2F2-F1 DPOAE SOURCES IN CONTRADICTION TO THE TWO-SOURCE/TWO-MECHANISM MODEL?

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Distortion product otoacoustic emissions (DPOAEs) can be separated into distortion (active/hair-cell-generator based) and reflection sources (passive/hydro-mechanically based). These sources are linked to specific physiological-acoustic events along the cochlear partition. Researchers have shown that the 2f1-f2 component (using parameters of f2/f1=1.22, 65/55 dB SPL) is dominated by the distortion source. However, the 2f2-f1 is far less well understood and rarely tested. Measured with presumed optimal parameters, f2/f1=1.08, 65/65 dB SPL it is likely dominated by the reflection source. Researchers rarely have described ripple characteristics of the 2f2-f1 fine structure (the function of magnitude versus frequency assessed using high-resolution analysis) well known for 2f1-f2. Differences are expected between components due to their putative differences of kind and place of production.

The purpose of this study was to determine how ripple characteristics differ between 2f1-f2 and 2f2-f1 using fine-structure DPOAE analyses elicited by parameters promoting robust responses for components using two sets of parameters: (1) f2/f1=1.22, 65/55 dB SPL and (2) f2/f1=1.08, 65/65 dB SPL. Inverse Fast Fourier Transform conversion of frequency into time–domain measures separated the sources.

The first prediction was 2f1-f2 would be dominated by the distortion source, given f2/f1=1.22, 65/55 dB SPL, and dominated by the reflection source with f2/f1=1.08, 65/65 dB SPL. The 2f2-f1 component, posited on theoretical grounds, would be dominated by the reflection source for both parameter sets. The second prediction was the two components would differ in ripple spacing, depth, and prevalence, presumably in deference to the diversity in their respective origins.

The following conclusions could be made: First, the distortion source was affirmed to be dominant for the 2f1-f2 DPOAE when measured using the f2/f1=1.22, 65/55 dB SPL parameter set for all participants (24/24). Furthermore, the reflection source was confirmed to be dominant for the other three conditions, with 100% occurrence for the 2f2-f1 DPOAE measured using the f2/f1=1.08, 65/65 dB SPL. There also were significant differences among the ripple characteristics measured under the four conditions. These results, while not contradicting two-source/two-mechanism model overall; nevertheless suggest need for some revision, as proposed. They also may help to promote greater interests in 2f2-f1, including applications.

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PREFACE

A short statement seems inadequate to express my appreciation and gratitude to those who have supported me throughout my doctoral program. I am a lucky woman to have such supportive family, friends, and colleagues in my life. You have each played a vital role in the realization of my dream. I wish you the same love and dedication as you have shown me.

1.0 INTRODUCTION

Otoacoustic Emissions (OAEs) are an indirect physiologic measure of the active responses from the outer hair cells to sound and of the health of the cochlea (Bonfils, Piron, Uziel, & Pujol, 1988; Gaskill & Brown, 1990; Lonsbury-Martin, Martin, Probst, & Coats, 1987). One measure of OAEs is distortion product OAEs (DPOAEs), which occur when two tones of differing frequency (f1 and f2, the primary tones) are presented to the ear simultaneously. The nonlinearity of the cochlea creates a third tone, the distortion product (DP) (Harris, Lonsbury-Martin, Stagner, Coats, & Martin, 1989). The frequency of the DP depends on the combination of the two primary tones. This third tone returns to the outer ear for measurement via backward traveling waves. The classification system of the backward traveling waves and the sources that create them is called taxonomy. Taxonomy is not just a classification nomenclature, but includes identification and description of concepts or principles.

Kemp's taxonomy for otoacoustic emissions (OAEs) was based on the absence or presence of evoking stimuli, separating spontaneous OAEs (SOAEs) from the others (*i.e.*, transient OAEs, stimulus frequency OAEs, and distortion product OAEs; Kemp, 1986). This taxonomy lasted until Shera and Guinan (1999) suggested a change that has gained wide-spread acceptance with other OAE researchers. The new taxonomy is based on the way in which backward traveling waves are created. Specifically, backward traveling waves are created by the nonlinear interaction of the primary-tone traveling waves creates the distortion source and the measurable linear reflections that accumulate from returning wavelets and the physical inhomogeneities of the cochlear partition create the reflection source. Both sources contribute to the formation of distortion product OAEs (DPOAEs) measured in the ear canal, though only one source dominates each measured distortion product and is dependent on the parameters used to shape the primary tones (Dhar, Talmadge, Long & Tubis, 2002). The 2f2-f1 component appears to be dominated by the reflection source (Wilson & Lutman, 2006). This differs from the 2f1-f2 component which may be dominated by either source depending on test parameters (Kalluri & Shera, 2001).

Most researchers who have described DPOAE sources used the 2f1-f2 component (Dhar, Talmadge, Long & Tubis, 2002; Gaskill & Brown, 1990; Kemp & Brown, 1984). This is no surprise as a majority of all DPOAE researchers have focused on the 2f1-f2 component and the frequency region (Fdp) below the primary tones (Kirby, Kopun, Tan, Neely, & Gorga, 2011). However, the 2f2-f1 component allows researchers to study the frequency region above the primary tones and to research in a more apical region of the cochlear partition; a frequency region known to negatively affect the measurement of the 2f1-f2 component (Gorga, Nelson, Davis, Dorn & Neely, 2000; Martin, Jassir, Stagner, Whitehead, & Lonsbury-Martin, 1998). The problem with using the 2f2-f1 component has been a lack of standardized parameters shown to improve its response magnitude (Knight & Kemp, 1999, 2000; Martin, Stagner, & Lonsbury-Martin, 2010). More recently, researchers have focused on finding the best test parameters for generating the 2f2-f1 component (Fitzgerald & Prieve, 2005; Horn, Pratt & Durrant, 2008).

Distortion product OAEs may be displayed using several techniques, such as the DP-gram or the input-output function, which will be described in a later section. For this study, the contribution of distortion and reflection sources were studied in small frequency ranges by using fine-structure DPOAEs. The fine-structure study of the 2f1-f2 and 2f2-f1 components provided targeted information of the cochlear partition above and below the primary tones, expanding knowledge of the way in which distortion and reflection sources, and their generating mechanisms, contribute to the formation of DPOAEs.

The overall aim of this study thus was to determine if the parameter combinations change the response magnitude for the fine structure of the 2f2-f1 DP component, affect the ripple characteristics of the fine-structure spectrum, and to determine which sources dominate the 2f1-f2 and 2f2-f1 components.

The following literature review will cover anatomy and physiology of the ear, macromechanical and micromechanical functions, acoustical concepts, OAEs in general, DPOAEs in specific, DPOAE generation theories, fine structure, and source separation techniques in order to provide background for the rationale and questions posed for the current study.

2.0 LITERATURE REVIEW

2.1 ANATOMY OF THE EAR

The outer ear, middle ear, and inner ear work together so that sound energy is encoded effectively by the hearing organ in order to excite the auditory nerve. Only a brief description of the relevant structures follows, but interested readers are referred to Geisler (1998) for an in-depth review.

2.1.1 Outer Ear

The outer ear is made up of the pinna and the ear canal that directs sound energy towards the tympanic membrane. Its presence influences the function of the middle ear due to its length. The ear canal measures 2.5 cm in humans and acts as a one-sided closed tube with the tympanic membrane acting as the closed end (Durrant & Feth, 2013). This format helps to transmit sounds above 1000 Hz in frequency and creates a short transmission time for signals traveling to the middle and inner ears. It should be noted that the ear canal may create a standing wave formation wherein incident and reflected waves interfere with sound transmission.

2.1.2 Middle Ear

The middle ear contains the tympanic membrane, the ossicles, and the outlet for the cochlea in the form of cochlear windows (oval and round). The middle ear is an impedance matching device between air and fluid environments. Impedance matching is most efficient in the mid-speech frequencies for humans. Ossicular motion provides a source of energy on the forward path of sound to the cochlear nerve and a backward path to the outer ear as is seen in otoacoustic emissions, a test of the inner ear. Beneficial to the measurement of the ear, the middle ear does not produce nonlinear distortion; it is linear over the practical dynamic range in hearing (Guinan & Peake, 1967).

2.1.3 Inner Ear

2.1.3.1 Overall Anatomy/Organization The inner ear comprises three scalae – the scala vestibuli, scala media, and scala tympani. These three channels narrow as they approach the helicotrema-end of the cochlea. The scala vestibuli and scala tympani are channels filled with perilymph, a sodium-based fluid, whereas the scala media is filled with endolymph, a potassium-based fluid, with the exception of the fluid in the tunnel and spaces of Nuel (see below).

The scala media is a fluid channel that encapsulates the anatomical structures of the cochlear partition. Within the cochlear partition is the organ of hearing (or organ of Corti) that contains the sensory cells needed to transfer energy to the eighth cranial nerve. The organ of Corti is defined by the reticular lamina on top and by the basilar membrane on the bottom (Lim, 1980). It contains the inner and outer sensory hair cells, supporting cells, and cortilymph (a sodium-based fluid in the spaces of Nuel). In contradiction to the shape of the perilymph-filled scalae, the cochlear partition widens at the helicotrema-end of the cochlea.

The organization of the cochlea is tonotopic. This is the phenomenon by which the frequencies within the inner ear are encoded. High frequencies have peak displacement at the base of the cochlear partition with frequencies decreasing as the apex is approached. This was discovered by Helmholtz (1877), with the underlying macromechanical events demonstrated by Bekesy (1947), and this scheme allows for the cochlear partition to act as a frequency analyzer (Smoorenburg, 1972).

2.1.3.2 Surface of the Auditory Sensory Macula There are generally four rows of hair cells within in the cochlear partition, particularly in primates – one row of inner hair cells (IHCs) and three rows of outer hair cells (OHCs). The inner hair cells do not sit on the basilar membrane directly, but are surrounded by their supporting cells.

The OHCs sit atop of their supporting cells (Deiter's cells) whose phalanges comprise part of the reticular lamina along with the tops of the OHCs (Lim, 1980). The reticular lamina is the "tissue" from which the small hairs or stereocilia of the hair cells emerge. The OHC hairs or stereocilia form a "W" pattern in each row with the base pointed away from the IHCs. They are arranged in size from largest to smallest and are connected to each other by tiplinks. The stereocilia of the OHCs are embedded in the bottom of the tectorial membrane whereas those of the IHCs are not.

The tectorial membrane is a gel-like structure that lies above the hair cells with the stereocilia of the outer hair cells embedded within it. The outer edge of the tectorial membrane is loosely attached in the area of the Hensen's cells and the inner edge is attached at the lip of the spiral limbus (near the modiolus) (Lim, 1980).

2.1.3.3 Inhomogeneities Inhomogeneities include normally-occurring features such as areas of extra hair cells or missing hair cells. These features occur due to the imperfect nature of the mosaic called the reticular plate, but inhomogeneities also may occur due to damage along the cochlear partition (Lonsbury-Martin, Martin, Probst, & Coats, 1988). Damage may be due to illness, infection, or overuse (Talmadge, Long, Tubis, & Dhar, 1999; Wilson & Lutman, 2006). The location of the inhomogeneities varies for each person, but does not change location (*i.e.*, place-fixed). Inhomogeneities contribute to the formation of certain phenomena (*e.g.*, otoacoustic emissions).

2.2 FUNCTIONAL ACOUSTICS OF THE COCHLEA (MACROMECHANICS)

2.2.1 Stapedial Motion

The stapes moves in a piston-like motion in and out of the oval window (Guinan & Peake, 1967). As the stapedial footplate moves inwards, the cochlear partition is deflected towards the scala tympani and there is an outward displacement of the round window. When the stapedial footplate moves outwards, the cochlear partition is deflected towards the scala vestibuli and the round window moves inward.

2.2.2 Traveling Waves

Traveling waves were first demonstrated by Bekesy in 1947. In its simplest explanation, a traveling wave is a displacement of the cochlear partition corresponding to a pure tone input. The repeated displacement of the cochlear partition is called a traveling-wave envelope. The envelope of vibration shows increasing amplitude of vibration of the cochlear partition until the characteristic place per frequency of the stimulus is reached with a rapid decrease in vibration beyond. Pure tones stimulate specific frequency regions along the cochlear partition with high frequencies stimulated at the basal end and low frequencies stimulated at the apical end.

2.2.3 Backward Traveling Waves

Sound travels out of the ear as well. Given normal cochlear function, the backward-traveling waves partially create otoacoustic emissions that may be measured with a probe sealed in the outer ear. In 1955, Bekesy described backward traveling waves as a rare occurrence in his observation. Current researchers have shown that backward traveling waves occur often, but they are not amplified and therefore could not be seen in Bekesy's cadavers (de Boer, Nuttall, & Shera, 2007).

2.2.3.1 Proof of Existence Kemp (1979a) created the Evoked Cochlear Mechanical Response (ECMR) model to suggest a cochlear genesis for OAEs. His research suggested "retrograde" waves likely existed on the basilar membrane and were thought to be created from some component of the basilar membrane. Kemp hypothesized the retrograde wave was as large as the original traveling wave at low stimulus levels, although smaller with high stimulus levels. As such, the retrograde mechanism was considered to be nonlinear due to the violation of the principle of homogeneity. Kemp's views were echoed by other researchers as described in later sections of this review.

2.2.3.2 Not Convinced Some researchers have argued against the existence of backward traveling waves. Ren and colleagues (Ren, 2004; Ren & Nuttall, 2006) maintained that OAEs return to the ear canal via fluid compression waves and not through backward traveling waves created along the cochlear partition. Using laser interferometry on gerbils, these researchers were not able to see backward traveling waves, but their research was compromised by issues such as low reflection of the basilar membrane at the level of 0.032% - meaning the recordings were noisy. It is possible the reflection was not observed because it was embedded in the noise.

2.2.4 Frequency-Dependent Encoding of Sound – Place Theory

Place theory was developed to explain that high frequencies, again, are encoded in the basal end of the cochlea and the low frequencies are encoded in the apex (Helmholtz, 1877). Originally, it was thought that the cochlear partition was segmented into strips and that each strip had a characteristic frequency (Helmholtz, 1877). It is known now that the cochlear partition is not a series of strips or strings, but arranged in tonotopic frequency regions. The frequency regions can be analyzed from their place of origin on the cochlear partition before that information reaches the auditory nerve (Galambos & Davis, 1948). From this theory, the brain can determine the frequency of signals by understanding from what part of the cochlear partition the sound arises. However, place theory does not preclude frequency encoding by temporal cues, and indeed both mechanisms are embraced by modern theory.

2.2.5 Behavior of the Cochlear Partition – Historical Perspective

In 1953, Davis reported differences that existed between the function of the organ of Corti and the neural network of the brain. Essentially he was trying to account for the differences between cochlear and neural tuning mechanisms. He attributed the difference between cochlear and neural functions to the existence of primary and secondary neurons. The primary neurons of the organ of Corti were not as sharply tuned as the secondary neurons of the brain.

