairs ITD sensitivity and lateralization abilities (Best et al., 2007; Stellmack and Dye, 1993; Woods and Colburn, 1992). 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. 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 300 μ s. 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 \sim 500 to \sim 100 μ s); 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 (SAM) tone, a half-wave rectified, or a "transposed tone" 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 optimized for processing by the auditory periphery, analogous to our multi-electrode mixed-rate stimulation in BiCI listeners (Bernstein and Trahiotis, 2002, 2009; McFadden and Pasanen, 1976; 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 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 diotic randomization of high rate timing led to improving sensitivity to ITDs, thus inadvertently creating low rate fluctuations. 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 cochlear implants. 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. (2013) suggests that interchannel crosstalk is detrimental to ITD coding on the auditory nerve. 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 acrossfrequency 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 pps, 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.

V. 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.

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