

# Use of Research Interfaces for Psychophysical Studies With Cochlear-Implant Users

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## Abstract

A growing number of laboratories are using research interfaces to conduct experiments with cochlear-implant (CI) users. Because these interfaces bypass a subject's clinical sound processor, several concerns exist regarding safety and stimulation levels. Here we suggest best-practice approaches for how to safely and ethically perform this type of research and highlight areas of limited knowledge where further research is needed to help clarify safety limits. The article is designed to provide an introductory level of technical detail about the devices and the effects of electrical stimulation on perception and neurophysiology. From this, we summarize what should be the best practices in the field, based on the literature and our experience. Findings from the review of the literature suggest that there are three main safety concerns: (a) to prevent biological or neural damage, (b) to avoid presentation of uncomfortably loud sounds, and (c) to ensure that subjects have control over stimulus presentation. Researchers must pay close attention to the software–hardware interface to ensure that the three main safety concerns are closely monitored. An important area for future research will be the determination of the amount of biological damage that can occur from electrical stimulation from a CI placed in the cochlea, not in direct contact with neural tissue. As technology used in research with CIs evolve, some of these approaches may change. However, the three main safety principles outlined here are not anticipated to undergo change with technological advances.

## Keywords

cochlear implants, research interface, safety

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## Introduction

Cochlear-implant (CI) systems are designed to convert acoustic vibrations to direct electrical stimulation of the spiral ganglia and auditory nerve in patients with moderate-to-profound hearing loss. While clinical sound processors have been successful in enabling CI users to understand speech and to communicate using oral language, the variability in outcomes among patients is high. It is likely that variability in outcomes results from a combination of limitations within the processors, and individual differences among patients in how well they can respond to the electrical pulsatile stimulation provided by the CI. Researchers are often interested in evaluating patients' performance in various listening conditions, but if they test patients while they wear clinically fitted devices, then the performance of

both the subject and the sound processor are being simultaneously evaluated. This article describes research platforms that take one of two forms: research processors and research interfaces. A research processor is portable and similar to a clinical sound processor (it allows the researcher greater stimulus control than is typically available in a clinical system). A research interface is a tool that provides control over implanted devices by a

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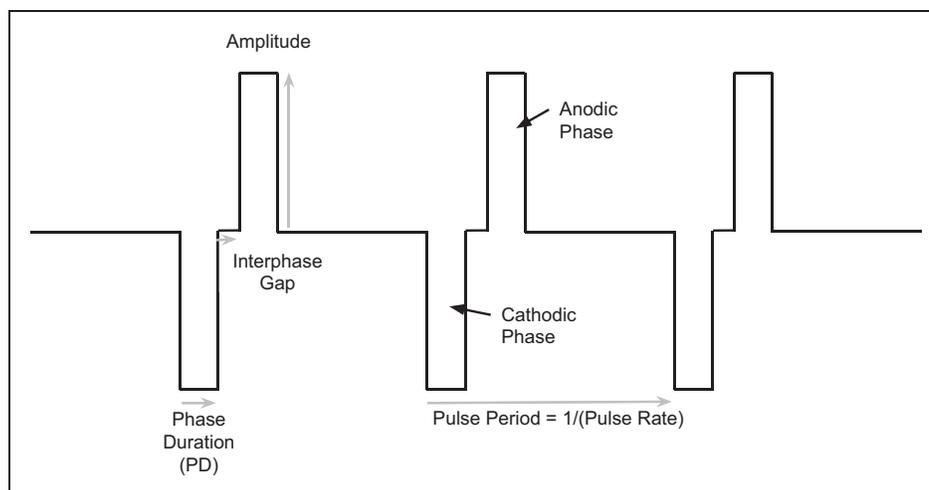
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**Figure 1.** A schematic of a pulse train is shown. Charge density is composed of the sum of the anodic and cathodic phases, shown as positive and negative portions of the phases. Parameters in the pulse train such as amplitude (shown as height of the pulses), duration (shown as the *phase duration* or the width of the pulses), and gap between phases (shown as *interphase gap*) can each be varied individually and are discussed in the text as parameters that can result in change in loudness. The pulse period is computed as  $1/\text{pulse rate}$ .

personal computer (PC) and is useful for the researcher who is interested in the fundamental capabilities of the subject without the restrictions and limitations of the specifics of the sound processor implementation (e.g., front-end processing, filter-bank implementation, and processing strategy). Research interfaces generally provide even more flexibility in stimulus control than a research processor but sacrifice the capability of being a wearable standalone processor. While research platforms allow for greater flexibility than a clinical system, using them requires a deeper understanding of issues concerning electrical stimulation of the auditory system with a CI to ensure subject safety.

Here we discuss the safety concerns that researchers face when using a CI research interface and identify ethical principles related to testing with CIs when research processors are used. This article does not take the place of what should be considered mandatory explicit training from an experienced researcher in a laboratory that is well established in this type of research. Three main safety concerns are discussed: biological safety (damaging tissue by providing too much current), overstimulation (playing an uncomfortably loud stimulus), and ensuring that the CI user has the ability and understanding to abort any stimulation immediately (e.g., removal of the transmitting coil). We provide some details on the principles of designing software and stimuli that maintain subject safety and comfort. In addition, we discuss the capabilities of research platforms that are available for working with all three U.S. Food and Drug Administration (FDA) approved CI brands, and the laboratory approaches necessary to ensure safety with electrical stimulation.

## Safety and Comfort

### Biological Safety

In the current article, biological safety is defined in the context of restricting electrical stimulation, such that no tissue or neural damage occurs. Biological safety with pulsatile stimulation is dependent on the amount of charge being delivered by the electrodes within a finite time period, as well as the surface area of the electrode contact. The charge of each phase is the product of the amplitude and phase duration (PD) of a pulse (see Figure 1), where a pulse can have multiple phases. Note that PD and pulse width are often used synonymously; however, we feel that PD is a more precise term because it represents only one phase of a pulse, and it is more exact about the referral to temporal duration, rather than *width* which can also refer to band width in the frequency domain.

Biological safety is partially ensured by providing biphasic pulses. The localized current carried during one phase is reversed during the second phase, so that there is no ionic imbalance and thus no electrochemical products are formed. The maximum charges used are those that are approved by government agencies that regulate and monitor trading and safety standards in the food and drug industries, for example, as per the FDA, which is the regulatory body of the United States. To ensure charge balance and prevent a buildup of charge, symmetric biphasic rectangular pulses of brief duration are typically used. With such pulses, charge is provided for a fixed amplitude and duration and then provided in the opposite polarity at the same amplitude

and duration after a short (0–10  $\mu$ s) interphase gap (illustrated in Figure 1). Advanced Bionics and MED-EL CIs can also produce pulses which deviate in shape from the symmetric biphasic rectangular pulses. These alternate pulsatile configurations also provide charge balance if the sum of the charges of all phases of a pulse is zero. Some examples with alternate configurations are discussed later in sections that specifically address Advanced Bionics and MED-EL devices. Logically, charge balancing should occur within a certain amount of time. Current studies use time scales up to  $\sim$ 5 ms (e.g., Carlyon et al., 2005; Macherey, van Wieringen, Carlyon, Deeks, & Wouters, 2006; Shannon, 1983; van Wieringen, Carlyon, Laneau, & Wouters, 2005). The field currently has no empirical evidence to suggest what the exact time window should be, despite its important ramifications for safety. Until this evidence is provided, a cautious and ethical researcher would keep this window small and comparable to the values used in the following studies.

With programming tools and libraries provided by the manufacturers or used with custom-made hardware, rigorous checks need to be made prior to electrical stimulation to ensure the safety of the subject. For example, best practices would dictate that verifying the output from research interfaces on an oscilloscope needs to be done, and the investigator should ensure that the stimuli are within safe charge densities. Most importantly, it is the researcher's responsibility to ensure that the parameters of stimulation do not generate pulses that might produce biological damage.

Information about safety comes from studies in animals. There are two noteworthy points regarding direct relevance to humans. First, a commonly accepted standard to avoid neural damage has been to respect the guidelines outlined in Shannon (1992). More recently, the guidelines from the FDA set a limit of 216  $\mu$ C/cm<sup>2</sup> for clinical applications. These guidelines on charge density are conservative because they are based on data collected with electrodes directly in contact with neural tissue. A clinical CI does not make direct contact with neurons; rather electrical current first passes through the cochlea and then stimulates the auditory nerve. Second, in these previous animal studies (McCreery, Agnew, Yuen, & Bullara, 1988, 1990, 1992, 1995), neurons were damaged primarily by excitotoxicity. McCreery et al. (1990) found that 100  $\mu$ C/cm<sup>2</sup>/phase resulted in mild-to-moderate neural damage in three of four testing sites when using an electrode with 0.01 cm<sup>2</sup> surface area. This stimulus was delivered over 400  $\mu$ s, so the current was  $1/400 = 2.5$  mA. Note that a 400- $\mu$ s PD is relatively long compared with the PDs used in current CI sound processors. What remains unclear is whether the damage was caused by sending 2.5 mA through a

0.01 cm<sup>2</sup> electrode, or by delivering a total of 1  $\mu$ C through that electrode. In other words, there was no way to determine whether it was charge density ( $\mu$ C/cm<sup>2</sup>) or current density ( $\mu$ A/cm<sup>2</sup>) that caused the damage. Thus, based on research to date, there is little definitive information regarding this issue.