Other researchers looked at the differences between the neural and cochlear data, and created the concept of the second filter (Evans & Wilson, 1973). The tuning of the cochlea was not as sharp as that of the neural fibers (Allen, 1980) and researchers thought there must be some sort of secondary filter to help the cochlear fibers become as sharply tuned as the neural ones (Allen, 1980; Davis, 1981). It was suggested that the second filter acted as a resonator (Davis, 1981). Then it was hypothesized that the second filter was a physical mechanism within the cochlea, likely a micromechanical function (Allen, 1980). Other researchers hypothesized that the filter was located in the organ of Corti (Davis, 1981; Russell & Sellick, 1977). This assumption was based on two beliefs. First, the second filter was vulnerable to physiological changes (Davis, 1981; Rhode, 1980). Second, Russell and Sellick (1977) had found inner hair cell tuning to be very sharp, thereby eliminating any post-hair-cell sharpening mechanism. Rhode (1980) speculated that cochlear nonlinearity appeared to reduce the discrepancy between cochlear and neural tuning. In truth, there was, and is, no second filter in the mechanism. Differences found between the early cochlear and neural tuning data are likely due to poor or insensitive measurement techniques and/or dead hair cells.

Some researchers came close to present-day knowledge of cochlear function. In 1970, Kiang, Moxon, and Levine studied kanamycin-damaged hair cells in cats. They obtained cochlear tuning curves for normal-hearing and hearing-impaired cats. The tuning curves for the normal-hearing cats were sharp whereas the tuning curves of the damaged ears were wider and/or required louder intensity to be measured. They also observed hair-cell damage in the highest frequency regions of the cochlea, with greater damage for the outer hair cells than the inner hair cells. The researchers could not show neural degeneration following kanamycin injection indicating a mechanistic difference between cochlear and neural function.

Dallos and colleagues in the late 1960s and early 1970s described a two stage process for cochlear distortion by studying cochlear microphonic potentials (Dallos, Schoeny, Worthington, & Cheatham, 1969; Durrant & Dallos, 1972). They saw cochlear distortion as both a high- and low-intensity stimulus phenomenon, based on the intensity of the stimulus used to elicit the cochlear microphonic. Dallos *et al*. found an electromechanical phenomenon (*i.e.*, hair cells) accounted for distortion from low-level stimulus intensities whereas a hydromechanical phenomenon (*i.e.*, cochlear fluids) accounted for distortion from high-level stimulus intensities. Durrant and Dallos (1972) identified the two-stage, stimulus-intensity phenomenon for cochlear distortion in harmonic distortion products. They found that 85-95 dB SPL was the transition level between the electromechanical and hydromechanical distortions. Their data argued that the cochlea was the source of the distortion although the distortion mechanisms remained an issue. The concept of two sources as the basis for cochlear phenomenon remains today, although considerably transformed (see below) and with attention focus on the lower side of the dynamic range, although it was at relatively lower SPLs that Dallos and his co-workers suspected the source to be the hair cells themselves, most likely the OHCs.

2.3 MICROMECHANICS – OVERVIEW OF CURRENT THEORY

2.3.1 Motile Responses of OHCs

Outer hair cells (OHCs) have a motile response meaning that the cells lengthen and shorten when vibrated. Hair cell motility is caused by a voltage change across the top of a hair cell (Geisler, 1998). The motility elements of the OHC are located on the lateral surface (or walls) of the cells (Geisler, 1998; Dallos, 1996). When the stereocilia are displaced towards the tallest stereocilia of the hair cell, it is depolarized (a change in the membrane potential toward less negative), causing the cell to somewhat contract in length. A push in the opposite direction hyperpolarizes the cell relative to its quiescent operating point, causing the cell to lengthen. In this manner, vibration of the cell amplifies the vibration of the cochlear partition.

2.3.2 Hair Cell Transfer Function – Output Not Simply Proportional to Input

Hair cells can amplify the power of a signal during energy conversion (Geisler, 1998). OHCs can contract and lengthen in response to extra- and intra-cellular currents (Kros, 1996) and thanks to relatively tight coupling of their stereocilia to the tectorial membrane, as noted earlier. Stereocilia of IHCs are not connected to the tectorial membrane and are pushed-pulled by velocity of the surrounding fluid. Hair cells have a limited or asymmetric output.

2.4 ACOUSTICAL CONCEPTS

Previous sections focused on the peripheral auditory system and foundational functions for this work. There are certain additional acoustical concepts that also need to be considered prior to discussing otoacoustic emissions in more depth.

2.4.1 Distortion

Distortion is defined as a change in a signal from the input to the output of a system (Rosen & Howell, 1991). In its most basic definition distortion is a warping of a sound (or object). Distortion may arise from more than one source. There are several types of distortion including frequency, phase, and amplitude. The focus of this study is on amplitude distortion.

Amplitude distortion is defined as the difference between input and output amplitudes and occurs when the limits of a signal are exceeded leading to nonlinearity. It is not merely an issue of attenuation or amplification if these operations are strictly proportionally applied. Amplitude distortion violates the assumptions of homogeneity (all constituents are of the same nature, in proportion) and additivity (the whole equals the sum of its parts). Two types of amplitude distortion exist: Harmonic and intermodulation. Harmonic distortion is the result of a sine wave being distorted and thus creating harmonics related to its fundamental frequency. Intermodulation distortion is a type of amplitude distortion that occurs when there is an interaction among two or more sine waves and their respective harmonics (Allen & Fahey, 1993; Stover, Neely, & Gorga, 1999). This interaction creates sum and difference tones, yielding distortion products that occur above and below the frequencies of the primary tones (Durrant & Feth, 2013).

2.4.2 Manifestations of Nonlinearity

Nonlinearity, again, occurs when the input and output are not proportionate (Durrant & Feth, 2013). It may occur in any system. Although a common sign of system dysfunction, perhaps ensuing failure, it will be shown here that this is not necessarily the case, and, in any event, a few more terms will be useful.

2.4.2.1 Distortion Products Distortion products (DPs) occur, again, due to the interaction between primary tones and their harmonics. The DPs are mathematically related to their primary tones (Plomp, 1965). These are phenomena that occur in any physical system, though the focus of this paper is on distortion products produced in the inner ear and ultimately the concept of the "essential" nonlinearity that is inherent to normal auditory end-organ function (Durrant & Feth, 2013).

2.4.2.2 Theories of DP Generation Gold (1948) put forth a hypothesis of an inherently regenerative component of cochlear function, insisting that the cochlea is not a passive organ, rather that there must be an active aspect to it. The category of mechanism implied is that of positive feedback, analogous to a classical radio receiver of relatively simple electronic design that uses such a regenerative circuit to facilitate sensitivity. He investigated two recognized electromechanical transducer actions – the cochlear microphonic effect and the audibility of electrical signals – to find a term that would negate the natural viscosity of cochlear fluids and the damping effect they have on the basilar membrane. For the cochlear microphonic, sound waves applied to the ear resulted in an electrical potential of significant voltage as to be measured even outside of the cochlea. Furthermore, a large electrical field applied outside of the cochlea has been shown evoke a sensation of hearing (also called the "reverse cochlear microphonic effect", although more broadly known as the "galvanic effect", Gold & Pumphrey, 1948). Gold reasoned that the cochlear microphonic occurred due to a feedback channel within the cochlea. He posited this feedback channel counteracted the damping caused by cochlear fluids which, in turn, he assumed to reduce the selectivity (Q) of tuning of the hearing organ to a given frequency (Gold & Pumphrey, 1948). Therefore, the cochlea cannot function by mere passive absorption of the incoming sound energy, rather by actively adding to it. He suggested that the likely anatomical location of this active cochlear process is between the organ of Corti and the bottom of the tectorial membrane. While this model does not focus on DPs specifically, Gold's suggestion of an "active" process is important as future researchers worked to confirm his notions in concept, indeed that the outer hair cells provide the structures of the active cochlear process (Sun, Schmiedt, He, & Lam, 1994).

Distortion in the ear has long been known, but Goldstein (1967) designed two tasks to further determine perceptual limits of detection of aural DPs. He created listening tasks for the simple/first-order difference tone (f2-f1) and another for two higher-order DPs (2f1-f2 and 2f2-f1). These DPs were measured in two ears, one belonging to Goldstein (JLG) and another belonging to a colleague (GM), controversial evidently but argued by JLG to be the only way to be certain that the subjects were listening for the right tones (and in fact "hearing out" specific DPs is a demanding task). The first study was a suppression task to determine if distortion products could be attributed to an inner ear phenomenon. Prior to 1967, scientists often attributed distortion to the outer and middle ears (Helmholtz, 1877; Newman, Stevens, & Davis, 1937). The second study was a loudness-balancing task to validate the suppression task. The stimulus level for the lower tone (L1) was held at 50 dB SPL with the stimulus level of the higher tone (L2) varied from 10-70 dB SPL. The difference tone and 2f1-f2 could be heard by both participants, whereas 2f2-f1 was inaudible. The listeners were best able to perceive the 2f1-f2 DP, better than the 2f2-f1 (a priori) and the difference tone f2-f1, respectively. Goldstein's work suggested that an essential mechanical nonlinearity exists within the cochlear function and not the outer or middle ears.

Hall (1974) created a computational model of the basilar membrane to study the generation and propagation of DPs f2-f1, 2f1-f2, and 2f2-f1. Hall created the model to represent the whole length of the basilar membrane and thus included nonlinearity as a factor. From his work with this model, he was the first to suggest that DP energy travels from its generation site to the base of the cochlea. Also, Hall found that the 2f1-f2 and 2f2-f1 were generated at the f2 place.

Kim, Siegel, and Molnar (1979) tested the generation and propagation of the f2-f1 and 2f1-f2 distortion products. They digitally synthesized the DP spectra and presented them to the normally hearing ears of adult chinchillas and cats. From their data, they determined that nonlinear interactions were created among DP components and propagated for both the f2-f1 and 2f1-f2. This led to the conclusion that, in general, DPs are propagated along the basilar membrane by the same mechanism as single pure tones.

Kim, Molnar, and Matthews (1980) hypothesized that distortion begins at one source and then moves in two directions (apicalward and basalward) along the cochlear partition. Therefore the source must be a place on the partition that can transmit apically and basally to generate the DP (Kemp & Brown, 1983). This model is contrary to Bekesy's original work that showed only "forward" traveling waves, though (again) he did find backward traveling waves later (called paradoxical waves; Bekesy, 1955).

2.4.3 Temporal Nuances

Phase and latency are two metrics of time that also manifest in distortion products. Phase is a mathematical term referring to a “fraction of a wave cycle that has elapsed relative to the origin” of a wave, commonly measured in degrees or radians of angle. Yet, there is the temporal view as a cycle is fundamentally characterized by its period. Phase may be additive or subtractive; two waves that are in-phase may synergize to form a wave of greater response amplitude, though two waves that are out-of-phase may augment or diminish the net response. Thus, measurement of phase is of potential interest in DP analysis.

Latency is a time delay between the initiation of a stimulus and its response. Given the tonotopic organization of the inner ear, it is expected that high-frequency tones will have a shorter latency than low-frequency tones at their characteristic place of excitation. However this common concept becomes complicated when measuring the latency of DPs with effectively continuous tones, but is potentially derivable from the measurement of phase.

2.5 OTOACOUSTIC EMISSIONS (OAES): AN OVERVIEW

Kemp (1978) created an ear-level probe system to measure the putative active mechanisms within the human ear. With this probe, he confirmed one of Gold’s predictions that of an outward propagating signal from the inner ear attributed to backward traveling waves generated within the cochlea (discussed in more detail below). This emitted signal would later be called otoacoustic emissions (Zurek, 1981).

Otoacoustic emissions were classified originally by the presence or absence of an input stimulus, *i.e*., stimulus evoked versus spontaneous (Kemp, 1986; Moulin & Kemp, 1996a; Shera, 2004; Shera & Guinan, 1999). Current taxonomy, as developed by Shera and Guinan (1999), uses the method by which backward traveling waves are generated, from coherent linear reflection (as in spontaneous, transient evoked, and stimulus frequency OAEs) or by nonlinear distortion (distortion product OAEs).

Spontaneous OAEs (SOAEs) occur without external stimulation, generally in the most sensitive of normally hearing participants (thresholds less than 15 dB HL) (Probst, Lonsbury-Martin, Martin, & Coats, 1987). The SOAEs thus are not measureable in all clinically normally hearing people. They also occur more often in the right ear than the left and in women twice as often as men (Bilger, Matthies, Hammel, & Demorest, 1990; Strickland, Burns, & Tubis, 1985). They were first measured by Kemp in 1979. Their origin is in the minor structural irregularities (*i.e*., inhomogeneities) of the cochlear partition such as a fourth row of outer hair cells and the linear reflections of the backward traveling waves (Kemp, 1986; Lonsbury-Martin *et al*., 1988; Shera, 2003, 2004). The SOAEs are measured by a low-noise probe placed in the ear canal with noise filtered out in the 300-500 Hz range or using a synchronized click-evoked program from the Institute of Laryngology and Otology (ILO) software (called synchronized spontaneous OAEs). The SOAEs, at face value, provide the most compelling proof of an active cochlear mechanism (Gold, 1948; Murphy, Talmadge, Tubis, & Long, 1995; Talmadge, Tubis, Wit, & Long, 1991), namely that energy is added to the sound energy absorbed by the sensory cells and, together with other considerations, are not mere reflections.

Transient OAEs (TEOAEs) are inner-ear phenomena stimulated in response commonly to the presentation of broadband clicks and appear nearly instantly after the presentation of the stimulus. The ILO software used to elicit TEOAEs, in its default nonlinear mode, uses four stimuli in each set (Glattke & Robinette, 2007; Kemp, Ryan, & Bray, 1990). The set includes three clicks of same phase and amplitude and the fourth click of opposite phase (*i.e.*, 180 degrees out of phase) and three times the amplitude of the other three; these parameters are reversed for the next sequence. The responses from each set of stimuli contain linear and nonlinear components. The responses from the linear components are summed, cancelling each other out, leaving the resulting nonlinear response (Glattke & Robinette, 2007). The TEOAEs are measured, using a low-pass filter to exclude internal and environmental noise, in normally hearing people and tend to be most robust in the 1000-4000 Hz frequency range (corresponding to the middle-ear transfer function) with roll-off towards the 6000-Hz region imposed by the frequency limit for responses without stimulus artifact (Kemp, 1978). The TEOAEs exist in the frequency range below 1000 Hz, but are masked by environmental and physiological noise (Kemp *et al*., 1990). Therefore, researchers have restricted the time window in the low-frequency region in order to improve the signal-to-noise ratio for the higher frequency response region (Hills & Glattke, 1996; Whitehead *et al*., 1995a).

Stimulus frequency OAEs (SFOAEs) are stimulated using a low-level continuous, pure-tone. A single frequency is input into the cochlea twice, recording with one stimulus level and then the other (*e.g*., 10 dB SL and 40 dB SL) creating two tracings (Furst, Rabinowitz, & Zurek, 1988; Kemp & Brown, 1983). The SFOAEs are detected by separating the linear from nonlinear components of the two tracings, leaving the nonlinear component as the response (Kemp, 2007). They are thought to be generated by the coherent linear reflection of the backward traveling waves to the middle ear (Kalluri & Abdala, 2015; Kemp, 2007). The SFOAEs are the cause of threshold microstructure (see below) and thought to be the precursor to SOAEs (Gaskill & Brown, 1990; Kemp & Brown, 1983).

Distortion product OAEs (DPOAEs) are demonstrated by testing for the presence of intermodulation distortion in the OAEs, both in deference to the earlier work on cochlear distortion and expectations from still other work showing that the hair cell generators demonstrate asymmetrical nonlinearities (see for example Dallos & Cheatham, 1976). They thus are created when tones of differing frequencies (called primary tones) are presented simultaneously in the ear canal. Brown and Kemp (1984) demonstrated a broad family of DPs to be observable in OAEs. This diversity is evident in the presence of multiple upper and lower sideband DPs arising from the frequency regions above and below the primary tones, respectively. By far the most studied DPOAE component is 2f1-f2, followed by 2f2-f1. The DPOAEs thus are direct manifestations of distortion produced in the cochlea and, these particular products are the focus of this dissertation.

2.6 DISTORTION PRODUCT OTOACOUSTIC EMISSIONS (DPOAES)

2.6.1 DPOAE Test Parameters

The DPOAE primary tones are designed and described by the following test parameters. These include higher versus lower test frequencies (f2 and f1, respectively, in Hz), frequency ratio (f2/f1), stimulus levels (L2 versus L1 in dB SPL), stimulus level differences (dB), and response magnitude. The effects of the parameters to be discussed are, by far, best known for the 2f1-f2 product, and these effects will be favored for reference and simplicity in the following, initial, discussions of DPOAE assessment.

2.6.1.1 Frequency Parameters The DP-grams often are plotted showing response magnitude (µPa) or response level (dB SPL) on the ordinate with test frequency (f2, Hz) on the abscissa (typically scaled logarithmically, *e.g.*, octave frequency spacing). However, some researchers (*e.g.*, the Martin/Lonsbury-Martin laboratory and their colleagues) prefer to use the geometric mean (GM, Hz) (Lonsbury-Martin *et al*., 1987; Martin *et al*., 1998; Martin, Villasuso, Stagner, & Lonsbury-Martin, 2003) as they felt it better represented the place of the DP on the cochlear partition. The GM is an average of numbers using the product of its values, not its sums, and is logarithmically scaled. This is accomplished using the equation: $GM = [(f1 \times f2)^{0.5}]$ (Martin *et al*., 1998).

However, the f2 layout is favored for two reasons: (1) the f2 frequency is nearest in location to the generation process of the DPOAE, and (2) this is assumed to occur at the maximum overlap between the traveling waves of the primary tones (f1, f2), considered to be near the f2 place (Allen & Fahey, 1993). The test frequency on the DP-gram abscissa thus is generally representative of the f2 primary tone.

The frequency ratio (f2/f1) is another parameter for describing the relationship between the two primary tones (f1, f2). DPOAE test systems are capable of measuring frequency ratios greater than or equal to 1.0, up to 1.5. Frequency-ratio tuning curves help to determine that the optimal frequency ratio (humans 1.22) with some variability noted from person to person (*e.g.*, see Vento, Durrant, Sabo, & Boston, 2004).

2.6.1.2 Stimulus Levels and Level Differences The primary tones represented at f1 and f2 have representative stimulus levels called L1 and L2, respectively. Optimal DPOAE responses are considered to occur at moderate stimulus levels (approximately 65 dB SPL) with diminishing reliability of recording significant responses below 40 dB SPL. Stimulus levels above 70 dB SPL are not considered to be dominated by OHCs; as such they are not DPOAEs.

Stimulus level difference is defined as L1-L2, *i.e*., the stimulus level of the lower-frequency tone minus the stimulus level of the higher-frequency tone. Primary tones may be measured at equal (L1-L2=0) or different stimulus levels (L1-L2>0). Primary tones presented at moderately high stimulus levels create "best" DPOAE responses at near equal levels, but primary tones presented at low stimulus levels create "best" DPOAE responses with a substantial stimulus-level difference (*e.g*., L1-L2=15 dB SPL) (Kummer, Janssen, & Arnold, 1998). This concept has been described by Kummer and colleagues by evoking the image of a pair of scissors, that is, by analogy to increasingly different lengths of the blades away from the joint.

2.6.1.3 Response Magnitude Magnitude represents how large the DPOAE response is. It is measured by subtracting the value of the trough from the peak-to-trough sound pressure, but generally as the root-mean-square (RMS) value and then transformed to dB SPL. The plotting of these values was presented briefly in overview, but requires further discussion in order to follow the methodology of this study.

2.6.1.4 DP-Grams The conventional (clinical) DP-gram is naturally attractive for resemblance to an audiogram. Common test frequencies are thus presented approximately by ½-octaves (*e.g.*., 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz). Measurement of DPOAEs is coarse using this format. An example is presented in Figure 1. Despite popularity, extensive research, and continued value in certain clinical applications, it proves to provide inadequate frequency resolution for more critical analyses and an incomplete picture of DPOAE output overall.

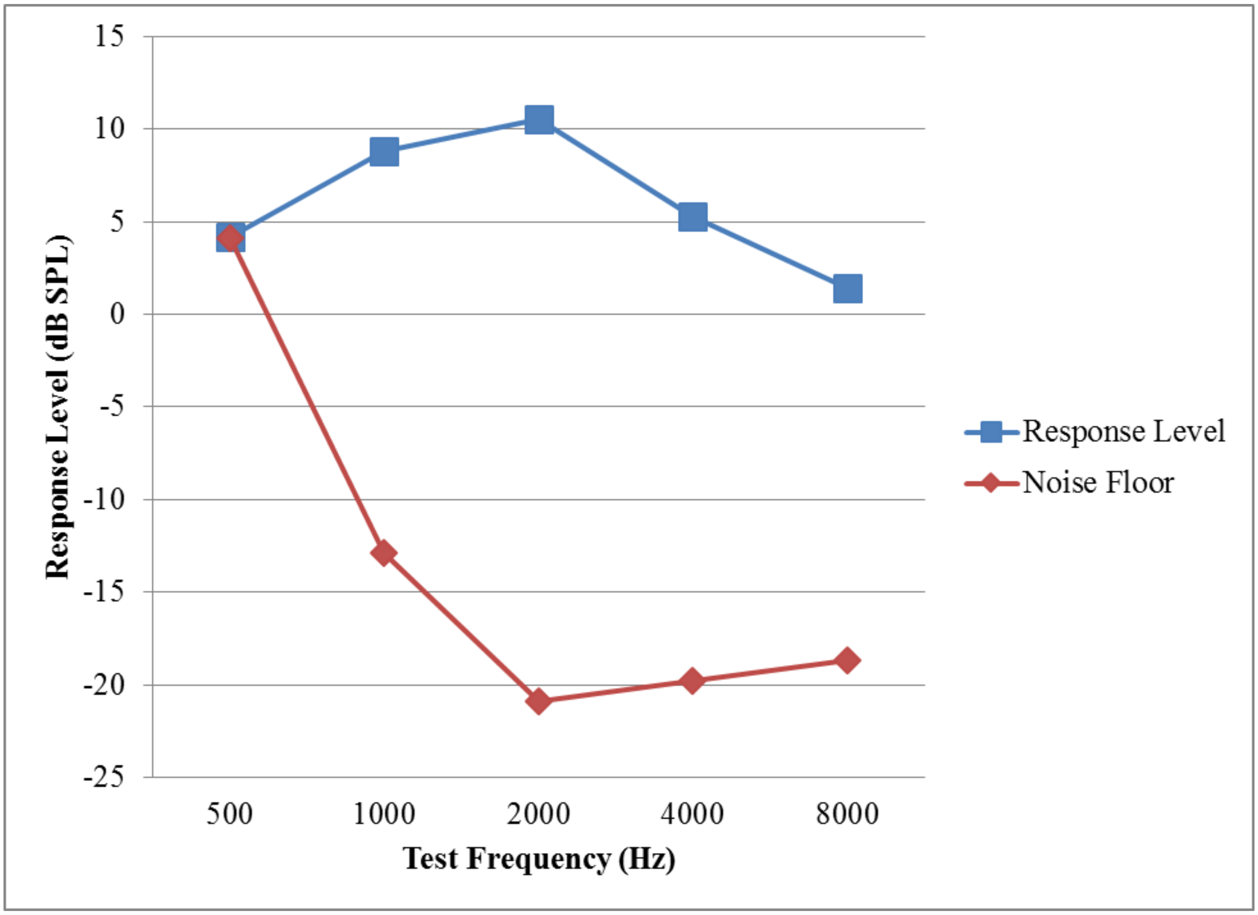


Figure 1. Example of clinical DP-gram from the EMAV program (see Methods) replotted using Microsoft Excel™.

2.6.1.5 Input-Output Functions (I/O) Traditionally in evoked response measurement, a still more fundamental but useful measurement is that of the input-output function. Here, the response level is plotted relative to the input stimulus level. Although not attracting substantial clinical interests (to-date), they have attracted interests in research. Examples of DPOAE input-output functions are presented in Figure 2, in this case for the 2f2-f1 product.

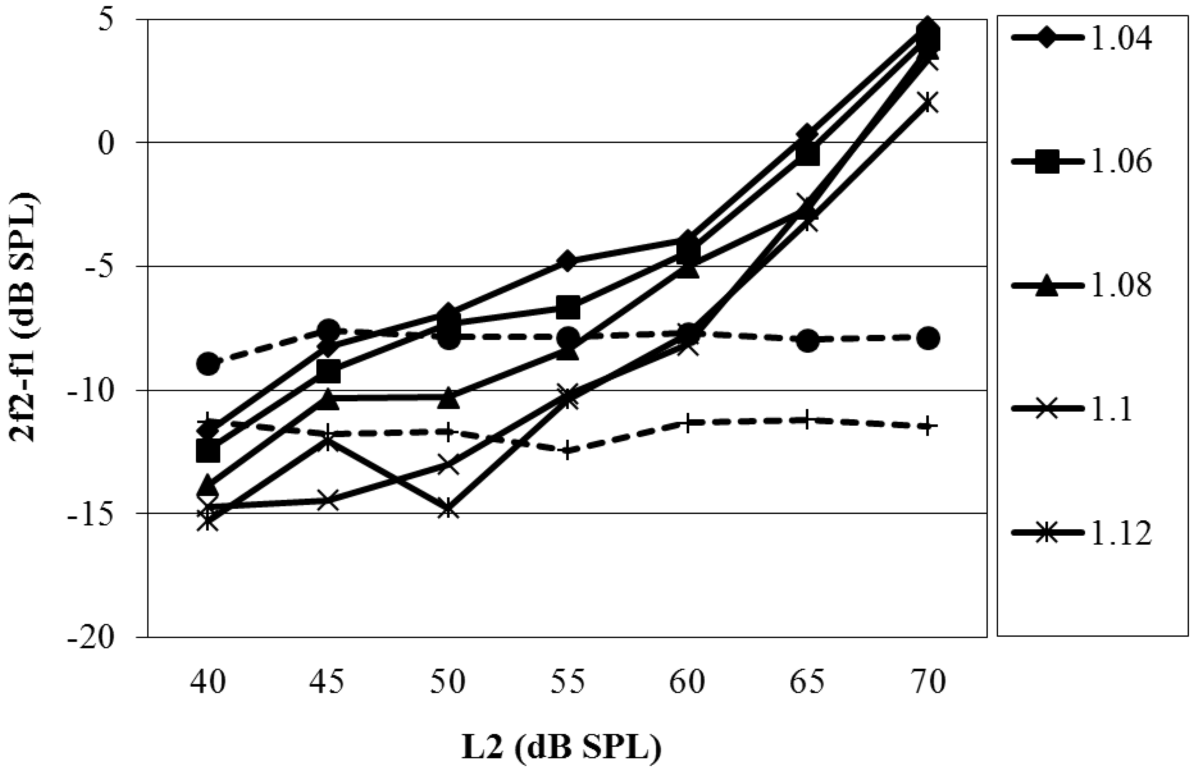


Figure 2. Example of an input-output function. (Reprinted with permission from Horn, J.H., Pratt, S.R., & Durrant, J.D., JSLHR, 51, 1620-1629 (2008). Copyright 2008, American Speech-Language-Hearing Association.)

2.7 DPOAES: TYPES AND MECHANISMS

The DPOAE mechanisms were thought to be nonlinear mechanical events along the cochlear partition with no greater specificity to their nature (Kemp, 1979b). Prior to 1979 it was assumed that OAEs arose by the mechanical nonlinear distortion property of the basilar membrane traveling in one direction, towards the cochlear base (Kemp, 1979a). However, Kemp (1979a) speculated that there must be a retrograde traveling wave that augments OAEs. Though he could not name the mechanism by which the traveling waves arose from the basilar membrane, he suggested that certain auditory phenomena (such as OAEs) could not be explained from any other mechanism.

In 1996, Kemp and Moulin described DPOAEs as arising from two mechanisms – wave-fixed and place-fixed (Moulin & Kemp, 1996b). The wave-fixed mechanism is tied to the traveling-wave envelope of the higher frequency tone (*i.e.,* f2), whereas the place-fixed mechanism is tied to the inhomogeneities that occur on the organ of Corti noted earlier (de Boer & Nuttall, 2006; Dhar, Long, Talmadge, & Tubis, 2005; Dong & Olson, 2010; Harris *et al*., 1989; Kalluri & Shera, 2001; Keefe, 2002; Mauermann, Uppenkamp, van Hengel, & Kollmeier, 1999a; Shera & Zweig, 1993; Schneider, Prijs, & Schoonhoven, 2003; Talmadge, Tubis, Long, & Piskorski,1998). The locations of the inhomogeneities on the cochlear partition (again) do not move, therefore they are place-fixed (Kalluri & Shera, 2001; Moulin & Kemp, 1996a; Knight & Kemp, 1999, 2000). However, they are randomly distributed.

2.7.1 DPOAE Classes

The DPOAE classes today are defined by the mechanism by which they occur, invoking in turn concepts such as backward-traveling waves. Backward-traveling waves occur due to the nonlinearity of the cochlea and conceptually help to distinguish the two classes of DPOAEs: Distortion-source and reflection-source.