The association for the advancement of medical instrumentation released guidelines for biologically safe stimulation in cochlear implants. The document underwent review by representatives of four CI manufacturers (Advanced Bionics, Cochlear, Med-El, and Oticon Medical), clinicians, scientists, and the FDA. The consensus document was approved on 6th of January 2017 and is available from the association for the advancement of medical instrumentation ([http://my.aami.org/aamiresources/previewfiles/1706\\_CI86Preview.pdf](http://my.aami.org/aamiresources/previewfiles/1706_CI86Preview.pdf)). Section 17 of this document specifically addresses safe stimulation waveforms, charge and charge-density limits, and stimulation modes. Although the document is specifically written from the perspective of commercial implementation, the guidelines generally apply to research investigations, such as the kinds that are discussed in this article. The safe upper limit of charge density is usually defined as 216  $\mu$ C/cm<sup>2</sup> for commercial applications. The FDA has not provided specific guidelines for the safe upper limit of charge density in a research environment; however, 100  $\mu$ C/cm<sup>2</sup> has sometimes been considered by the FDA. For any research software that is used under an investigational device exemption (IDE), stimulation limits have been and are presently approved on a case-by-case basis for a given IDE submission (V. Dasika, personal communication).

Regarding best practices with human CI research, a conservative practice based on the animal studies and FDA recommendations would carefully consider situations where increases in PD, the interphase gap, the stimulation rate, pulse amplitude, and the distance between electrode and stimulated neurons (as well as possibly other factors) could move a safe current in the direction of an unsafe one. Clearly these parameters interact, potentially nonlinearly, and therefore best practices would suggest extreme caution when varying more than one of these parameters simultaneously.

Future research that would be immensely beneficial to the field would be to determine charge density that can cause biological damage for a CI placed in the cochlea. This would include parametric studies on level, stimulation rate, pulse shape, grounding configuration, and so on. As sound processing strategies and electrical stimulation patterns become more sophisticated, such knowledge is necessary to ensure biological safety for future technologies. It also sets appropriate limits for researchers to safely explore these novel stimulation patterns and modes.

The manufacturers also have their own set of safe guidelines for their devices. The appropriate charge-density limits are dependent on properties including the area of the electrode contact and the distance from the stimulated neural population. It is worth noting that, even within the same manufacturer, charge-density limits can vary across electrode arrays. *Hence, to ensure biological safety, the onus is on the manufacturers of both the CI and the research interface, to provide guidance on safe parameter values that are within acceptable limits; in turn, the onus is on the researcher to ensure that checks are in place to ensure that these limits are not exceeded.*

### Authorization and Oversight

Research interfaces that are described here are not available to individual investigators unless they reach an agreement with the interface manufacturer and conduct the research under an approved institutional review board (in the United States), or equivalent board in other countries. Interface manufacturers have an interest in ensuring that their tools are used with the utmost care and concern for patient safety by sufficiently knowledgeable researchers. Therefore, the manufacturers typically engage in a vetting process with potential researchers and release tools only when they are confident in the researcher's ability to use the interfaces safely and responsibly. Furthermore, in the United States, direct approval from the FDA is not required. Some devices may be designed to be used outside the laboratory (such as those used to implement new processing strategies). In these cases, the investigator may or may not require additional authorization from the FDA in the form of an IDE. In general, an IDE is designed to allow the use of an investigational device in a clinical study, for the purpose of collecting data on safety and effectiveness. Investigators who are using devices in a clinical trial should contact the FDA to determine whether they are required to apply for an IDE before the study is initiated.

### Ensuring Comfort by Controlling Loudness

It is imperative that uncomfortably loud stimulation (i.e., one that is greater than the maximum acceptable loudness or MAL) be avoided. Protection from overly loud stimulation is required for direct stimulation research by most institutional review boards. There are numerous stimulus parameters that can be controlled by the experimenter that affect loudness and therefore must be carefully adjusted during an experimental session. In addition, the values of stimulation parameters that produce an appropriate loudness will vary across subjects and electrodes. Thus, the experimenter must measure

the appropriate values for each stimulus with each subject and each electrode individually.

To measure an appropriate loudness of a given stimulus, the typical practice is to provide initial stimulation below audible threshold (T) and gradually increase the current, until the desired loudness is achieved. This process mimics the typical protocol of a clinical audiologist measuring T and MAL levels. Once these levels have been measured for each stimulus, it is important that stimulation remains below the MAL levels. However, for some subjects, MALs can change over the course of an experiment. Thus, remeasuring when time permits is a reasonable approach. In either case, when taking breaks from testing, it is important to verify that subjects continue to perceive the stimulation not uncomfortably loud when testing is resumed. For a researcher, since MAL levels have already been safely collected by a trained audiologist for a specific set of parameters, one should ask for a copy of the clinical maps to obtain a general idea about a safe and appropriate starting point and loudness levels for each specific experiment.

Although clinically appropriate levels can be provided by the audiologist, it is likely that the research will use stimulation patterns with parametric values that differ from the clinical parameters. Therefore, because perceived loudness is dependent on many parameters, new T and MAL levels should be measured when possible, particularly if the new stimuli are likely to produce loudness changes. For example, stimuli with differing degrees of amplitude modulation, PD, or stimulation rate should all have their T and MAL levels measured independently. It is especially important to note that when stimulating multiple electrodes, the loudness percept is greater than each of the single electrodes presented in isolation. Therefore, if there is any question about overstimulation with the addition of other electrodes, stimulation should be conservatively reduced to the levels near T, and the loudness should be rechecked. Clinically, audiologists typically measure MAL levels and then perform gross adjustments to all electrodes when the sound processor is fully activated. This often results in an overall reduction in levels because the multielectrode stimulation is typically too loud for comfortable everyday listening. Such information should be kept in mind for relatively basic multielectrode direct stimulation but also when designing multielectrode direct stimulation speech processing strategies. This procedure should be performed until stimulation is perceived to be comfortably loud for the maximum number of channels that can be presented simultaneously or sequentially interleaved (e.g., McKay & Henshall, 2003; McKay, Remine, & McDermott, 2001). In the following section, a detailed presentation of parameters that affect loudness is provided.

It is important that CI subjects can immediately abort any stimulation in case of an error that would yield an

uncomfortably loud stimulation when using a research interface. With modern CIs, a removal of the transmitting coil immediately halts stimulation from the device. Each CI user should be instructed that in the case of an unpleasant sound, they should immediately remove the transmitting coil. During the experiment, CI users' hands should be free so that nothing prevents them from removing the transmitting coil.

## Parameters Affecting Loudness Perception

### *Amplitude ( $\mu\text{As}$ ) and PD ( $\mu\text{s}$ )*

The loudness of a pulse is related to its charge, which is a product of amplitude and PD. Both amplitude and PD have a complex relationship with loudness perception (e.g., Chatterjee, Fu, & Shannon, 2000; McKay et al., 2001). Figure 1 shows a schematic of biphasic pulses. Amplitude, PD, and overall duration can each be varied independently, such that the experimenter can monitor the effect of changing parameter values on loudness. For example, for a fixed amplitude, increasing the PD will typically increase loudness. Similarly, for a given PD, increasing the amplitude will typically increase loudness. Changing charge by manipulating amplitude generally produces a greater change in loudness compared with the change in charge due to manipulation of the PD (Zeng, Galvin, & Zhang, 1998). Therefore, when either the PD or amplitude is changed, researchers may elect to obtain new T and MAL levels.