The distortion-source class occurs from the nonlinear interaction of the traveling waves of the primary tones and occurs near the f2 place (Dhar, Rogers, & Abdala, 2011; Kalluri & Shera, 2001; Konrad-Martin, Neely, Keefe, Dorn, & Gorga, 2001; Martin, Stagner, Lonsbury-Martin, 2010; Parazzini *et al*., 2005; Prijs, Schneider, & Schoonhoven, 2000; Shera & Guinan, 1999). These DPOAEs have a constant phase because this source follows the traveling waves of the primary tones, creating a nearly flat frequency response (Abdala, Dhar, & Kalluri, 2011; Dhar *et al*., 2002; Kalluri & Shera, 2001; Knight & Kemp, 1999; Martin *et al*., 2010; Parazzini *et al*., 2005). This distortion-source class also has short latencies due to the relatively short paths in and out from the cochlea (Shera & Guinan, 1999).

The reflection-source class is generated by the inhomogeneities on the cochlear partition and the scattered wavelets due to those inhomogeneities. This class occurs with smaller frequency ratios (less than 1.1) and occurs near the Fdp place (Abdala *et al*., 2011; Dhar *et al*., 2011; Knight & Kemp, 2000, 2001; Reuter & Hammershoi, 2006; Shera & Guinan, 1999). This class is sensitive to changes to the cochlear amplifier (Shera, 2004), and thus why they too are linked to active cochlear (micro-) mechanics. These DPOAEs have a steep phase over place/frequency because it changes with each inhomogeneity (Knight & Kemp, 2000; Martin *et al*., 2010; Parazzini *et al*., 2005). Longer latencies occur due to phase changes at each frequency increasing the group latency (Kemp, 1979).

Researchers have shown that the latency that separates the distortion- versus reflection-source DPOAEs is 2 ms (Wilson & Lutman, 2006). The distortion source shows dominance with the largest peak prior to 2 ms and the reflection source with the largest peak after 2 ms.

2.7.2 2f1-f2 Component

The 2f1-f2 DPOAE component again is the most robust DPOAE, and warrants additional characterization, namely as a way to then understand (and ultimately test) theories of generation of 2f2-f1. The location of the 2f1-f2 Fdp occurs on the apical side of the primary tones. Its most robust responses occur in the mid-high test frequency range, with frequency ratios above 1.1, and at low-to-moderate stimulus levels. This parameter combination is known to separate the normal-hearing from the impaired-hearing populations. Yet, other combinations are not without interest.

Consequently, the 2f1-f2 component also may be classified as distortion-source dominant or reflection-source dominant depending on the frequency ratio used for testing. Distortion-source dominance occurs with frequency ratios above 1.1, whereas reflection-source dominance occurs with frequency ratios below 1.1 (Kalluri & Shera, 2001; Knight & Kemp, 1999, 2000; Konrad-Martin *et al*., 2001; Schneider *et al*., 2003). Both sources occur simultaneously, but again one is dominant. The measured 2f1-f2 component is then the vector sum of the distortion and reflection sources as well as resulting reflected spectra from the oval window (Lopez-Poveda & Johannesen, 2009; Reuter & Hammershoi, 2006; Schneider *et al*., 2003; Shera, 2004; Talmadge *et al*., 1999).

2.7.3 2f2-f1 Component

As noted in the Introduction, the 2f2-f1 DPOAE component is a far less-studied phenomenon. Several researchers have tried to establish the parameters that elicit the largest response levels for 2f2-f1 component. The most successful has been Fitzgerald and Prieve (2005), whose findings ostensibly were confirmed by Horn, Pratt, and Durrant (2008), in turn providing additional insights toward the optimization of this product. Fitzgerald and Prieve (2005) established that an f2/f1 ratio of 1.08 with L1=L2=65 dB SPL best elicited a strong 2f2-f1 component, especially at lower test frequencies (*i.e.*, below 1000 Hz). Knowing the parameters that produce the largest DPOAE amplitudes for the 2f1-f2 and 2f2-f1 components can help researchers and clinicians alike to use these components to determine the status of specific locations on the basilar membrane.

Still the 2f2-f1 component is not used clinically because a set of test parameters that differentiates ears with normal cochlear function from ears with abnormal cochlear function in a large percentage of the population has yet to be established. Fitzgerald and Prieve's study was performed on 150 ears. Also, it appears that the response levels of the 2f2-f1 component are never quite as large as those of 2f1-f2 (Gorga *et al.*, 2000; Moulin, Collet, Veuillet, & Morgon, 1993; Wable, Collet, & Chery-Croze, 1996). Martin and colleagues (1998) indicated that 2f2-f1 amplitude is smaller because of the smaller amplitude of the traveling waves at the putative places where they are generated (at least in terms of basilar membrane displacement per stapes displacement). Another view was offered by Schroeder (1975) who suggested that because 2f2-f1 is generated in a region basalward to the f2 place its response amplitude is attenuated, not amplified. Yet another theory suggests that the reverse traveling wave is amplified but vibration at its Fdp location it is not amplified as much as that of 2f1-f2 (Talmadge *et al.*, 1998).

Originally the 2f2-f1 DPOAE was thought to originate from the same place on the basilar membrane as the 2f1-f2 DPOAE, but it is now presumed that these two components have different sites of origin (Gorga *et al.*, 2000; Withnell, Shaffer, & Talmadge, 2003). The main source of the 2f2-f1 DP is likely the Fdp place (Erminy, Avan, & Bonfils, 1998; Gorga *et al.*, 2000; Knight & Kemp, 1999, 2000; Martin, Lonsbury-Martin, Probst, Scheinin, & Coats, 1987; Martin *et al*., 1998; Moulin, 2000; Moulin & Kemp, 1996b; Prijs *et al.*, 2000; Wilson & Lutman, 2006). This is an important distinction because it allows for recognition that the 2f1-f2 and 2f2-f1 components are measuring responses at two separate areas of the basilar membrane.

However, there are situations in which the 2f2-f1 component presents comparable response levels to those of the 2f1-f2 component. Researchers who have used animal models have shown, regardless of test parameters, comparable 2f1-f2 and 2f2-f1 DPOAE response magnitudes (Kettembeil, Manley, & Siegl, 1995; Lasky, 1998; Lonsbury-Martin *et al.*, 1987; Zurek, Clark, & Kim, 1982). In humans, the 2f2-f1 component has equal or better response magnitudes than the 2f1-f2 component at low test frequencies ($\leq$ 1000 Hz) because the noise floors surrounding the 2f2-f1 component are much smaller at these frequencies (Gorga *et al.*, 2000). Frequency ratio does not affect the 2f2-f1 source of generation as it does with the 2f1-f2 DP. For 2f2-f1, the most robust responses occur with f2/f1 close to 1.0 (Fitzgerald & Prieve, 2005; Horn *et al*., 2008; Knight & Kemp, 2000; Talmadge *et al.*, 1998). Using small frequency ratios could bring the 2f2-f1 emission place nearer to the frequency region of the primary tone traveling waves (Knight & Kemp, 1999). Equal-level primaries allow for an increase in the nonlinear distortion effect on the basilar membrane, which helps promote the recording of the 2f2-f1 DP (Knight & Kemp, 1999). Also, the 2f2-f1 component displays its largest amplitudes with moderate to high stimulus levels (Erminy *et al.*, 1998; Fitzgerald & Prieve, 2005).

Basalward DPOAEs are more robust at higher stimulus levels because the broadening traveling waves of the primary tones overlap on the basilar membrane more, thereby saturating the emission mechanism (Knight & Kemp, 1999; Talmadge *et al.*, 1998). In summary, the highest amplitudes for 2f2-f1 DPs appear to be elicited with equal-level primaries, low frequency ratios (less than 1.1), and low frequency stimuli (contrary to Knight & Kemp, 1999).

Smaller frequency ratios give the 2f1-f2 component a different phase than seen when recording 2f1-f2 DPOAEs with higher frequency ratios (Knight & Kemp, 1999). As it takes time for the primary tones to move along the basilar membrane there is an inherent delay in the generation of OAEs and therefore the phase of each OAE is dependent on its frequency (Knight & Kemp, 2000). For 2f2-f1 DPOAEs, longer latencies are seen with low frequency ratios relative to higher frequency ratios (Moulin & Kemp, 1996a).

Originally researchers considered the 2f2-f1 component to be unmixed (*i.e.*, not a combination of the distortion and reflection sources). However, recent research has shown that both mechanisms can be measured, to some extent, within this DPOAE (Wilson & Lutman, 2006). As the 2f2-f1 Fdp is basalward to the primary tones and their overlap region, this may be true.

2.8 THEORIES OF DPOAE GENERATION

Since Kemp's first revelations of OAEs and their several manifestations, new theories of DPOAE generation have been offered potentially to account better for emergent insights into the micro-anatomy, physiology, and molecular biology of the organ of Corti.

2.8.1 Shera and Guinan

In 1999, Shera and Guinan created a new taxonomy for classifying OAEs based on the model first proposed by Kim *et al*. in 1980. They based their taxonomy on the sources (classes) and mechanisms thought to create 2f1-f2 DPOAEs. Their classification is called the Two-Source/Two-Mechanism Model as there are two distinct locations and mechanisms of generation.

To reiterate, distortion-source class arises from the wave-fixed mechanism located at the f2 place and is considered dominant for the 2f1-f2 DPOAE component. The reflection-source class arises from the place-fixed mechanism located at the Fdp place and is considered dominant for TEOAEs, SFOAEs, and SOAEs.

Figure 3 is an illustration of Shera and Guinan's model. Two stimuli (f1, f2) enter the outer and middle ears represented by the rectangle. The spectra of each stimulus travel along the cochlear partition until they encounter the nonlinear distortion region near the peak of f2 as denoted by D. Some of the energy from the distortion region (D) then travels a short distance apically to the coherent reflection region near the peak of Fdp as denoted by R and some of the energy is reflected (via reverse-propagation) back to the middle and outer ears. The energy from the Fdp site (R) is also reflected back to the middle ear. The reflected wavelets are represented by Fdp waves. Reflected Fdp waves rebound from the tympanic membrane with some energy returning to the ear canal, mixing together, and then recorded with an ear-level microphone.

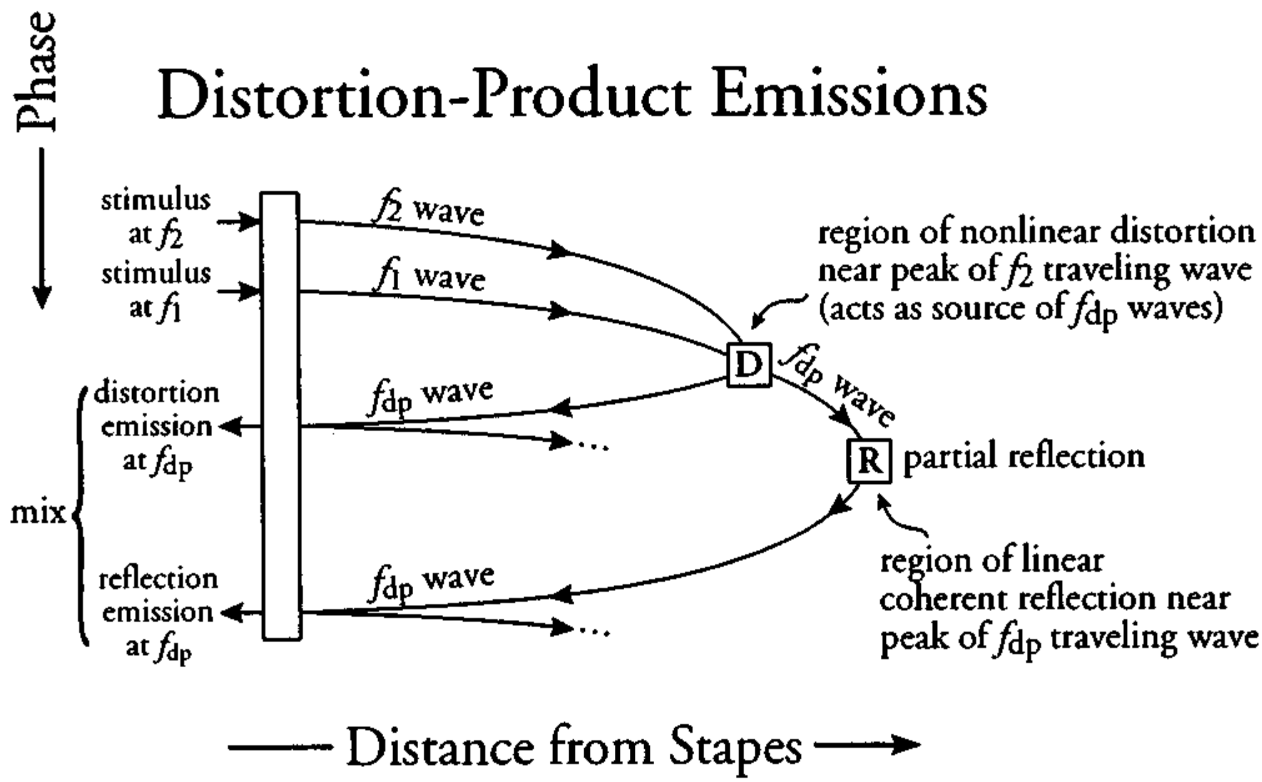


Figure 3. Model presented by Shera and Guinan (1999). (Reprinted with permission from Shera, C.A & Guinan, J.J., Jr. Journal of the Acoustical Society of America, 105, 782-798 (1999). Copyright 1999, Acoustical Society of America.)

2.8.2 Wilson and Lutman

Wilson and Lutman (2006) developed a model for 2f2-f1 DPOAE generation based on Shera and Guinan's model for 2f1-f2 DPOAE generation, illustrated in Figure 3. Wilson and Lutman also accounted for the inhomogeneities that occur on the organ of Corti.

Again, the two stimuli enter the outer and middle ears, represented by the rectangle. The higher frequency stimulus (f2) travels directly to the distortion region near the peak of the f2 traveling wave (D). This energy returns to the middle ear. Inhomogeneities, indicated by the I box, are encountered prior to reaching the distortion and reflection areas which occur at the same location on the cochlear partition (the Fdp). All of the energy from the reflection area travels back through to the middle ear to the outer ear for recording in the ear canal. Both the distortion and reflection sources produce reflected wavelets. Wilson and Lutman describe the same pathway for both 2f1-f2 and 2f2-f1 DPOAE components.

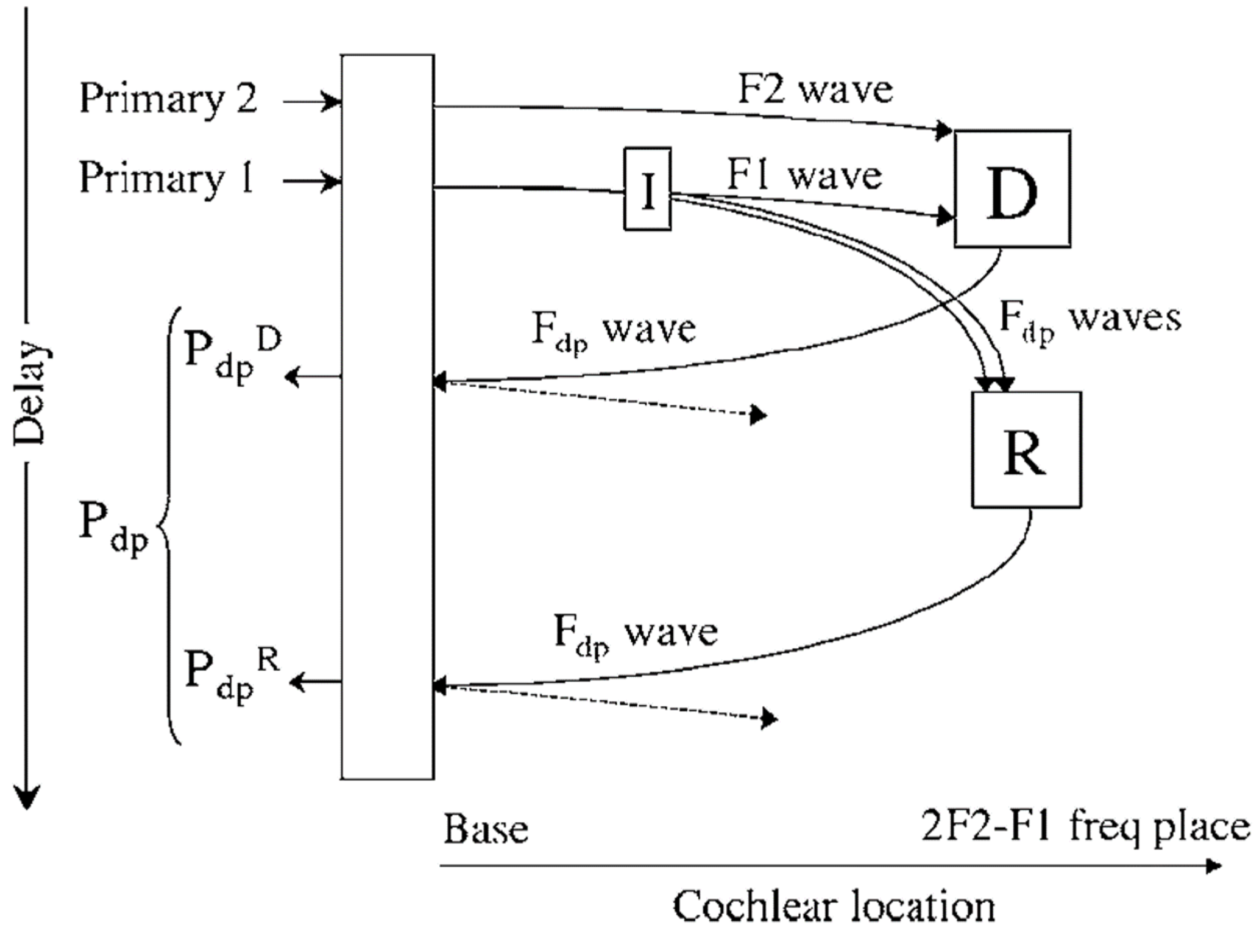


Figure 4. Model presented by Wilson and Lutman (2006). (Reprinted with permission from Wilson, H.K. & Lutman, M.E. Journal of the Acoustical Society of America, 120, 2108-2115. Copyright 2006, Acoustical Society of America.)

2.8.3 Fine Structure Measurements of DPOAEs

In concert with (if not signaling the need for) further theoretical development (as summarized above), the virtually iconic DP-gram, which remains the primary DPOAE clinical tool, bore further refinement. However, it suffered essentially the same weakness that may be claimed of the conventional audiogram, a matter that motivated interests of Kemp himself. These conventional analyses are simply carried out along a frequency axis that is too coarse to fully understand the observed phenomena.

Fine structure analysis was first described by Elliot in 1958. He was not measuring OAEs as they had not been discovered at that time. Rather he analyzed hearing thresholds along frequency axis in far greater detail than the clinical DP-gram. Thomas (1975) discovered an average difference of 12-dB between maxima and minima for auditory microstructure and Cohen (1982) found threshold fluctuations of 2-14 dB. Kemp's cochlear reflection hypothesis of OAEs was developed from his knowledge of threshold microstructure as representative of the sensitivity of the cochlear partition (Kemp, 1978, 1979a, b).

Fine structure DP-grams thus differ from a standard DP-gram in that the test frequencies on the abscissa are presented with greater resolution (*e.g.*, 1/8-cotave, 1/32-octave, or 1/64-octave). Fine structure is not just a description of a testing output, but a description functionally of the cochlear partition. Fine structure is caused by the mixing or interference of the energy traveling from the f2 place and that traveling from the Fdp place to the ear canal. Interference of these energies creates the appearance of maxima and minima as a function of frequency (*i.e.*, a "rippling" pattern). The rippling (or fine structure) disappears with extreme damage to the cochlear partition (*e.g.*, hearing loss). Therefore, fine structure provides the basis of another tool to tease apart DPOAE components and by which to critically test theories of DPOAE production. It might be argued that even clinical DPOAE testing ought to employ a fine-structure test paradigm, although it is substantially more time consuming. At the very least, the coarseness of the clinical DP-gram potentially misses the random peaks and/or dips in the DPOAE output allowing for possible misinterpretation—false negatives or positives.

2.8.3.1 Fine-Structure DP-gram: Effects As with the conventional DP-gram, fine structure is affected by DPOAE test parameters such as stimulus level and frequency ratio. Low to moderate stimulus levels increase measurability of fine structure, whereas the use of high stimulus levels results in decreased rippling. Using higher stimulus levels creates broadened traveling waves stimulating greater areas of the cochlear partition.

Frequency ratio affects fine structure. In recent study, Martin, Stagner, and Lonsbury-Martin (2013) measured DPOAEs in rabbits across a range of frequency ratios (1.01-1.25), and the researchers found that narrower frequency ratios influenced the dominance of basalward sources, as these sources occurred first in the time domain. This influence was reasoned to be caused by interaction between out-of-phase sources.

Also the presence of SOAEs may affect DPOAE fine structure in hearing thresholds as well as DPOAEs, as minima are likely to fall near SOAEs (Talmadge *et al*., 1998). The decrease of SOAE-adjacent hearing thresholds causes micro-hearing losses in those areas of the cochlear partition (Smurzynski & Probst, 1998).

2.8.3.2 Fine-Structure Characteristics Fine structure is described by three characteristics: Ripple spacing, ripple depth, and ripple prevalence, as follows.

Ripple spacing is defined as the width between two successive maxima. The difference between these maxima should be less than or equal to 25 Hz ($Maxima_1$-$Maxima_2$ $\leq$25 Hz; Abdala, Mishra, & Williams, 2009). Consistent with the tonotopic organization of the inner ear, ripple spacing decreases with increasing frequency (Reuter & Hammershoi, 2006).

Ripple depth is the difference between the maxima and minima of a single peak. The difference between the maxima and minima should be greater than or equal to 2.5 dB ($Maxima_1$-$Minima_1$ $\geq$2.5 dB; Abdala *et al.*, 2009).

Ripple prevalence is defined as the number of maxima in a 1/3-octave frequency band. Young adults have 1.5 to 3 maxima per 1/3-octave band for studies using the 2f1-f2 DPOAE component (Abdala & Dhar, 2010).

2.8.4 Studies of 2f1-f2 Fine Structure

The following section is a review of fine structure studies performed using the 2f1-f2 component. These studies provide an in-depth view of how fine-structure DP-grams may be affected by chosen parameters. A summary of the following studies may be seen in Table 1.

He and Schmiedt (1993) were interested in observing the changes in response magnitudes associated with the changes in primary-tone level, specifically how high-primary-tone levels affected the rippling pattern of the fine structure. The authors tested 10 normal-hearing young adults. The frequency ratio was set at 1.2. For the first part of the experiment, primary tones were presented at equal levels (L1=L2=50 dB SPL) while f2 was centered approximately at 2000, 3000, 4000, and 6000 Hz with frequency steps of 3/32 octave. For the second part of the study, the fine structure was measured at f2=2000 and 4000 Hz with L1=L2=45 to 65 dB SPL in 2.5-dB steps. In the first experiment the fine structure was measurable across the chosen frequency region. Response magnitudes often were largest for the 2000 Hz stimulus. The patterns of the fine structure varied with participant. From the second experiment the researchers found that fine-structure amplitude was not significantly affected by high stimulus levels when f2 was at or below 4000 Hz. However, there was a small shift in the fine structure pattern towards lower frequencies when the stimulus levels were high. The authors suggested that this event might be attributed to the place-fixed mechanism of the 2f1-f2 component. This finding supports more recent research that revealed better 2f2-f1 DPOAE amplitudes at low frequencies and high stimulus levels (Gorga *et al*., 2000).

Later, He and Schmiedt (1996) studied changes in four groups of participants – young adults with normal hearing, older adults with normal/near normal hearing, older adults with high-frequency hearing loss, and young adults with normal/near normal hearing (similar to the older adults). The DPOAEs were measured with f2/f1=1.2 and L1=L2=50 dB SPL. Test frequencies (f2) included 2000, 3000, 4000, and 6000 Hz with frequency steps of 1/32 octave. The authors contended that fine structure could be measured as long as DPOAEs were present. For both the normal-hearing young adults and the near normal/normal-hearing older adults the largest DPOAE levels were recorded with f2=2000 Hz. The decrease in OAE amplitudes for the higher test frequencies (*i.e*., 3000, 4000, & 6000 Hz) was greater for the older adults than the younger adults, though both groups did show smaller amplitudes for the higher test frequencies. As for high-frequency hearing loss, the effect on DPOAEs was as expected – there was a reduction in response level with increasing test frequency. That is, the test frequencies that fell within the region of hearing loss produced lower response levels than those that fell within the normal-hearing region. The authors speculated it was the damage to the outer hair cells in the region of hearing loss that resulted in the decreased response levels of the DPOAEs. However, they also commented when comparing the response levels from the normal hearing young adults and near normal/normal hearing older adults, that it was the older adults who had smaller response levels than the young. This finding led the authors to speculate a loss of sensitivity that contributed to this response. In summary, the peak amplitude for older participants was smaller than that for younger participants, especially at the higher test frequencies, though the distance between the peaks of the fine structure did not change with age or hearing status. The results of this study provided good rationale for the use of normally hearing young-adult participants for more basic/theoretically motivated research. This study (1996) also provided expectations for 2f1-f2 fine structure behavior.

Talmadge *et al.* (1998) mathematically modeled OAE fine structure in order to describe fine structure of hearing threshold, the relationship between the fine structures of different OAEs, and DPOAE filter shape. Most important to the present study is the work on DPOAE fine structure. The authors considered both apicalward and basalward DPOAEs. Modeling of the basalward DPOAEs showed the frequency ratio that best elicited this DP was closer to 1.0 in value; this is consistent with other literature (Fitzgerald & Prieve, 2005). The researchers also found there was a difference in amplification of the basalward versus apicalward traveling waves. The forward-traveling wave was enhanced by 40-60 dB whereas the backward traveling wave was reduced by 20-30 dB. However, the authors indicated that there was still some amplification of the backward traveling wave. Amplification of both forward- and backward-traveling waves occurred near the tonotopic location of that wave. Differences seen between the apicalward and basalward DPOAEs were related to their respective regions of generation, specifically related to mass versus stiffness issues. According to the authors, the apicalward DPOAEs were generated in a stiffness-dominated area but the basalward DPOAEs were generated in a mass-dominated region. The authors further contended that because basalward DPOAEs were mass-dominated, they needed higher stimulus levels and smaller frequency ratios in order to be observed, such as speculated with the 2f2-f1 component. The higher primary tone levels (again) allowed for a broadening of the traveling wave. This broadening of the traveling waves created a larger overlap between the primary tones. The issues of amplification of the backward-traveling wave and the location of this amplification will be important to future investigations.

Kalluri and Shera (2001) tested four normal-hearing adults for a study regarding the two-mechanism model of DPOAE generation. The authors measured the fine structure of the 2f1-f2 component in 15-Hz steps with parameters of L1=L2=45 and 60 dB SPL with a frequency ratio of 1.2. They used suppression and time windowing to separate the sources. (These separation methods will be described in later sections.) This study is relevant because (1) the authors described what happens to the sources when mixed and unmixed and (2) showed how the two separation procedures produced a similar effect apropos the 2f1-f2 distortion source.

Dhar and Abdala (2007) investigated the maturation of the peripheral human auditory system. They performed fine-structure DPOAEs on newborns and normal-hearing young adults with test frequencies equaling 500 through 12,000 Hz in the adults and 996-4020 Hz in the newborns to accomplish this task. Other parameters included the use of 1.22 for the frequency ratio and L1/L2 equaling 65/55. The fine structure was most distinct in the adults in the 1000-1500 Hz range, whereas the fine structure was distinct across the newborn-test-frequency range. The authors contended that they found less examples of fine structure from 2f1-f2 DPOAEs elicited with low-test frequencies. This observation is consistent with past research that showed smaller amplitudes for 2f1-f2 DPOAEs recorded with low-frequency stimuli than for mid-frequency stimuli (Fitzgerald & Prieve, 2005). The Dhar and Abdala study is similar to that of Knight and Kemp (1999; reviewed in the next section) in that they used 2f1-f2 component across a large frequency range, though dissimilar frequency ratio, intensity levels, and intensity level differences. However, Dhar and Abdala did not measure the 2f2-f1 component.

Martin, Stagner, and Lonsbury-Martin (2013) assessed the nature of the inverted U-shaped frequency-ratio function in rabbits with f2 equaling 1600-20550 Hz in 0.1-octave steps. Notches were found in the resulting frequency function. Then the frequency domain data were converted into the time domain using inverse FFT (IFFT). After converting the data into the time domain, the researchers examined the time output before and after turning off the f2 tone for six seconds, following five seconds of presentation. They noted that complexities arose when the f2 was turned off. Complexities were defined as "abrupt variations in the time-waveform magnitude and phase" (p. 343) and occurred most often in the narrow-frequency-ratio output. Martin and colleagues determined that the notches arose from phase differences between the DPOAE sources whereas the complexities arose from time differences due to the locations of the DPOAE sources on the cochlear partition (*i.e.*, apicalward vs. basalward of the primary tones). Complexities are not the same as inhomogeneities as they exist within different domains (*i.e.*, frequency vs. time).

Table 1. Parameters used in previous 2f1-f2 fine structure research studies.