It is worth noting that although an increase in amplitude produces an increase in perceived loudness, the relationship varies across subjects. Zeng and Shannon (1994) argued that for lower stimulation rates ( $\sim 100$  pulses per second [pps]), loudness is best modeled as a power function of pulse amplitude, and for higher stimulation rates ( $> 300$  pps), loudness is best modeled as an exponential function of pulse amplitude. Sanpetrino and Smith (2006) found loudness growth typically to be expansive for most postlingually deafened CI users but observed that for some prelingually deafened CI users, loudness growth functions were more linear. As a result, when determining the maximum comfortable loudness, one must be careful during the mapping process. This is because the loudness growth function usually has expansive characteristics, but this varies across individuals. In addition, within individual subjects, loudness can grow differently across electrodes, another factor that needs to be carefully considered. As a result, a fixed increase in amplitude in the lower portion of the dynamic range will likely produce a smaller change in loudness than the same increase in amplitude at a higher portion of the dynamic range. Thus, one must take care when changing amplitude, especially at the higher end of the dynamic range, because one or two clinical current units could

produce larger jumps in loudness perception than at lower levels.

### *Interphase Gap ( $\mu\text{s}$ )*

The interphase gap is the time between subsequent phases in a multiphasic pulse (see Figure 1 for an example of a biphasic pulse; McKay & Henshall, 2003). The pulses have two phases with opposing charges, cathodic and anodic (their particular order is not important), but the balance of charge between the two phases is designed to prevent irreversible corrosion of electrodes and the potential deposit of metal oxides at the electrode-tissue interface. The magnitude of loudness increases as a function of increase in interphase gap but varies across subjects and may be related to local neural survival (Prado-Guitierrez, Fewster, Heasman, McKay, & Shepherd, 2006; Ramekers et al., 2014). Other factors likely to affect loudness include the number of phases in a pulse and the order and signs of those phases.

### *Stimulation Rate (pps)*

An increase in stimulation rate may yield an increase in loudness because more charge is provided per unit time. This is particularly important to consider for experimental changes in pulse or stimulation rate. Because one cannot assume that different rates will produce the same loudness perception, it is important that T and MAL levels be assessed for each subject, and at every rate. It is worth noting that a change in loudness with increased stimulation rate is greater at relatively low rates (e.g., Hong & Rubinstein, 2003; McKay et al., 2001). In McKay et al. (2001), rates of 250, 500, and 1000 Hz were tested, and a greater adjustment in current was needed at the 1000 Hz rate than the lower rates in order for subjects to perceive changes in loudness.

### *Stimulation Mode (i.e., Multipolar Stimulation)*

Stimulation mode refers to the configuration of stimulating and reference electrodes at any given moment in time. The configuration is determined by the number of electrodes simultaneously stimulated, their relative locations along the array, amplitudes, and polarities. Examples of common modes used in clinical and research devices are as follows: (a) common ground (e.g., Busby, Whitford, Blamey, Richardson, & Clark, 1994) in which all nonstimulating intracochlear electrodes are shorted together and act as a return electrode, (b) monopolar (MP; e.g., Shannon, 1983) in which one intracochlear electrode provides stimulation while the return electrode is extracochlear, (c) current focusing modes (e.g., bipolar, Busby et al., 1994; tripolar,

Bierer, 2007) in which one or more intracochlear return electrodes are used, (d) virtual channels (e.g., Donaldson, Kreft, & Litvak, 2005; Firszt, Koch, Downing, & Litvak, 2007), in which multiple intracochlear electrodes stimulate simultaneously in-phase to move the peak of stimulation of the electrical field, and (e) stimulation modes using combinations of intracochlear and extracochlear return electrodes as well as possibly multiple intracochlear stimulating electrodes. These stimulation modes include the partial tripole (e.g., Landsberger, Padilla, & Srinivasan, 2012; Zhu, Tang, Zeng, Guan, & Ye, 2012), the quadrupolar virtual channel (e.g., Landsberger & Srinivasan, 2009), the virtual tripole (e.g., Padilla et al., 2017), and phantom stimulation (e.g., Saoji, Landsberger, Padilla, & Litvak, 2013; Saoji & Litvak, 2010). Each stimulation mode has unique relationships to perceived loudness, and an experimenter needs to exercise caution when stimulating in each mode and particularly when changing between modes. Typically adding stimulation on multiple electrodes in the same phase (such as a virtual channel) increases the perceived loudness for a fixed amplitude (e.g., Frijns, Kalkman, Vanpoucke, Bongers, & Briaire, 2009; Landsberger & Galvin, 2011), while stimulating multiple electrodes out-of-phase (such as in bipolar or tripolar stimulation) reduces the loudness for a fixed amplitude (e.g., Berenstein, Mens, Mulder, & Vanpoucke, 2008; Chatterjee, 1999; Landsberger & Srinivasan, 2009). Figure 2 of Landsberger et al. (2012) specifically shows the relationship between increasing the amount of current focusing and the increase in charge required to maintain equal loudness. Therefore, stimulation at an appropriate amplitude with a tripolar stimulus would likely greatly exceed comfortable limits in MP mode with the same amplitude.

### Multichannel Loudness Summation

Psychophysical experiments can either be conducted using single- or multichannel stimulation. Single-channel stimulation is the most basic stimulation pattern available via a CI. MAL levels are often determined on single channels. However, loudness summation can occur when multiple channels are stimulated; therefore, care must be taken to evaluate loudness with each multichannel condition. The degree of loudness summation is dependent both on the level of stimulation within the subject's dynamic range and the mode of stimulation (McKay et al., 2001; Padilla & Landsberger, 2014). According to McKay and Henshall (2003), each pulse of a stimulus contributes to the perceived loudness, and this loudness summation is insensitive to intracochlear place of stimulation. The model assumes that each pulse is sequential (i.e., that pulses do not overlap in time). If pulses overlap in time,

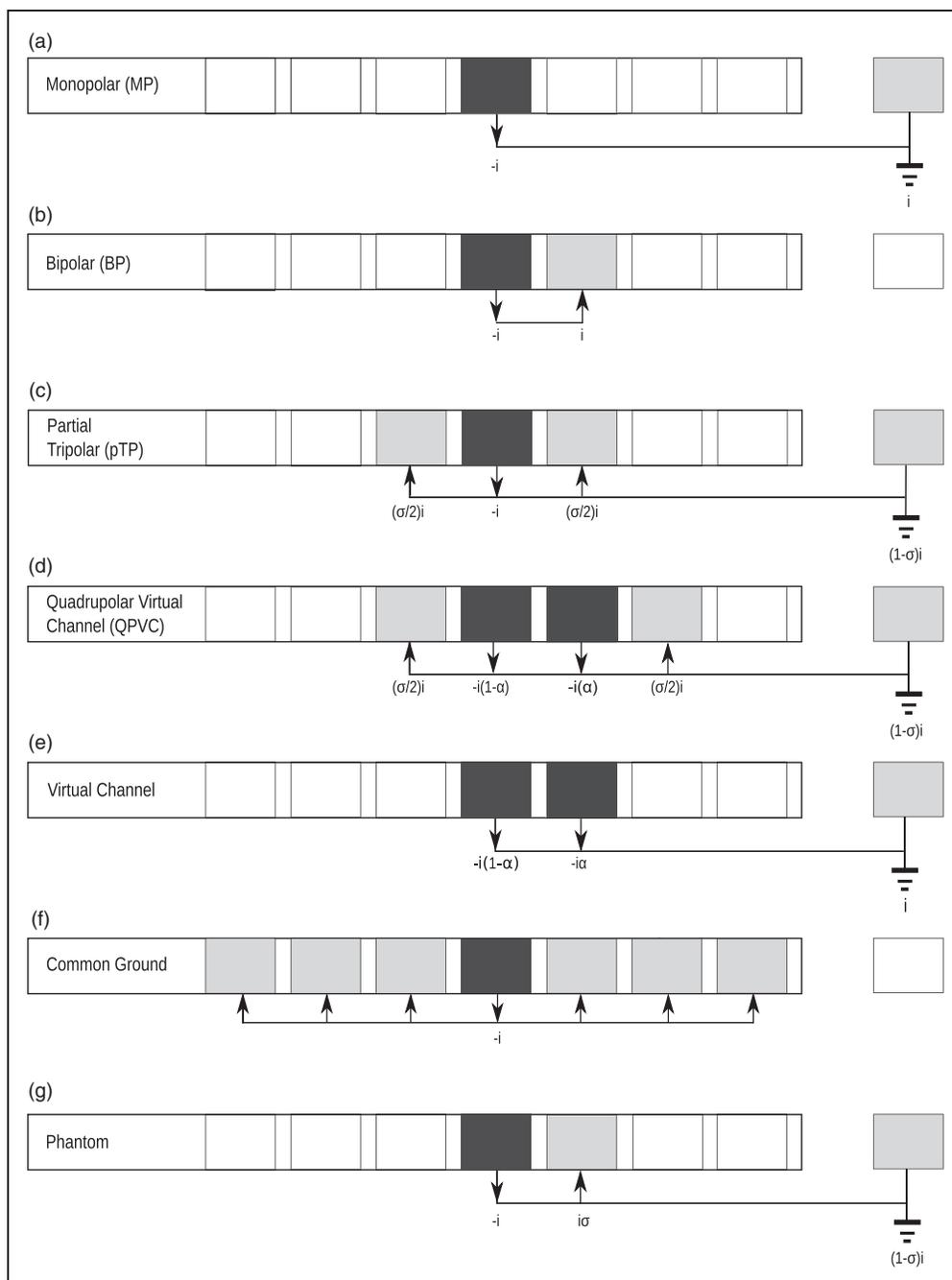
they should be considered a *multipolar* stimulus, as described in the previous section.

### Compliance

CIs have a maximum supply voltage that cannot be exceeded. A stimulus is called *out of compliance* when it requires more voltage to produce a specified current than the CI can provide. If a CI is unable to provide appropriate voltage, then the shape of the stimulating pulse or waveform will be distorted. In extreme cases, if the distortion is asymmetric for anodic and cathodic phases, a charge imbalance will occur. To protect from charge imbalances, MED-EL and Advanced Bionics devices have inline capacitors to ensure that any remaining charge is dissipated. Devices from Cochlear require a shorting of all electrodes after each phase of stimulation to remove any residual charge (which is why there is a minimum interphase gap and interpulse delay for devices from Cochlear). One indication that a stimulus may be out of compliance is that an increase in amplitude from the CI does not provide a corresponding increase in loudness.

The voltage (V) provided by a CI with a current source (see Table 1) is equal to the current (I) produced by the source multiplied by the local impedance (Z). However, because the local impedance is related to the electrode surface area and cochlear positions, it is impossible to know the current that would cause a stimulus to be out of compliance without measuring the impedance at the corresponding electrode for a given subject. Ideally, one should measure impedance at every electrode to determine the maximum current that can be provided without exceeding compliance levels. Using research tools, measuring impedance is not performed automatically as it is with clinical software. Instead, some tools allow the researchers to write software to measure the impedances while other tools do not allow the capability at all. If it is not possible to measure impedance, then it is important to ensure that for every stimulus used in an experiment, adding additional current produces additional loudness, up to the MCL.

Best practices, in terms of following ethical research conduct, would suggest that care should be taken regarding design of the stimuli. Moreover, researchers should be careful not to make assumptions about changes in loudness that results from an alteration of one of the stimulation parameters and apply that information broadly to all stimuli, or to all electrodes. This is especially important when these parameters are changed between conditions in any given experiment, and even more so if the experimenter chooses to vary multiple parameters at once. In such a case, there is a greater risk of producing unexpected and uncomfortably loud stimulation.



**Figure 2.** Schematic rendition of various stimulation modes used in research and clinical practice. These include: (a) Monopolar, one active electrode and one return (ground) electrode outside the cochlea. Monopolar stimulation is the most commonly used configuration in current sound processing strategies and provides the largest current spread. (b) Bipolar, two adjacent electrodes are paired as active and return. Bipolar stimulation is designed to have smaller current spreads than monopolar. (c) Partial Tripolar, three adjacent electrodes. The middle electrode is active while the two adjacent intracochlear electrodes provide out of phase stimulation to reduce the spread of current. Some of the current ( $\sigma$ ) stays within the cochlea while some of the current goes to an extra cochlear ground ( $1-\sigma$ ). Partial tripolar is a current focused stimulation mode designed to provide a greater reduction in spread than bipolar. (d) A quadrupolar virtual channel is a current focused stimulation similar to partial tripolar. In a quadrupolar virtual channel, four adjacent electrodes are used. The middle active electrode of a partial tripole is replaced by two adjacent electrodes. The amplitudes of the two middle electrodes can be adjusted (using a variable  $\alpha$ ) to manipulate the location of the peak (or centroid) of the combined electric fields, allowing for place of stimulation resolution greater than stimulation at a location corresponding to a physical electrode. (e) Virtual channel, two adjacent electrodes are active, and the return ground is sent to a ground electrode outside the cochlea. Current is steered between the two active electrodes using the variable  $\alpha$ . (f) Common ground, where all nonactive intracochlear electrodes are used as ground electrodes. The distribution of charge at each electrode is dependent on the local impedances. (g) Phantom electrode is a partial bipolar configuration where grounds consist of an intracochlear and extracochlear electrode, attenuating current from the active electrode near the intracochlear ground electrode. Phantom electrodes are typically used to provide stimulation beyond the electrode array (e.g., beyond the most apical electrode).

**Table 1.** List of the internal devices from each manufacturer, and the research tools that can be used for each device.

Manufacturer	Internal Name	Marketing Name	Tools	V or R Source	Telemetry?
Advanced Bionics	C I	C I	None Supported	Voltage	YES
Advanced Bionics	C II	C II	BEDCS, BEPS+	Current	YES
Advanced Bionics	HiRes90K	HiRes90K	BEDCS, BEPS+	Current	YES
Advanced Bionics	HiRes90K Advantage	HiRes90K Advantage	BEDCS, BEPS+	Current	YES
Cochlear	CI22M	Nucleus 22	HEINRI	Current	NO
Cochlear	CI24M	Nucleus 24 (Straight, Double Array)	NIC, UTD, HEINRI, SPEAR3	Current	YES
Cochlear	CI24R	Nucleus 24 (Contour, Contour Advance), Nucleus 24k (Straight)	NIC, UTD, HEINRI, SPEAR3	Current	YES
Cochlear	CI24RE	Nucleus Freedom (Contour Advance, Straight), Cochlear Nucleus CI422, Cochlear Hybrid L24	NIC, UTD, HEINRI, SPEAR3	Current	YES
Cochlear	CI500 Series	Cochlear Nucleus CI512	NIC, UTD, HEINRI, SPEAR3	Current	YES
Cochlear	Profile Series	Cochlear Nucleus CI512, CI522, CI532	NIC, UTD, HEINRI, SPEAR3	Current	YES
MED-EL	COMBI 40+	COMBI 40+	RIB 2	Current	NO
MED-EL	Pulsar	Pulsar	RIB 2	Current	YES
MED-EL	Sonata	Sonata	RIB 2	Current	YES
MED-EL	Concert(o)	Concert(o)	RIB 2	Current	YES
MED-EL	Synchrony	Synchrony	RIB 2	Current	YES

Note. BEDCS = Bionic Ear Data Collection System; BEPS+ = Bionic Ear Programming System; HEINRI = House Ear Institute Nucleus Research Interface; NIC = Nucleus Implant Communicator; UTD = University of Texas Dallas; SPEAR3 = Sound Processor for Electric and Acoustic Research, rev. 3; RIB2 = Research Interface Box 2.

## Stimulus and Software Design

It is important when using research processors and interfaces that the above safety and comfort issues are addressed. It is also important that any research software for CIs maintain subject safety and comfort. This can be achieved by inspecting and verifying amplitude of the currents, PDs, interphase gaps, and pulse rates (as shown in Figure 1) using an oscilloscope or data acquisition card. In addition, software checks should be used to ensure that subject-specific MAL levels are never exceeded; that is, parameters such as amplitude, PD, interphase gap, pulse rate, polarity, and so on should be limited to appropriate values to maintain safe loudness levels. Because modifying stimulus parameters (such as stimulation mode or rate) often requires changes in other stimulus parameters to remain within safe limits (see section on Parameters affecting loudness perception), it is suggested that software be designed to ensure that the experimenter cannot change one parameter without consideration of the other parameters. Therefore, researchers must pay close attention to the software–hardware interface to ensure that the three main safety and comfort concerns are closely monitored.

Best practices mean that the experimenter (and the software engineer if they are different people) needs to have a proper understanding of the properties of electrical stimulation, which can cause either damage or patient discomfort. The best way to achieve proper understanding is to be trained in a lab which has sufficient and appropriate expertise to work with research interfaces and provide electrical stimulation to CI users. In addition, before running the experiment, it is important that the software is verified to provide the correct and appropriate output (using an oscilloscope) both by the developer while creating the software and by the experimenter before using the software.

## Ethical Concerns

Experiments that utilize research processors and interfaces are different from experiments involving the presentation of stimulation using a clinically fitted sound processor (i.e., those performed in the free field or using a direct audio input). Unlike the clinical setting, where there are inherent safety features built into the device programming, such features are missing in research processors. Subjects who can typically control

the stimulation in these ways are adult subjects and children who are old enough to understand the instructions and convey their needs to the experimenter.

Finally, behavioral tests in CI patients often take multiple, long sessions, and can therefore be tiring for subjects, thus frequent breaks are typically needed. Without frequent breaks, fatigue and lack of attention have the potential to affect the data in ways that lead to weaker reliability and replicability.