Author	Year	2f1-f2	2f2-f1	F2 (kHz)	F2/f1	L1 (dB SPL)	L1-L2 (dB)
He & Schmiedt (Exp 1)	1993	Yes	No	2-6	1.2	50	0
He & Schmiedt (Exp 2)	1993	Yes	No	2, 4	1.2	45-65 (2.5 dB steps)	0
He & Schmiedt	1996	Yes	No	2-6	1.2	50	0
Kalluri & Shera	2001	Yes	No	1-1.6	1.2	45, 60	0
Dhar & Abdala	2007	Yes	No	5-12 (adults) 1-4 (newborns)	1.22	65	10
Martin *et al*.	2013	Yes	No	1.6-20.55	1.01-1.25	65	0-20

2.8.5 Studies of 2f2-f1 Fine Structure

In 1999, Knight and Kemp performed a study that focused on DPOAE and TEOAE characteristics as well as their relationship to auditory thresholds. Focusing, for purposes here, uniquely on the DPOAE, the authors measured 2f1-f2 and 2f2-f1 fine structure DP-grams, using several parameter combinations. They examined nine ears of normal-hearing young adults and focused on 16 frequencies (f2) centered at and within a half-octave of 2000 Hz (1660-2392 Hz). Stimulus levels (L1, L2) were 65, 70, and 75 dB SPL, while intensity level differences (L1-L2) were 0, 5, and 10 dB. Frequency ratios were 1.05, 1.2, 1.27, and 1.32. The 2f1-f2 component was measured in all ears for all parameter combinations. The 2f2-f1 component was measured in all ears as well, but some parameter combinations did not provide responses with sufficient amplitude to record values above the software noise floor. The study results included larger response levels of the 2f1-f2 component over those of the 2f2-f1 component, except for the condition where L1=L2 with a frequency ratio of 1.05. Responses for the 2f1-f2 component, when measured with the smallest frequency ratio, had the smallest response magnitude. The largest magnitude for the 2f1-f2 component was measured when L1-L2=10 and the frequency ratio was 1.32. For the 2f2-f1 component the largest magnitudes were recorded when the frequency ratio was 1.05 and L1=L2. At this specific parameter combination the 2f2-f1 response level was larger by 2-2.5 dB. Responses for the 2f2-f1 component were reduced (in response magnitude) when there was stimulus level separation and/or the frequency ratio was above 1.1. Generally, the response levels from the 2f1-f2 component were larger across all frequencies (by almost 20 dB in some cases) than those recorded from the 2f2-f1 component. Knight and Kemp contended that the 2f2-f1 component was more variable than 2f1-f2 when repeating measurements. They also posited that this increased variability was likely from noise influences. The results from this study were consistent with those of Erminy *et al.* (1998) and were replicated by Fitzgerald and Prieve (2005).

Knight and Kemp (1999) further addressed the issue of DPOAE fine structure by testing one participant across an extended frequency range of f2=500-7000 Hz. Responses were recorded from both DPOAE components (2f1-f2, 2f2-f1) across the frequency range. The researchers performed an extended DP frequency sweep using stimulus parameters of f2/f1 of 1.05 and L1=L2=70 dB SPL. These parameters promote the recording of the 2f2-f1 component (Fitzgerald & Prieve, 2005; Horn, Pratt, & Durrant, 2008), as the low frequency ratio and lack of stimulus-level difference have been shown to do for the 2f2-f1 DPOAE component. Unlike the studies from Erminy *et al.* (1998), Fitzgerald and Prieve, and Horn *et al*. (2008), this study showed larger response magnitudes for the 2f2-f1 component at higher test frequencies (f2; 1800, 2400, 3400, & 4800-5900 Hz) and smaller magnitudes from lower test frequencies. Otherwise, the largest response levels corresponded to the 2f1-f2 component. Past reports have described the response levels for the 2f2-f1 component as larger for low test frequencies (f2<1000 Hz) (Gorga *et al.*, 2000). However, for this individual, the response levels of the 2f1-f2 component were larger for f2<1000 Hz. This was a direct contradiction to the authors' previous statement regarding their participants' having larger magnitudes for the 2f2-f1 component at f2/f2=1.05 with L1=L2 (on p. 1424). Given that the test parameters should promote the 2f2-f1 component, the DPOAE results from this participant appeared to be inconsistent with expectations backed by the literature (Erminy *et al.*, 1998; Fitzgerald & Prieve, 2005; Horn *et al.*, 2008). The authors did not provide any further discussion on the fine structure of the DPOAE components for this individual. Therefore it is not possible to determine which aspect(s) of testing (*i.e.*, software, hardware, and/or participant) might have influenced these contraindicated results. Nor was there a description of the fine structure for either the 2f1-f2 or 2f2-f1 components thereby leaving no way to determine how or if the fine structure differed between the two components. Moreover, this extended study was performed on only one participant making it difficult to generalize the results. Nevertheless, the issues that this study highlighted are worth noting and included: (1) The 2f2-f1 DP appears to have a fine structure. No previous study had described the 2f2-f1 DP as having a fine structure. (2) There was an unexpected frequency effect found on the extended range fine structure DP-gram. It was unexpected that the 2f2-f1 DPOAE would have better response levels (greater amplitude) at higher frequencies (*e.g.*, 2000 Hz) over lower frequencies (*e.g.*, 500 Hz). (3) The authors contended that the poorer low-frequency emissions of 2f2-f1 were due to noise influence on the component. More recently researchers have shown larger amplitude 2f2-f1 DPOAEs when using low frequencies (below 1000 Hz) to elicit a response as it is unlikely to be as affected by noise as the 2f1-f2 component (Fitzgerald & Prieve, 2005).

Knight and Kemp (2000) studied 2f1-f2 and 2f2-f1 DPOAEs in the context of the primary-tone areas on the basilar membrane. The authors tested two adults with normal hearing. Stimulus levels were L1=L2=60, 70, and 75 dB SPL. Test frequencies were 1000 to 4100 Hz with a 12-Hz step size and an f2/f1=1.22. The researchers then measured DPOAEs with both f1-sweep (f2 remains fixed) and f2-sweep (f1 remains fixed) methods. Fine structure was present for both 2f1-f2 and 2f2-f1 DPOAEs for L1=L2=60 and 75 dB SPL. Schneider *et al.* (2003) reported that distortion and reflection sources and their contribution to DPOAEs measured depended on the test parameters (in this case, frequency ratio and stimulus level) used to elicit them. Knight and Kemp (2000) showed shallow phase contours for intermediate and high-frequency ratios (1.1-1.3), but steep phase contours for low-frequency ratios (1.05). The 2f1-f2 component moved from distortion-source dominant to reflection-source dominant at a frequency ratio of approximately 1.15 (Knight & Kemp, 2000; Schneider *et al.*, 2003). This study provided more detailed information regarding phase for the 2f1-f2 and 2f2-f1 components, but did not provide further explanation on how the fine structure description varied between the two components.

Table 2. Parameters used in previous 2f2-f1 fine structure research studies.

Author+	Year	2f1-f2	2f2-f1	F2 (kHz)	F2/f1	L1 (dB SPL)	L1-L2 (dB)
Knight & Kemp (Exp 1)	**1999**	**Yes**	**Yes**	**2**	**1.05, 1.2, 1.27, 1.32**	**65, 70, 75**	**0, 5, 10**
Knight & Kemp (Exp 2)	**1999**	**Yes**	**Yes**	**1.3-3**	**1.05**	**70**	**0**
Knight & Kemp	**2000**	**Yes**	**Yes**	**1.3-3**	**1.01-1.5**	**60, 70, 75**	**0**

+All studies that used the 2f2-f1 DPOAE component are presented in bold.

2.8.6 Separation Techniques of DPOAE Sources

The sources of fine structure DP-grams again may be separated, or unmixed, using suppression and inverse FFT (IFFT) also known as time windowing, as well as pulsing one of the primary tones on and off during primary-tone presentation (Dhar *et al.*, 2002, 2005; Kemp & Brown, 1983). Researchers studying the 2f2-f1 component have used suppression and time windowing (Martin *et al.*, 1987, 1998, 2003; Wilson & Lutman, 2006). The focus of this section thus is on the use of suppressor tones and time windowing via IFFT to separate the distortion and reflection sources of 2f1-f2 and 2f2-f1 DPOAE components.

2.8.6.1 Suppression Suppression is a technique by which a part or source of a response is reduced. In the case of DPOAEs the two primary tones are joined by a third--the suppressor — tone (f3) that differs in frequency from the primary tones. The suppressor tone may be higher or lower in frequency than the Fdp (Dhar *et al.*, 2011; Kettembeil *et al.*, 1995; Konrad-Martin *et al.*, 2001; Moulin & Kemp, 1996b). The most effective suppressor tones (for separating DPOAEs sources) vary by frequency and stimulus levels indicating suppressor tones have variable effect on fine structure (Dhar & Shaffer, 2004; Mauermann & Kollmeier, 2004). In all cases of effective suppression the reflection source is what is eliminated (suppressed). Table 3 provides a summary of the test parameters of the following articles. Table 4 presents the results of suppression studies that included 2f1-f2 and 2f2-f1 components.

Suppression works on fine structure by minimizing the effect of the reflection source and the multiple reflections along the cochlear partition (Martin *et al.*, 2010; Talmadge *et al.*, 1999). The maxima and minima of fine structure are reduced when a suppressor tone is of a frequency near the Fdp (Dhar *et al.*, 2011; Konrad-Martin *et al.*, 2001). Suppressor tones reduce DP energy coming from Fdp region so energy is measured only from f2 place (Dhar & Shaffer, 2004; Knight & Kemp, 2001; Rhode & Cooper, 1993). Essentially the addition of a suppressor tone divides the emission components by their place on the cochlear partition (Knight & Kemp, 2001). Another description is the suppressor tone affects/minimizes the 'long latency components of the response' (*i.e.*, the reflection source) (Konrad-Martin *et al.*, 2001). It should be noted that it is possible to have an incomplete suppression of the reflection source (Dhar & Shaffer, 2004). Adding a suppressor tone to individuals with strong reflection sources may enhance the magnitude of the fine structure, a phenomenon called facilitation, as it "equalizes" the reflection and distortion sources (Dhar & Shaffer, 2004; Kettembeil *et al.*, 1995).

Brown and Kemp (1984) studied the effects of suppression of the 2f1-f2 component in humans and gerbils. They recorded suppression tuning curves (STCs) for L1=L2=60 dB SPL for a frequency ratio of 1.32 at frequencies (f2) of 1750, 3500, and 5800 Hz for gerbils and 1850 Hz for humans. The pure-tone suppressor level was increased or decreased in intensity as suppressor frequency (f3) was changed. Suppressor level ranged from +20 down to -10 dB re: primary tone intensity level (*i.e.*, 60 dB SPL). DPOAE magnitude decreased when the frequency-specific suppressor tone was used. Suppression peaked at frequencies near f2. The authors observed that higher frequencies (f2) and smaller frequency ratios (1.16) resulted in sharper tuning and tones closer to f2 were easiest to suppress.

Martin and colleagues (1987) tested the effects of suppression on rabbits using 2f1-f2 and 2f2-f1 STCs. They collected STCs using equal-level primary tones (L1=L2=65 dB SPL), frequency ratio of 1.25, and primaries that evoked DPs at 2000 and 4000 Hz for 2f1-f2, and 4000 and 8000 Hz for 2f2-f1. Maximum suppression for 2f1-f2 occurred when the suppressor tone was close in frequency to the primary tones, whereas 2f2-f1 was most suppressed when the suppressor tone was close to or higher than the Fdp. However, suppression did not occur for the highest frequencies tested for 2f2-f1. In fact, the amplitude of the 2f2-f1 response sometimes increased in the “suppressor” condition. Martin *et al.* concluded that suppression of the 2f2-f1 component is unpredictable.

Kettembeil and colleagues (1995) tested suppression effects on birds using 2f1-f2 and 2f2-f1 DPOAE STCs. They tested chickens using only 2f1-f2 and starlings using both 2f1-f2 and 2f2-f1. They tested f1 of 900 through 4000 Hz for f2/f1 of 1.01-1.7 and 40-90 dB SPL. The suppressor tone did not match f1, f2, or Fdp in frequency. Similar to human studies they found 2f2-f1 was almost always smaller in magnitude than 2f1-f2, and there were fewer suppression measures for 2f2-f1 as compared to 2f1-f2. Effects for the 2f1-f2 component showed a change in characteristic frequency (CF) with suppression in 50% of the cases; however, the direction of the suppression depended on the stimulus frequency. For stimulus frequencies (f1) of 2800 and 4000 Hz the CF shifted up in frequency whereas for stimulus frequencies of 900 and 1400 Hz the CF shifted down in frequency. Also, the CF shifted down in frequency with increasing primary tone intensity level. As described earlier, facilitation is the growth of response magnitude in the presence of f3. For 2f1-f2, facilitation occurred at frequencies below and above CF and tended to be grouped, whereas facilitation for 2f2-f1 only occurred above the CF at the 2f2-f1 Fdp (7 of 19 cases, 37%). Also for the 2f2-f1 component, a second region of suppression was recorded for 47% (9 of 19) of the cases. This study showed that suppression has a variable and somewhat unpredictable effect on the 2f2-f1 component.

Martin *et al.* (1998) tested young adults for suppression of 2f1-f2 and 2f2-f1 DPOAE components. They tested geometric means equaling 250-8000 Hz at f2/f1=1.21 and L1=L2=75 dB SPL. Suppression was added at 3000, 4000, and 6000 Hz. The DPOAEs were considered present when greater than 3 dB above the noise floor. Suppression was scored as such when there was a 6-dB drop in the DPOAE amplitude. Similar to their 1987 study, the 2f2-f1 component originated from an area near or at the 2f2-f1 Fdp. Interestingly, the STC tips for 2f1-f2 appeared to mark a similar place along the cochlear partition (near the primary tones) but the 2f2-f1 STC tips were distributed along a larger swath of the cochlear partition (though still centered at the 2f2-f1 Fdp). Using the parameters listed above, the 2f2-f1 component has smaller amplitude than 2f1-f2 at all frequencies. The authors concluded that 2f2-f1 suppression is more variable than 2f1-f2 in both frequency and amplitude.

Kalluri and Shera (2001) looked at source separation by suppression and time windowing. Only suppression will be discussed in this section; time windowing will be discussed in the next section. They postulated suppression would remove the influence of the reflection source on the DPOAE via unmixing. Kalluri and Shera (2001) measured 2f1-f2 fine-structure using 60/45 stimulus levels and a 1.2 frequency ratio. The suppressor was added at a frequency 44 Hz below the DP frequency. Suppression level was approximately 50-55 dB SPL. The suppressor tone was successful at separating the distortion and reflection sources by limiting the reflection source. This process occurs by diminishing the amplitude of the reflection waves. The resulting spectrum is "smoother" as the fine structure (*i.e.*, the roughness aspect) has been removed because the reflection source is no longer interfering with the distortion source.

Konrad-Martin *et al.* (2001) measured 2f1-f2 fine-structure DPOAEs at 2000 and 4000 Hz with L1 – L2 = 10, and L2 = 25, 35, and 45 dB SPL. Suppression was used to separate the distortion and reflection sources. The authors found the suppressor tone (f3; 15.6 Hz below the 2f1-f2 Fdp) suppressed the reflection source. The authors contended that the reflection source was suppressed by f3 because reflection is a secondary source at the 2f1-f2 Fdp. This is relevant in that it shows suppression will not promote the reflection source, a reasonable expectation to better study the 2f2-f1 component.