## Research Interfaces and Processors Provided by the Manufacturers

Numerous research platforms are available from the different manufacturers (discussed in this section) as well as other providers (discussed in the following section). When using these platforms, researchers must pay close attention to the software–hardware interface to ensure that safety and comfort concerns are sufficiently addressed. Because there are a large variety of experimental parameters that can be manipulated, the onus is jointly on the researcher and manufacturers of the research system to ensure the safety of the subject. In addition, because researchers are always stimulating internal devices, regardless of the external interface, it is important that researchers working with research processors be familiar with the features of the devices and the clinical fittings used with these devices.

Table 1 contains a list of the internal devices from each company and the research tools that can be used for each device. The available research platforms are summarized in Table 2. Research platforms that are supplied by the manufacturers are typically accompanied by a range of software tools that vary in their ability to ensure subject safety. A summary of available software tools is presented in Table 3.

### Advanced Bionics

Advanced Bionics presently supplies two different research systems: bionic ear data collection system (BEDCS) and bionic ear programming system (BEPS+) interface. Both platforms enable experimentation with mono- and multipolar stimulation modes using charge-balanced pulsatile waveforms of varying shapes.

**BEDCS.** Researchers can directly control the Advanced Bionics CII and HiRes90K CIs through BEDCS. BEDCS is a bench-top, or standalone, software package that uses clinical hardware to connect to the CI. There are presently two versions of BEDCS (1.X and 2.X). BEDCS 1 uses a clinical programming interface (CPI-2) and a platinum series processor body-worn speech processor connected to the CPI-2 with a programming cable. BEDCS 2 uses a CPI-3 and one or two Naida CI

**Table 2.** The Available Research Platforms Are Summarized Here, and Example References for Published Research Using These Platforms Are Provided.

Research interface	Devices supported	Stimulation modes supported	Pulse shapes supported	Only allows charge balanced stimulation	Bilateral stimulation support	Example reference
NIC2	Cochlear Nucleus 24 and later	MP, BP, CG (in MATLAB only MP)	Symmetrical biphasic rectangular pulses	Yes	Yes	Kan et al. (2013)
NIC3	Cochlear Nucleus 24 and later	MP, BP, CG (in MATLAB MP and BP)	Symmetrical biphasic rectangular pulses	Yes	Yes	2 x L34
SPEAR3	Cochlear Nucleus 24 and later	MP, BP, CG	Symmetrical biphasic rectangular pulses	Yes	Yes	RF Gen. XS van Hoesel et al. (2009); Loizou et al. (2009)
BEDCS	Advanced Bionics CII, HiRes90K, HiRes90K Advantage	MP, BP, TP, QPVC, VTP, Phantom	Biphasic, triphasic, pseudomonophasic, custom pulse shapes	Yes	Yes	Srinivasan et al. (2012); Landsberger et al. (2012)
RIB2	Combi C40H or newer	MP	Biphasic, triphasic	Yes	Yes	Majdak et al. (2006)
HEINRI	All Cochlear Nucleus Implants	MP, BP, CG	Symmetrical biphasic rectangular pulses	Yes	Yes	Shannon et al. (1990)
University of Texas-Dallas PDA	Cochlear Nucleus 24 and later	MP	Symmetrical biphasic rectangular pulses	Yes	Yes	Ali et al. (2013)

Note. PDA = Personal Digital Assistant; HEINRI = House Ear Institute Nucleus Research Interface; RIB2 = Research Interface Box 2; BEDCS = Bionic Ear Data Collection System; SPEAR3 = Sound Processor for Electric and Acoustic Research, Rev. 3; NIC = Nucleus Implant Communicator. MP = monopolar; BP = bipolar; CG = common ground; TP = tripolar; QPVC = quadrupolar virtual channel; VTP = virtual tripolar.

**Table 3.** Research Platforms That Are Supplied by the Manufacturers Are Typically Accompanied by a Range of Software Tools That Fall Along a Spectrum in Their Ability to Ensure Subject Safety.

Research interface	Devices supported	Purpose of software	Distributor	URL
APEX	Nucleus 24 or later, Acoustic	Psychophysical front end for sound cards and Cochlear Nucleus Devices	KU Leuven	<a href="https://expori.med.kuleuven.be/web/index.php/Public:Software/APEX">https://expori.med.kuleuven.be/web/index.php/Public:Software/APEX</a>
PACTS	Advanced Bionics CII, HiRes90K, HiRes90K Advantage	Psychophysical front end for BEDCS 1	Advanced Bionics	
ART-Research	MED-EL i100 platform (Pulsar, Sonata, Concert(o), Synchrony)	Record ECAPS	MED-EL	
Volta	Advanced Bionics CII, HiRes90K, HiRes90K Advantage	Record ECAPS	Advanced Bionics	
Psychophysics	Nucleus 24 or later with NIC, All Nucleus Devices with HEINRI	Run basic psychophysical experiments	Emily Shannon Fu Foundation / Tiger Speech Technology	<a href="http://tigerspeech.com/tst_psy-chophysics.html">http://tigerspeech.com/tst_psy-chophysics.html</a>
Nucleus MATLAB Toolbox	Nucleus 24 or later	MATLAB implementation of Nucleus speech processors	Cochlear	
BEPS+	Advanced Bionics CII, HiRes90K, HiRes90K Advantage	Research Speech Processor Fitting Software	Advanced Bionics	

Note. BEPS+ = Bionic Ear Programming System.

Q70 processors. To ensure biological safety, BEDCS is only capable of providing charge-balanced stimulation with a maximum charge of 120 nC. Furthermore, the default settings in BEDCS 1 require that the MAL must be measured for each different stimulus for each subject before stimulation can be presented in an experiment. This is done to prevent accidental delivery of overly loud stimulation. However, this check can be disabled by the experimenter. This option is allowed so researchers can write their own software which includes their own safety verifications to control BEDCS. In BEDCS 2, all controls to ensure that an overly loud stimulus is not presented to the subject must be written into custom software developed by the researcher.

BEDCS is a highly flexible platform that allows custom pulse shapes and stimulation modes. It can be used for basic psychophysical experiments. In addition, BEDCS 1 can be used for recording of intracochlear potentials and impedance. This capability is not yet available for BEDCS 2. Both versions of BEDCS are limited by the relatively small buffer memory in the processors, which prohibits the use of BEDCS for speech processing. BEDCS 1 can only be used unilaterally, while BEDCS 2 can provide bilateral stimulation. BEDCS 1 has a built-in interface for running basic psychophysical experiments directly within the package. However, researchers are not limited to using the BEDCS 1 interface for running experiments. Instead, researchers can write their own software to control the stimulation. In this case, the custom research software would pass stimulation parameters to BEDCS 1 using the Microsoft ActiveX interface. BEDCS 2 is a library without a stand-alone package which requires the experimenter to write their own software to communicate with the implant.

One of the strengths of BEDCS is that it allows the user to define custom stimulation modes (such as MP, bipolar, and tripolar modes) and pulse shapes (such as an asymmetric rectangular pulse; e.g., Macherey et al., 2006), a nonrectangular pulse (Ballesterio et al., 2015), or even an analog waveform (Morse, Morse, Nunn, Archer, & Boyle, 2007). However, to ensure biological safety, BEDCS verifies that every stimulus is charge balanced and will not stimulate if the charge is not balanced. It is important to note that although BEDCS ensures charge balancing, the experimenter is still responsible for maintaining appropriate loudness, as loudness will be different for different stimulation modes and shapes.

The effects of different pulse shapes and modes on loudness are clearly important and need to be well understood. As discussed earlier, the relevant parameters for any given combination of pulse shape and mode are similar to those outlined for symmetric biphasic rectangular pulses. Therefore, it is important to verify appropriate

loudness settings for each different combination of pulse shape and mode used.

BEDCS 1 can be used to measure impedances, which is important for ensuring stimulation within compliance. In addition, it can be used to measure voltage field spread (e.g., Tang, Benitez, & Zeng, 2011), electrically evoked compound action potentials (Hughes & Stille, 2010), electrocochleography (Dalbert et al., 2015), as well as central potentials by combining multiple recordings (K. Koka, personal communication). However, BEDCS 2 does not presently have the ability to make recordings and therefore cannot measure impedances, voltage field spread, or potentials.

**BEPS+.** BEPS+ is a highly flexible research processor fitting system. It is designed to implement novel sound processing strategies into behind-the-ear processors, allowing subjects to experience the new strategies in a portable platform without being tethered to a PC. One of the important capabilities of BEPS+ is the ability of researchers to deliver complex signals such as speech. Presently BEPS+ programs processors (Harmony or Naida Q70) connected to the PC via the CPI-2 or CPI-3 box. Several parameters can be changed in BEPS+ that cannot be changed in the clinical fitting software packages from any of the manufacturers. In addition, BEPS+ ensures that charge per phase shall be below the FDA limit (120 nC for Advanced Bionics' smallest electrode size). The FDA limit is  $100 \mu\text{C}/\text{cm}^2$ ; given the smallest electrode size,  $0.3 \times 0.4 \text{ mm}$ , this translates to charge of 120 nC. Similar to BEDCS, custom pulse shapes and stimulation modes can be implemented in BEPS+. Appropriate loudness for the user is set in the same manner as a clinical system with a user interface that is very similar to a clinical fitting software package.

### **Cochlear Ltd**

For subjects with Cochlear Ltd. CIs (except for the Nucleus 22), research experiments can be conducted using the nucleus implant communicator (NIC) research software tools provided by Cochlear Ltd. The tools allow direct control of the stimulation amplitude, PD, stimulation rate, and stimulation mode for each electrode. There are currently two versions of the NIC software tools, NIC2 and NIC3. They are both software libraries that provide an interface in Python and MATLAB (programming in NIC2 is also available in C). The NIC2 software communicates with the internal device through a Laura34 (L34) or Freedom processor, while NIC3 supports the L34 and the bilateral radio frequency (RF) generator XS.

NIC2 has been used extensively in psychophysical experiments and can deliver synchronous bilateral stimulation by setting up a master or slave pair of

synchronized L34 processors and using the external trigger of the programming pod, allowing for the generation of interaural timing differences down to  $1 \mu\text{s}$ . However, some researchers have reported that after many hours of use following an initial synchronization trigger, a pair of L34's can lose synchronization with each other because their clocks can never be exactly matched. To ensure better and longer term synchronization between CIs, the RF generator was developed as a new bilateral streaming platform for NIC3, which is one device with a shared clock for both channels. NIC2 can access the intracochlear potential measurement capabilities of the nucleus implants when using the Freedom processor, while for now NIC3 has no intracochlear potential measurement capabilities. For MATLAB, an additional Nucleus MATLAB Toolbox is provided by Cochlear for simulating many aspects of clinical sound processing strategies, such as the advanced combination encoder (ACE) and continuous interleaved sampling (CIS). When making measurements of electrically evoked compound action potentials, and when using different modes of stimulation (MP or bipolar), C and Python are both usable. NIC2 cannot perform low-latency streaming of stimuli, and the duration of a stimulus is limited by the buffer size of the L34 or Freedom processor. NIC3, however, can use the L34 for low-latency streaming ( $<100 \text{ ms}$ ) for an unlimited amount of time but only unilaterally. In addition, NIC3 allows researchers to stream stimuli through bipolar stimulation mode using MATLAB or Python 2.7. All these streaming platforms only provide charge-balanced biphasic pulses with a maximum charge per pulse of 255 nC. While biological safety is ensured by the Cochlear Ltd. implants when using the NIC tools, the onus is on the experimenter to ensure subject comfort by finding the appropriate MAL for each stimulus and having their software check that the MAL is not exceeded. However, if the experimenter is using the Nucleus MATLAB Toolbox, subject comfort can be ensured by using a map generated using Cochlear Ltd.'s clinical software, Custom Sound.

### **MED-EL**

MED-EL does not directly provide a research interface for direct stimulation. Instead, MED-EL will instruct potential researchers to use a third-party research device (Research Interface Box 2 [RIB2]) made available from the University of Innsbruck. More details on this device are provided in the following section.

### **Other Research Systems**

There are a few custom-designed research systems that have been used by various investigators. These are listed in Table 1. Here, we provide brief details of custom-

designed interfaces that are currently in use in laboratories around the world. While some of these interfaces are strictly designed to be used in the laboratory, others are designed to be portable and can be used outside of the laboratory.

### *University of Texas Dallas Personal Digital Assistant*

The University of Texas Dallas personal digital assistant is a portable, bilaterally synchronized, research processor designed to work with Cochlear Nucleus24 and newer Nucleus Devices. It supports unilateral, bilateral, and bimodal stimulation modes. It was originally designed for take-home testing of new speech processing strategies and enhancement or noise reduction algorithms. The first version of the system consists of a custom-made circuit board that interfaces between the CI and a Windows Mobile 5.0 personal digital assistant. Biological safety is ensured in the firmware, where stimulation levels are not allowed to exceed the maximum charge-density levels for the internal electrode array and maximum pulse width is not allowed to exceed 400 nC per phase. Software is written in the C++ programming language, and implementations of the continuous interleaved sampling and advanced combination encoder strategies are available. Subject comfort is ensured through a map, similar to that used in clinical processors. A matlab interface is provided via a DLL, which means it can be programmed with any language, so it is not matlab specific. But also, it has an Android device interface which is probably much more important and makes it the conceptual analog to the first generation, i.e. a take home system as described in the beginning of the paragraph.

### **SPEAR3**

A custom-built research processor, known as the SPEAR3 (Sound Processor for Electric and Acoustic Research, rev. 3), was developed at the hearing cooperative research center in Melbourne (Australia) to work with the Cochlear Nucleus CIs and with hearing aids (<http://www.hearworks.com.au/technology/spear3>).

When used with CIs, the SPEAR3 transmits RF signals to the subject's receiver coils and can be used for both unilateral and bilateral stimulation studies, with MP, bipolar, or common-ground stimulation. This device can control bilateral pulse timing within 2.5  $\mu$ s for chosen pairs of electrodes in the right and left ears, because it has a single digital signal processor controlling the stimulation in both ears. A custom software program allows the user to control stimulation parameters such as PD and amplitude for each electrode. The SPEAR3 can be used as a real-time sound processor to encode acoustic signals via the auxiliary (audio) input of the processor.

The SPEAR3 can also be used to deliver controlled and predetermined stimulation to any electrodes, such as bin-aural stimulation (e.g., Litovsky, Jones, Agrawal, & van Hoesel, 2010; Lu, Litovsky, & Zeng, 2010; van Hoesel & Clark, 1997). The SPEAR3 programming system interface is used to connect the SPEAR3 processor to a computer through a serial communication port. The developers provide a core speech coding program that is a configurable version of the SPEAK strategy, which can be configured to emulate various speech coding strategies that are available in the clinical speech processors. When using the SPEAR3, the experimenter can set parameters of the speech processor program using the SeedSpeak interface, including the T and comfortable levels of stimulation and the clinical frequency-allocation tables for the number of electrodes to be used in the experiment. Researchers who prefer to develop their own applications for testing speech processing or for conducting psychophysics experiments can get access to software development tools. Thus, source code can be developed to configure and access peripherals (such as the programmable amplifier, codec, etc.) in the SPEAR3 processor. Assembler tools are also provided (Motorola DSP563xx), as well as some application source code. In addition, left and right volume controls are provided as means for balancing loudness across ears. Notably, when the SPEAR3 is used for direct stimulation experiments with custom psychophysics software, the same issues regarding biological safety and listening comfort apply as those discussed earlier for the NIC.

### *University of Southern California Cochlear Implant Research Interface (Formerly House Ear Institute Nucleus Research Interface and Boys Town Nucleus Research Interface)*

The University of Southern California Cochlear Implant Research Interface was originally developed at Boys Town National Research Hospital (Shannon, Adams, Ferrel, Palumbo, & Grandgenett, 1990) and was known as the Boys Town Nucleus Research Interface (BTNRI). In 1989, the design was brought to the House Ear Institute where it was updated to support the newer Nucleus protocols and implants. While at the House Ear Institute, the interface box was given the name House Ear Institute Nucleus Research Interface (HEINRI), which is the name by which the interface is best known (Shannon, 2015). Recently, after the group developing the HEINRI relocated to the University of Southern California, the device has been renamed the University of Southern California Cochlear Implant Research Interface. As the devices are interchangeable, most publications refer to the device as HEINRI (e.g., Chatterjee & Peng, 2008;

Chen, Ishihara, & Zeng, 2005; Luo & Fu, 2007; Sanpetrino & Smith, 2006). The HEINRI allows control over PD, interphase gap, and amplitude for each pulse. The amplitudes are specified in terms of the Cochlear clinical units. Therefore, the highest output amplitude from the HEINRI is the same as the highest amplitude level allowed by the internal receiver or stimulator of the Cochlear Nucleus CI, and this level is different across the Cochlear models. The charge per phase can also be modified by changing the phase duration, which can be changed in increments of  $2\ \mu\text{s}$  for all Nucleus devices except the Nucleus22 which can be changed in increments of  $4\ \mu\text{s}$ . The HEINRI also has a software component that restricts total charge ( $\mu\text{A} \times \mu\text{s}/\text{phase}$ ) to be less than the guidelines outlined in Shannon (1992). In terms of its utility, the HEINRI is similar to the NIC. It is capable of delivering synchronous bilateral stimulation using two HEINRIs setup in a master or slave configuration. The HEINRI (unlike the NIC) works with the Nucleus22 devices, facilitating bilateral research with subjects who have a Nucleus22 in one ear and a later model Nucleus device in the contralateral ear. Custom software can be written in any language that can interface with a Windows Dynamic-Link Library (DLL).