Martin *et al.* (2003) tested the interference response area in young adults. As suppression does not always result in the suppressing of a response (as often seen in 2f2-f1 DPOAEs), these researchers used the term "interference" instead of "suppression". The 2f1-f2 and 2f2-f1 DPOAEs were collected at 1000, 2000, 3000, and 4000 Hz with f2/f1=1.22 and L1=L2=75 or 85 dB SPL or L1/L2=65/55 dB SPL. Martin *et al.* found interference (*i.e.*, whether suppression or facilitation) at frequencies above f2 for both components; however 2f2-f1 responses were more variable. Once again, the 2f2-f1 DPOAE showed variable response to suppression. Interestingly, the tips of 2f2-f1 interference curves were more sharply tuned than those for 2f1-f2.

Later, Martin *et al.* (2010) performed an interference tone study on three young female rabbits to search for basal (*i.e.*, high-frequency) DPOAEs. They measured 2f1-f2 and 2f2-f1 DPOAEs using various parameter combinations including f2/f1=1.25, f2=1600–20550 Hz, and eleven intensity level differences (tones of equal and differing levels). They found that the reflection source was dominant for the 2f1-f2 component at low-frequency ratios and for the 2f2-f1 at most frequency ratios. In addition, they found that an interference tone located 1/3-octave above f2 removed the reflection source in rabbits, as it has in humans. They, therefore, suggested a basal generation site for the reflection source and the 2f2-f1 DPOAE component.

From the above studies it appears that suppression well separates the sources of the 2f1-f2 component, but the same is not true for the 2f2-f2 component. The sources of the 2f2-f1 component may be suppressed, facilitated, or unaffected by the suppression process. This response variability makes the use of suppression on 2f2-f1 DPOAEs highly suspect.

Table 3. Parameters used in 2f1-f2 and 2f2-f1 DPOAE suppression studies.

Author	Year	2f1-f2	2f2-f1	Participants	F2 (kHz)	F2/f1	L1 (dB SPL)	L1-L2 (dB)	Test Measure	F3	Suppression Criterion (dB)
Brown & Kemp	1984	Yes	No	Gerbils, Humans	1.75, 3.5, 5.8 (gerbil); 1.85 (human)	1.32 (gerbil); 1.2 (human)	40-70	0	STCs	Varied	6
Kalluri & Shera	2001	Yes	No	Humans	0.8-2.4	1.2	60	15	DP-gram	44 Hz below 2f1-f2 DP	Not noted
Konrad-Martin *et al.*	2001	Yes	No	Humans	2, 4	1.2	35-55	10	DP-gram	15.6 Hz below 2f1-f2 DP	6
Martin *et al.*+	**1987**	**Yes**	**Yes**	**Rabbits**	**2, 4 (2f1-f2) 4, 8 (2f2-f1)**	**1.25**	**65**	**0**	**DP-gram**	**1-12 kHz**	**6**
Kettembeil *et al.*	**1995**	**Yes**	**Yes**	**Birds**	**0.9-4**	**1.01-1.7**	**40-90**	**0**	**I/O, STC**	**≠ f1, f2, Fdp**	**Various freq & intensity levels**
Martin *et al.*	**1998**	**Yes**	**Yes**	**Human**	**0.25-8**	**1.21**	**75**	**0**	**STC**	**0.25-10 kHz**	**6**
Martin *et al.*	**2003**	**Yes**	**Yes**	**Human**	**1, 2, 3, 4**	**1.22**	**65, 75, 85**	**0, 10**	**STC**	**0.25-9.5 kHz**	**DPOAE level minus NF avg plus 2 SD**
Martin *et al.*	**2010**	**Yes**	**Yes**	**Rabbits**	**1.6-20.55**	**1.025-1.5**	**45-75**	**0-25**	**DP-gram**	**1/3-oct above f2, 44 Hz below Fdp**	**Not noted**

+ All studies that used the 2f2-f1 DPOAE component are presented in bold.

Table 4. Results from suppression studies including 2f2-f1 DPOAEs.

Author	Year	2f1-f2 Results	2f2-f1 Results
Martin *et al.*	**1987**	Max. suppression with F3 near primary tones	Suppression is highly variable – facilitation sometimes noted with f3
Kettembeil *et al.*	**1995**	50% of cases: STC CF shifted down with low f1; STC CF shifted up with high f1 or increased L2s	Suppression occurred only in 37% (7/19 cases); no obvious change in patterns; a 2nd suppression region occurred in 47% (9/19 cases)
Martin *et al.*	**1998**	STC tips grouped at or slightly below geometric mean frequencies	STC tips "scattered" above geometric mean frequencies; largest magnitude in 500-1000 Hz range
Martin *et al.*	**2003**	Interference occurred at frequencies > f2	2f2-f1 STC tips grouped near Fdp; low suppression thresholds noted; more sharply tuned than 2f1-f2

2.8.6.2 Time Windowing Time windowing is accomplished using the inverse FFT (IFFT) to convert data from the frequency domain into the time domain and has the advantage of not diminishing or removing either source from the original DPOAE measure, rather than just interfering with the reflection source. Specifically, he IFFT uses the group delay differences to separate the distortion and reflection sources (Knight & Kemp, 2000, 2001; Konrad-Martin *et al.*, 2001). As described previously, the distortion source has a short latency while the reflection source has a long latency. In the time window, the peak that occurs prior to two milliseconds is the distortion source, and the primary peak that occurs just after two milliseconds is the reflection source (Stover, Neely, & Gorga, 1996). The peak that is largest in amplitude, whether it occurs before or after 2 ms, represents the dominant source for that DPOAE component.

Various researchers have used time windowing to make observations regarding the sources of fine-structure DPOAEs. Below are summarized several articles describing the findings of studies in which time windowing was performed on fine-structure DPOAEs. Table 5 provides a summary of the parameters examined, and Table 6 presents the results of time windowing studies that included the 2f2-f1 component.

Stover *et al.* (1996) researched the issue of latency as the indicator of source-of-generation for 2f1-f2 DPOAEs. Normal-hearing young adults were tested for f2 equaling 2000-8000 Hz in 25-Hz steps with frequency ratios of 1.3-1.5. The researchers used IFFT to determine source latency. They found that latency does indicate the location of a source and, as expected, there was an increased latency when using low stimulus levels to elicit DPOAE responses.

Knight and Kemp (2000) tested 2f1-f2 and 2f2-f1 fine structure in two participants for DPOAE frequencies of 1000-4100 Hz for various frequency ratios. The authors found that small frequency ratios resulted in larger peaks after two milliseconds on the time-window representation, corresponding to larger amplitude for the reflection source. The 2f1-f2 DPOAE with a larger frequency ratio was dominated by the distortion source whereas the 2f1-f2 DPOAE with a small frequency ratio and the 2f2-f1 DPOAE no matter the frequency ratio were dominated by the reflection source. These results promote the argument for the use of small frequency ratios to improve the response amplitude of 2f2-f1 DPOAEs. The results of this study also suggested the importance of reflection sources to both 2f1-f2 and 2f2-f1 DPOAEs.

Kalluri and Shera (2001) looked at source separation by suppression and time windowing. Only time windowing will be discussed in this section as suppression was discussed previously. They postulated that time windowing would separate the sources for the 2f1-f2 component by their latencies. Kalluri and Shera obtained 2f1-f2 DPOAEs using 60/45 dB SPL stimulus levels and a 1.2 frequency ratio. These authors found that suppression and time windowing had the same net result in that the 2f1-f2 sources were well-separated using either method. If these separation procedures have the same net result then it would seem that the use of time windowing is a valid separation procedure for this study as it: (1) separates DPOAE sources well but (2) does not diminish the reflection source. This is important because time windowing does not enjoy the long history of research applications as suppression, yet offers clear advantages.

Konrad-Martin *et al.* (2001) used 2f1-f2 fine-structure DPOAEs to look at the reflection source and its dependence on test parameters. Both suppression and time windowing were used to separate the sources, only time windowing will be discussed here. The IFFT analyses were performed on the 2f1-f2 component to separate the distortion and reflection sources based on their phase. Peaks corresponding to both sources were found in the time domain. In addition, Konrad-Martin and colleagues found that primary levels that enhanced the 2f1-f2 component also enhanced the distortion-source peak of the time domain. It could then be reasoned that the reflection-source peak of the time domain would be enhanced by certain 2f2-f1 parameters (L1=L2=65 dB SPL, f2/f1=1.08).

Dhar *et al.* (2002) tested the fine structure of the 2f1-f2 DPOAE component in order to determine the effect of reflections along the cochlear partition. The authors attributed reflections on the cochlear partition to be due to impedance mismatch at the oval window. DPOAEs were measured between 1500 and 2500 Hz with 4-Hz and 8-Hz spacing, respectively. Multiple frequency ratios, intensity levels, and intensity level differences were used. Dhar and colleagues found the reflection source for the 2f1-f2 DPOAE was largest with the 1.11 frequency ratio. These results are consistent with those of Knight and Kemp (2000) - that the 2f1-f2 reflection source is affected by the frequency ratios used to elicit it.

Withnell *et al.* (2003) tested DPOAE amplitude and phase in guinea pigs using 2f1-f2 and 2f2-f1 DPOAE fine structure. The authors assumed 2f2-f1 had both distortion and reflection sources and that those sources came from the 2f2-f1 Fdp only. Withnell and colleagues found both sources existed for 2f2-f1 DPOAEs in guinea pigs. They also found 2f2-f1 was dominated by the reflection source even when using the 1.2 frequency ratio, which is known to enhance the distortion source in 2f1-f2 DPOAEs. These authors described both the 2f2-f1 distortion and reflection sources as coming from similar places along the cochlear partition. The author of the current literature review (JHH) argues that 2f2-f1 distortion and reflection sources come from their respective places (f2, Fdp) along the basilar membrane. Nevertheless, Withnell's conclusion regarding the reflection source as dominant for the 2f2-f1 component even with an f2/f1=1.2 is consistent with other research.

Mauermann and Kollmeier (2004) were interested in seeing how the reflection source affects a 2f1-f2 DPOAE input-output (I/O) function. They measured the 1500 through 4500 Hz range in 18-Hz steps and performed the IFFT on the resulting data separating them into short- and long-latency responses. The latencies resulted in two peaks in the time domain, and the reflection source was largest at low test frequencies (*i.e.*, 1300-1700 Hz), approximately equal to the distortion source at 2400 Hz, and smallest at the higher test frequencies. Also observed was a decrease for the reflection source across all frequencies with increasing stimulus level, this effect also was noted by Konrad-Martin *et al.* (2001). The results also were consistent with past studies in which increased magnitude responses for the 2f2-f1 component were found with lower test frequencies and low f2/f1 (Fitzgerald & Prieve, 2005).

Dhar *et al.* (2005) measured 2f1-f2 fine structure to determine how frequency ratios affected distortion and reflection sources. The ears of three adults with hearing thresholds <10 dB HL were assessed with L1=L2=45, 65, and 75 dB SPL and L1=65 with L2=45, 50, 55, 60 dB SPL at f2/f1=1.053-1.36 in 0.02-0.04 Hz steps. The distortion source had its greatest amplitude at a frequency ratio of 1.22 and reflection was largest at 1.11. Dhar *et al.* also found that the distortion source was largest at higher test frequencies, but the reflection source was largest at lower frequencies – a finding consistent with the results of Mauermann and Kollmeier (2004).

Wilson and Lutman (2006) investigated the possible generation mechanisms (and sources) of the 2f2-f1 DPOAE. They studied 20 young adults with normal hearing (thresholds ≤20 dB HL). They used frequency ratios of 1.05, 1.1, 1.22, and 1.32 for f2s equaling 1000-2500 Hz in 16-Hz steps. Stimulus tone levels were set at L1=65 dB SPL and L2=60 dB SPL. They considered an emission to be "present" when its amplitude was measured more than one standard deviation above the noise floor. The short-latency aspects (the distortion source) were seen prior to two milliseconds, while the long-latency aspects (the reflection source) were seen after that time. The distortion and reflection sources of the 2f1-f2 component and the distortion source of the 2f2-f1 component were present in all participants and the reflection source of the 2f2-f1 component was present in 18 of 20 people. The authors confirmed that both distortion- and reflection-source classes existed within the 2f2-f1 DPOAE. They explained that the distortion source component dominated the 2f2-f1 component because it was measurable across all participants. This is contradictory to results of previous studies that suggested the reflection source to dominate the 2f2-f1 component. The authors also explained how frequency ratio seemed to separate 2f1-f2 and 2f2-f1 DPOAEs. The distortion source of the 2f1-f2 component was dependent on the frequency ratio whereas neither the distortion nor the reflection sources of 2f2-f1 were affected by the frequency ratio.

Wilson and Lutman tested participants with hearing levels up to 20 dB. Previous literature has shown that thresholds equal to or below 10 dB HL ($\leq$10 dB HL) are better for eliciting the most robust 2f2-f1 components (Gorga *et al.*, 2000). In addition, the researchers did not test lower frequency primary tones known the help distinguish the 2f2-f1 component. Using parameters that enhance the 2f2-f1 component presumably will result in the presence of distortion and reflection sources for all participants. The 2f2-f1 component apparently is influenced most consistently by a well-defined set of parameters (moderate stimulus intensity levels, equal-level stimulus intensities, and small frequency ratio). Any deviations are likely to affect this component adversely and, therefore, its dominant source. Finally, Wilson and Lutman did not describe the fine structure similarities and differences between the two components.

Table 5. Parameters used in DPOAE time windowing studies.

Author	Year	2f1-f2	2f2-f1	Participants	F2 (kHz)	F2/f1	L1 (dB SPL)	L1-L2 (dB)	Test Measure
Stover *et al.*	1996	Yes	No	Humans	2-8	1.3-1.5	20-75	10	I/O
Kalluri & Shera	2001	Yes	No	Humans	0.8-2.4	1.22	60	15	DP-gram
Konrad-Martin *et al.*	2001	Yes	No	Humans	2, 4	1.2	35-55	10	DP-gram
Dhar *et al.*	2002	Yes	No	Humans	1.5-2.5	1.053-1.36	45, 65, 75	0-20	DP-gram
Mauermann & Kollmeier	2004	Yes	No	Humans	1.5-4.5	1.2	20-80	Varied	DP-gram
Dhar *et al.*	2005	Yes	No	Humans	1.5-2.5	1.053-1.36	45, 65, 75	0-20	DP-gram
Knight & Kemp+	**2000**	**Yes**	**Yes**	**Human**	**1-4**	**1.01-1.5**	**60, 70, 75**	**0**	**DP-gram**
Withnell *et al.*	**2003**	**Yes**	**Yes**	**Guinea Pigs**	**7-13**	**1.2**	**45, 55**	**0**	**DP-gram**
Wilson & Lutman	**2006**	**Yes**	**Yes**	**Human**	**1-2.5**	**1.05, 1.1, 1.22, 1.32**	**65**	**5**	**DP-gram**

+ All studies that used the 2f2-f1 DPOAE component are presented in bold.