## RIB2

The RIB2 is a research interface that can communicate directly to all MED-EL CI models released since the Combi 40H. The RIB2 is available from the University of Innsbruck. Originally, the RIB2 consisted of custom hardware and a DLL library. To connect the RIB2 custom hardware to a PC, a National Instruments board is required. The latest version of the RIB2 DLL also allows the latest clinical fitting interface (the MAX) to be used instead of the custom hardware. The RIB2 can provide both biphasic and triphasic pulses. To ensure biological safety, the RIB2 is only capable of providing charge-balanced stimulation. The maximum electrical charge per phase is  $283\ \text{nC}$ , thus limited to prevent damage to cochlea and electrodes even after prolonged stimulation.

The RIB2 requires all research software to be custom written in either C++, MATLAB, Python, Visual Basic, or any other language that can interface to a Windows DLL. The RIB2 hardware (and MAX) drives a left and right transmitting coil, allowing easy control for bilateral stimulation. The two coils are run with the same clock from the same hardware, eliminating the need for two devices in a master or slave configuration (as is used in the NIC and HEINRI systems). The RIB2 also allows for recording of intracochlear potentials. Although no sound coding strategy algorithms are provided, the researcher can pre-render stimulus patterns derived from audio signals and present them via the RIB2.

Real-time speech coding strategies can potentially be implemented using double buffering. As is the limitation with the MED-EL CIs, stimulation can only be in MP mode. However, because the MED-EL CIs have independent current sources for each electrode, parallel stimulation can be provided by the RIB2.

## Conclusion

To date, numerous research laboratories worldwide have conducted psychophysical experiments with CI users. One approach is to use research interfaces, which have the advantage of bypassing the subjects' clinical sound processors, and enabling precise control over stimulus parameters that are under investigation. Because of the growing interest in these approaches, this article aimed to identify several concerns regarding safety and to outline best-practice approaches for how to safely and ethically perform this type of research. In this article, we discussed the three main safety and comfort concerns. First, there is a need to ensure that biological or neural damage is avoided. Second, it is important to ensure that sounds are played at levels that are not perceived by the subjects as being uncomfortably loud. Third, it is important to ensure that subjects have control over stimulus presentation. While some laboratories implement their own software packages, others obtain software from colleagues or from manufacturers of the interfaces. Thus, researchers must pay close attention to the software-hardware interface to ensure that the three main safety and comfort concerns are closely monitored. Future development of other interfaces may take place, and CI technology used in research with CIs may evolve. The way that these changes may impact the approaches described here is not predictable but must be carefully monitored.

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## References

- Ali, H., Lobo, A. P., & Loizou, P. C. (2013). Design and evaluation of a personal digital assistant-based research platform for cochlear implants. *IEEE Transactions on Biomedical Engineering*, *60*(11), 3060–3073. doi:10.1109/TBME.2013.2262712
- Ballester, J., Recugnat, M., Laudanski, J., Smith, K. E., Jagger, D. J., Gnansia, D., & McAlpine, D. (2015). Reducing current spread by use of a novel pulse shape for electrical stimulation of the auditory nerve. *Trends in Hearing*, *19*. doi:10.1177/2331216515619763.
- Bierer, J. A. (2007). Threshold and channel interaction in cochlear implant users: Evaluation of the tripolar electrode configuration. *Journal of the Acoustical Society of America*, *121*(3), 1642–1653. doi:10.1121/1.2436712
- Berenstein, C. K., Mens, L. H., Mulder, J. J., & Vanpoucke, F. J. (2008). Current steering and current focusing in cochlear implants: Comparison of monopolar, tripolar, and virtual channel electrode configurations. *Ear and Hearing*, *29*(2), 250–260. doi:10.1097/AUD.0b013e3181645336
- Busby, P. A., Whitford, L. A., Blamey, P. J., Richardson, L. M., & Clark, G. M. (1994). Pitch perception for different modes of stimulation using the cochlear multiple-electrode prosthesis. *Journal of the Acoustical Society of America*, *95*(5 Pt 1), 2658–2669. doi:10.1121/1.409835
- Carlyon, R. P., van Wieringen, A., Deeks, J. M., Long, C. J., Lyzenga, J., & Wouters, J. (2005). Effect of inter-phase gap on the sensitivity of cochlear implant users to electrical stimulation. *Hearing Research*, *205*(12), 210–224. doi:10.1016/j.heares.2005.03.021
- Chatterjee, M. (1999). Effects of stimulation mode on threshold and loudness growth in multielectrode cochlear implants. *Journal of the Acoustical Society of America*, *105*(2, Pt 1), 850–860. doi:10.1121/1.426274
- Chatterjee, M., Fu, Q. J., & Shannon, R. V. (2000). Effects of phase duration and electrode separation on loudness growth in cochlear implant listeners. *Journal of the Acoustical Society of America*, *107*(3), 1637–1644. doi:10.1121/1.428448
- Chatterjee, M., & Peng, S. C. (2008). Processing F0 with cochlear implants: Modulation frequency discrimination and speech intonation recognition. *Hearing Research*, *235*, 143–156. doi:10.1016/j.heares.2007.11.004
- Chen, H., Ishihara, Y. C., & Zeng, F. G. (2005). Pitch discrimination of patterned electric stimulation. *Journal of the Acoustical Society of America*, *118*, 338–345. doi:10.1121/1.1937228
- Dalbert, A., Pfiffner, F., Roosli, C., Thoele, K., Sim, J. H., Gerig, R., & Huber, A. M. (2015). Extra- and intracochlear electrocochleography in cochlear implant recipients. *Audiology and Neurotology*, *20*(5), 339348. doi:10.1159/000438742
- Donaldson, G. S., Kreft, H. A., & Litvak, L. (2005). Place-pitch discrimination of single- versus dual-electrode stimuli by cochlear implant users (L). *Journal of the Acoustical Society of America*, *118*(2), 623–626. doi:10.1121/1.1937362
- Firszt, J. B., Koch, D. B., Downing, M., & Litvak, L. (2007). Current steering creates additional pitch percepts in adult cochlear implant recipients. *Otology and Neurotology*, *28*(5), 629–636. doi:10.1097/01.mao.0000281803.36574.bc
- Frijns, J. H., Kalkman, R. K., Vanpoucke, F. J., Bongers, J. S., & Briaire, J. J. (2009). Simultaneous and non-simultaneous dual electrode stimulation in cochlear implants: Evidence for two neural response modalities. *Acta Otolaryngol*, *129*, 433–439. doi:10.1080/00016480802610218
- Hong, R. S., & Rubinstein, J. T. (2003). High-rate conditioning pulse trains in cochlear implants: Dynamic range measures with sinusoidal stimuli. *Journal of the Acoustical Society of America*, *114*(6 Pt 1), 3327–3342. doi: 10.1121/1.1623785.
- Hughes, M. L., & Stille, L. J. (2010). Effect of stimulus and recording parameters on spatial spread of excitation and masking patterns obtained with the electrically evoked compound action potential in cochlear implants. *Ear and Hearing*, *31*(5), 679–692. doi:10.1097/AUD.0b013e3181e1d19e
- Kan, A., Stoelb, C., Litovsky, R. Y., Goupell, M. J., & Ye, D. (2013). Effect of mismatched place-of-stimulation on binaural fusion and lateralization in bilateral cochlear-implant users. *The Journal of the Acoustical Society of America*, *134*(4), 2923–2936. doi:10.1121/1.4820889
- Landsberger, D., & Galvin, 3rd., J. J. (2011). Discrimination between sequential and simultaneous virtual channels with electrical hearing. *Journal of the Acoustical Society of America*, *130*(3), 1559–1566. doi:10.1121/1.3613938
- Landsberger, D. M., Padilla, M., & Srinivasan, A. G. (2012). Reducing current spread using current focusing in cochlear implant users. *Hearing and Research*, *284*(1–2), 16–24. doi:10.1016/j.heares.2011.12.009
- Landsberger, D. M., & Srinivasan, A. G. (2009). Virtual channel discrimination is improved by current focusing in cochlear implant recipients. *Hearing and Research*, *254*(1–2), 34–41. doi:10.1016/j.heares.2009.04.007
- Litovsky, R. Y., Jones, G. L., Agrawal, S., & van Hoesel, R. (2010). Effect of age at onset of deafness on binaural sensitivity in electric hearing in humans. *Journal of the Acoustical Society of America*, *127*(1), 400–414. doi:10.1121/1.3257546
- Loizou, P. C., Hu, Y., Litovsky, R., Yu, G., Peters, R., Lake, J., ... Roland, P. (2009). Speech recognition by bilateral cochlear implant users in a cocktail-party setting. *The Journal of the Acoustical Society of America*, *125*(1), 372–383. doi:10.1121/1.3036175
- Lu, T., Litovsky, R., & Zeng, F. G. (2010). Binaural masking level differences in actual and simulated bilateral cochlear implant listeners. *Journal of the Acoustical Society of America*, *127*, 1479–1490. doi:10.1121/1.3290994
- Luo, X., & Fu, Q. J. (2007). Frequency modulation detection with simultaneous amplitude modulation by cochlear implant users. *Journal of the Acoustical Society of America*, *122*, 1046–1054. doi:10.1121/1.2751258
- Macherey, O., van Wieringen, A., Carlyon, R. P., Deeks, J. M., & Wouters, J. (2006). Asymmetric pulses in cochlear implants: Effects of pulse shape, polarity, and rate. *Journal of the Association for Research in Otolaryngology*, *7*(3), 253–266. doi:10.1007/s10162-006-0040-0
- Majdak, P., Laback, B., & Baumgartner, W.-D. (2006). Effects of interaural time differences in fine structure and envelope on lateral discrimination in electric hearing. *Journal of the Acoustical Society of America*, *120*(4), 2190–2201. doi:10.1121/1.2258390

- McCreery, D. B., Agnew, W. F., Yuen, T. G., & Bullara, L. (1990). Charge density and charge per phase as cofactors in neural injury induced by electrical stimulation. *IEEE Transactions on Biomedical Engineering*, 37(10), 996–1001. doi:10.1109/10.102812
- McCreery, D. B., Agnew, W. F., Yuen, T. G., & Bullara, L. A. (1988). Comparison of neural damage induced by electrical stimulation with faradaic and capacitor electrodes. *Annals of Biomedical Engineering*, 16(5), 463–481. doi:10.1007/BF02368010
- McCreery, D. B., Agnew, W. F., Yuen, T. G., & Bullara, L. A. (1992). Damage in peripheral nerve from continuous electrical stimulation: Comparison of two stimulus waveforms. *Medical and Biological Engineering and Computing*, 30(1), 109–114. doi:10.1007/BF02446202
- McCreery, D. B., Agnew, W. F., Yuen, T. G., & Bullara, L. A. (1995). Relationship between stimulus amplitude, stimulus frequency and neural damage during electrical stimulation of sciatic nerve of cat. *Medical and Biological Engineering and Computing*, 33(3 Spec No), 426–429. doi:10.1007/BF02510526
- McKay, C. M., & Henshall, K. R. (2003). The perceptual effects of interphase gap duration in cochlear implant stimulation. *Hearing and Research*, 181(1–2), 94–99. doi:10.1016/S0378-5955(03)00177-1
- McKay, C. M., Remine, M. D., & McDermott, H. J. (2001). Loudness summation for pulsatile electrical stimulation of the cochlea: Effects of rate, electrode separation, level, and mode of stimulation. *Journal of the Acoustical Society of America*, 110(3 Pt 1), 1514–1524. doi:10.1121/1.1394222
- Morse, R. P., Morse, P. F., Nunn, T. B., Archer, K. A., & Boyle, P. (2007). The effect of Gaussian noise on the threshold, dynamic range, and loudness of analogue cochlear implant stimuli. *Journal of the Association for Research in Otolaryngology*, 8(1), 42–53. doi:10.1007/s10162-006-0064-5
- Padilla, M., & Landsberger, D. M. (2014). Loudness summation using focused and unfocused electrical stimulation. *Journal of the Acoustical Society of America*, 135(2), EL102–EL108. doi:10.1121/1.4862877
- Padilla, M., Stupak, N., & Landsberger, D. M. (2017). Pitch Ranking with Different Virtual Channel Configurations in Electrical Hearing. *Hearing Research*, 348, 54–62. doi:10.1016/j.heares.2017.02.013
- Prado-Guitierrez, P., Fewster, L. M., Heasman, J. M., McKay, C. M., & Shepherd, R. K. (2006). Effect of interphase gap and pulse duration on electrically evoked potentials is correlated with auditory nerve survival. *Hearing and Research*, 215(1–2), 47–55. doi:10.1016/j.heares.2006.03.006
- Ramekers, D., Versnel, H., Strahl, S. B., Smeets, E. M., Klis, S. F., & Grolman, W. (2014). Auditory-nerve responses to varied inter-phase gap and phase duration of the electric pulse stimulus as predictors for neuronal degeneration. *Journal of the Association for Research in Otolaryngology*, 15(2), 187–202. doi:10.1007/s10162-013-0440-x
- Sanpetrino, N. M., & Smith, R. L. (2006). The growth of loudness functions measured in cochlear implant listeners using absolute magnitude estimation and compared using Akaike's information criterion. *Conference Proceedings of IEEE Engineering in Medicine and Biology Society*, 1, 1642–1644. doi:10.1109/IEMBS.2006.259984
- Saoji, A. A., Landsberger, D. M., Padilla, M., & Litvak, L. M. (2013). Masking patterns for monopolar and phantom electrode stimulation in cochlear implants. *Hearing and Research*, 298, 109–116. doi:10.1016/j.heares.2012.12.006
- Saoji, A. A., & Litvak, L. (2010). Use of “phantom electrode” technique to extend the range of pitches available through a cochlear implant. *Ear and Hearing*, 31(5), 693–701. doi:10.1097/AUD.0b013e3181e1d15e
- Shannon, R. V. (1983). Multichannel electrical stimulation of the auditory nerve in man. II. Channel interaction. *Hearing and Research*, 12(1), 1–16. doi:10.1016/0378-5955(83)90115-6
- Shannon, R. V. (1992). A model of safe levels for electrical stimulation. *IEEE Transactions on Biomedical Engineering*, 39(4), 424–426. doi:10.1109/10.126616
- Shannon, R. V. (2015). Auditory implant research at the House Ear Institute 1989-2013. *Hearing and Research*, 322, 57–66. doi:10.1016/j.heares.2014.11.003
- Shannon, R. V., Adams, D. D., Ferrel, R. L., Palumbo, R. L., & Grandgenett, M. (1990). A computer interface for psychophysical and speech research with the nucleus cochlear implant. *Journal of the Acoustical Society of America*, 87(2), 905–907. doi:10.1121/1.398902
- Srinivasan, A. G., Shannon, R. V., & Landsberger, D. M. (2012). Improving Virtual Channel Discrimination in a Multi-Channel Context. *Hearing Research*, 286(1–2), 19–29. doi:10.1016/j.heares.2012.02.01
- Tang, Q., Benitez, R., & Zeng, F. G. (2011). Spatial channel interactions in cochlear implants. *Journal of Neural Engineering*, 8, 046029. doi:10.1088/1741-2560/8/4/046029
- van Hoesel, R. J. M., & Clark, G. M. (1997). Psychophysical studies with two binaural cochlear implant subjects. *Journal of the Acoustical Society of America*, 102(1), 495–507. doi:10.1121/1.419611
- van Hoesel, R. J. M., Jones, G. L., & Litovsky, R. Y. (2009). Interaural Time-Delay Sensitivity in Bilateral Cochlear Implant Users: Effects of Pulse Rate, Modulation Rate, and Place of Stimulation. *Journal of the Association for Research in Otolaryngology*, 10(4), 557–567. doi:10.1007/s10162-009-0175-x
- van Wieringen, A., Carlyon, R. P., Laneau, J., & Wouters, J. (2005). Effects of waveform shape on human sensitivity to electrical stimulation of the inner ear. *Hearing and Research*, 200(1–2), 73–86. doi:10.1016/j.heares.2004.08.006
- Zeng, F. G., Galvin, 3rd., J. J., & Zhang, C. (1998). Encoding loudness by electric stimulation of the auditory nerve. *Neuroreport*, 9(8), 1845–1848.
- Zeng, F. G., & Shannon, R. V. (1994). Loudness-coding mechanisms inferred from electric stimulation of the human auditory system. *Science*, 264, 564–566. doi:10.1126/science.8160013
- Zhu, Z., Tang, Q., Zeng, F. G., Guan, T., & Ye, D. (2012). Cochlear-implant spatial selectivity with monopolar, bipolar and tripolar stimulation. *Hearing and Research*, 283(1–2), 45–58. doi:10.1016/j.heares.2011.11.005