Table 6. Results from time windowing studies including 2f2-f1 DPOAEs.

Author	Year	2f1-f2 Results	2f2-f1 Results
Knight & Kemp	**2000**	Distortion source with higher f2/f1; Reflection source with lower f2/f1	Smaller f2/f1 resulted in larger peaks after 2 ms 2f2-f1 was dominated by reflection source no matter f2/f1 size
Withnell *et al.*	**2003**	Distortion source dominates reflection source	Both sources found; 2f2-f1 was dominated by the reflection source even with the 1.22 f2/f1
Wilson & Lutman	**2006**	Distortion source = 20/20 cases Reflection source = 20/20 cases	Distortion source = 20/20 cases Reflection source = 18/20 cases

In summary, according to Kalluri and Shera (2001) and Konrad-Martin *et al.* (2001), time windowing and suppression have similar results for 2f1-f2 components (if suppression is fully implemented). However the same cannot be shown for the 2f2-f1 component. Suppression has variable effects on 2f2-f1 components and the ability to measure the reflection source, thought to be the dominant source for 2f2-f1, is lost as suppression removes its effects. Time windowing shows both sources and retains a high level of observation of both sources (100 and 90%, respectively) (Wilson & Lutman, 2006). Therefore, IFFT/time windowing is the preferable procedure for analyzing the reflection source and 2f2-f1 component of DPOAEs.

2.9 RATIONALE

The review of the literature demonstrates that great insight has been gained into the generation of the 2f1-f2 DPOAE but less so with the 2f2-f1 DPOAE. Despite limited numbers and/or extent of investigations, the 2f2-f1 DPOAE has been shown to be more robust than might have been expected, providing a nearly comparable dynamic range for testing the cochlear partition. The following is a recap of the most prominent models of DPOAE generation, upon which the rationale for the present work was developed.

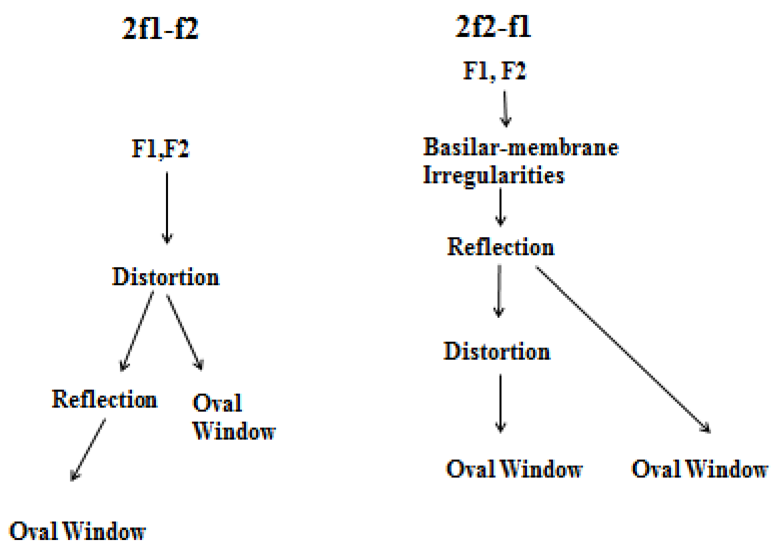


Figure 5. 2f1-f2 and 2f2-f1 generation mechanisms per Shera and Guinan (1999) and Wilson and Lutman's (2006) models.

Shera and Guinan (1999) developed the two-mechanism/two-source model to describe how 2f1-f2 DPOAEs are created by the cochlea. The basis for the model is the existence of backward traveling waves that are generated from two sources on the cochlear partition. These sources (distortion and reflection) are located at the f2 and Fdp places, respectively. For 2f1-f2 DPOAEs, the f2 place is basalward to that of Fdp. The primary-tone-traveling waves encounter f2 before Fdp as they travel from the base to the apex. The distortion source is known to dominate the 2f1-f2 component when using clinically accepted test parameters.

Shera and Guinan (1999) never explained the source of 2f2-f1 DPOAEs within the two-source/two-mechanism model. It is possible that 2f2-f1 DPOAEs do not (or should not) have two sources. However, Wilson and Lutman (2006) proposed a different model for DPOAE generation, one that includes the 2f2-f1 component. They proposed that distortion and reflection sources both occur at the 2f2-f1 Fdp on the cochlear partition. Also, Wilson and Lutman included inhomogeneities found on the cochlear partition. The addition of the inhomogeneities to the model prior to the reflection source integrates what is already known about cochlear physiology. That is (1) inhomogeneities help to make up the reflection source and (2) the 2f2-f1 component of the DPOAE is dominated by the reflection source. As such it is dependent on the inhomogeneities of the basilar membrane for its existence (Mauermann *et al.*, 1999a; Talmadge *et al.*, 1998). However, Wilson and Lutman were not able to record the 2f2-f1 reflection source in all of their participants. They attributed this result to emission levels occurring below the noise floor.

The purpose of the present study was to determine the sources generating the 2f2-f1 component wherein the 2f2-f1 fine structure is revealed. It was anticipated that the results of this study will serve to clarify the dominant source or sources generating the 2f2-f1 component, in reference to the broadly investigated 2f1-f2 component, by which the source or sources can be postulated definitively. In 2010, Martin and colleagues suggested that the two-source/two-mechanism model of DPOAE generation was not complete without addressing the generation of the 2f2-f1 component arising from an area of the cochlear partition basalward of the primary tones (Martin *et al.*, 2010). This suggestion lends credence to the need for the present study.

2.10 QUESTIONS, HYPOTHESES, AND PREDICTIONS

Both the Shera and Guinan (1999) and Wilson and Lutman (2006) models cited the f2 place as the location of the distortion source and the Fdp as the location of the reflection source. The Wilson and Lutman model, though seemingly an improvement, did not account for the difference in cochlear location of the Fdp sites of the 2f1-f2 and 2f2-f1 components.

The 2f1-f2 and 2f2-f1 DPOAEs require different parameters to elicit their largest magnitude responses because of their location on the cochlear partition (2f1-f2 Fdp is apicalward to the primary tones while 2f2-f1 Fdp is basalward). As DPOAEs are tied to their anatomy so are their distortion and reflection sources. As mentioned previously, past research has linked the distortion source to the f2 place and the reflection source to the Fdp. Therefore, the sources of the DPOAE will be affected by the parameters used to elicit them just as DPOAEs (the combination of those sources) are affected. Depending on the parameters used (and tonotopic organization), these Fdp sites may be quite removed from each other allowing researchers (and clinicians) to evaluate distinct areas of the cochlear partition simultaneously.

2.10.1 Questions and Hypotheses

1a. Is there a significant difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f1-f2?

$H1a_o$: There is no difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f1-f2.

$H1a_a$: There is a difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f1-f2.

1b. Is there a significant difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f2-f1?

$H1b_o$: There is no difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f2-f1.

$H1b_a$: There is a difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f2-f1.

2a. Is there an effect on fine-structure descriptors (ripple spacing, ripple depth, and/or ripple prevalence) when 2f1-f2 DP-grams are measured with differing parameter combinations?

$H2a_o$: There is no effect on fine-structure descriptors when 2f1-f2 DP-grams are measured with differing parameter combinations.

$H2a_a$: There is an effect on fine-structure descriptors when 2f1-f2 DP-grams are measured with differing parameter combinations.

2b. Is there an effect on fine-structure descriptors (ripple spacing, ripple depth, and ripple prevalence) when 2f2-f1 DP-grams are measured with differing parameter combinations?

$H2b_o$: There is no effect on fine-structure descriptors when 2f2-f1 DP-grams are measured with differing parameter combinations.

$H2b_a$: There is an effect on fine-structure descriptors when 2f2-f1 DP-grams are measured with differing parameter combinations.

2.10.2 Predictions

1. Enhancement of DPOAE magnitude output for the 2f1-f2 component broadly believed to be optimized by selective parameters of stimulation, and in turn enhances the most prominent source of this component. As noted earlier, several investigators have shown relative enhancements of the 2f1-f2 component over the wide range of stimulus parameters for which this component is measureable, as well as (again) to enhance one source over the other. These results were fully expected in the present study or, failing such findings, to permit more critical analyses of differences in between the present and earlier findings. Although optimal parameters for 2f2-f1 output differ from those of 2f1-f2, comparable effects from test parameters have been demonstrated in observed 2f2-f1 outputs. In order to scrutinize the difference in magnitude of the reflection source, 2f2-f1 DPOAEs were measured using parameters that optimize 2f1-f2 output (Question 1a) and versus conditions optimal for 2f2-f1 (Question 1b). The reflection component was larger in magnitude when measured with the 2f2-f1-enhancing parameters therefore the results of this study were consistent with the models described previously. The outcome per this question did not vary from the previous findings reported in the 2f1-f2 and 2f2-f1 literature, lending validity to the study.

2. The fine structure of the two DPOAE components differed with respect to ripple spacing, ripple depth, and ripple prevalence (Reuter & Hammershoi, 2006). From previous research for both 2f1-f2 and 2f2-f1 components, it was expected that ripple depth would be maximized using those parameters (*i.e.*, provide the largest amplitude). Second, ripple spacing was expected to decrease with increasing stimulus frequency thereby allowing for more ripples in the higher stimulus frequency regions (Engdahl & Kemp, 1996; Reuter & Hammershoi, 2006). The pattern of response of the distortion source on its own will have a more-flattened/less-rippled look (Mauermann & Kollmeier, 2004; Withnell *et al.*, 2003). Third, as the perturbations and reflections within the cochlea contribute to the creation of the reflection source it was predicted that the fine structure of the 2f2-f1 component (elicited by its best parameters) will have smaller/narrower ripple spacing and greater ripple prevalence than the 2f2-f1 component measured under optimizing conditions for 2f1-f2 per se, for 2f1-f2 measured under 2f2-f1 "best" parameters, or for 2f1-f2 output measured under 2f1-f2 optimizing parameters (See Table 7).

Table 7. Parameters that will elicit the narrowest ripple spacing and the greatest prevalence.

	DPOAE Component	**Dominant Source**	**f2/f1**	**L1 (dB SPL)**	**L1-L2 (dB)**
Narrower Ripple Spacing and Increased Prevalence	2f2-f1	Reflection	1.08	65	0
	2f2-f1	Reflection	1.22	65	10
	2f1-f2	Reflection	1.08	65	0
Wider Ripple Spacing and Decreased Prevalence	2f1-f2	Distortion	1.22	65	10

3.0 METHODS

3.1 PARTICIPANT RECRUITMENT

The participants were recruited from the staff, visitors, and patients of Desert Ear, Nose, and Throat and the Hearing Institute of the Desert in Rancho Mirage, California. The Hearing Institute of the Desert is a private audiology practice that is a subsidiary of Desert Ear, Nose, and Throat. Neither the Hearing Institute nor Desert ENT was associated with this study.

Permission was obtained from this otolaryngology practice to post flyers advertising for participants that qualify for this study. A letter of understanding from the Desert Ear, Nose and Throat was included in the University of Pittsburgh Institutional Review Board and consent form for this study. Each participant signed a consent form that had been approved by the University of Pittsburgh Institutional Review Board. The participants did not have to be native English speakers, but their oral and written English-language skills had to be sufficient to provide oral and written informed consent. A short questionnaire was completed by each participant in order to determine their audiologic and otologic histories including history of otitis media, pressure equalization tubes, or significant noise exposure (see Appendix A).

The preliminary and experimental procedures were conducted within a sound-treated booth at the Hearing Institute of the Desert (ANSI, 1999; Industrial Acoustics Co., Inc.). All participants were compensated $25 for their time.

3.2 NUMBER OF PARTICIPANTS

The number of participants was based on an effect size of *d* = .25 paired with a correlation of .7 to produce an adjusted effect size of .47 (Cohen, 1988). This effect size was judged to be sufficient to produce power of greater than .8 for the response magnitude of the 2f2-f1 DPOAE component measured with two different parameter combinations (1.22 with 65/55 dB SPL and 1.08 with 65/65 dB SPL), 24 participants, testing one ear per person, within a repeated-measures, mixed-model ANOVA. The initial medium effect size (.25) was chosen based on previous results from Horn *et al.* (2008), which resulted in significant main effects and interactions across nearly all measures.

3.3 PARTICIPANT INFORMATION

Twenty-four young female adults (20-35 years) with normal hearing participated in this study. Their gender, age range, and race are discussed below.

3.3.1 Sex

Female participants were chosen to eliminate any differences in anatomy or physiology contributed by sex and to minimize any possible negative effects on the data. A study by Moulin and Kemp (1996a) supports the decision to use women as it suggested latency differences for the

2f2-f1 component between male and female participants. A more recent study from McFadden and colleagues suggested there is little if any sex difference for DP latencies however they only used the 2f1-f2 component (McFadden, Pasanen, Leshikar, Hsieh, & Maloney, 2012).

3.3.2 Age

The participants were aged 21;8 to 35;9 years (mean = 29.86 years, SD = 2.49 years). Young adults were chosen for study because they have larger DPOAE response magnitudes and better frequency responses than older adults (He & Schmiedt, 1996; Stover *et al.*, 1996). In addition, they are less likely to have subclinical cochlear damage that might affect fine-structure measurement (He & Schmidt, 1996; Mauermann, Long, & Kollmeier, 2004). Recent studies on aging effects on DPOAEs have focused on the younger end of this sample's age range. Abdala and Dhar (2012) measured DPOAEs across seven age-groups ranging from 33-weeks gestation to 71 years. Their young-adult group included men and women aged 19-25 years and produced comparable response magnitudes to those seen in the current study. Rao, Tusler, and Formo (2014) assessed aging effects and found that middle-aged adults had decreased response magnitudes compared to the younger adults for the 2f2-f1 component. However, their middle-aged group was older, on average, than the participants of the current study.

3.3.3 Race

Participants of all races were welcomed to the study. No significant effects have been found for 2f1-f2 DPOAE response magnitudes across races (McFadden *et al*., 2012) and therefore not considered as a potential variable in this study.

3.3.4 Test Ears

Responses were measured from the right ear from each participant. Right ears were chosen as they have been shown to generate larger DPOAE responses than the left ear (Engdahl, 2002; McFadden, Martin, Stagner, & Maloney, 2009; McFadden *et al.*, 2012).

3.4 DPOAE EQUIPMENT

The screening and experimental DPOAE testing were performed with EMAV custom software developed by Neely and Liu (1993). The EMAV software was installed on a Windows XP-based personal computer (Dell Dimension E510) fitted with a high-quality 24-bit soundcard (CardDeluxe; Digital Audio Labs). This software allowed for primary-tone generation to occur on different channels of the soundcard. The primary tones were presented through ER-2 insert earphones (Etymotic Research) and mixed acoustically within the ear canal. The DP response then was carried by the earphones to the probe microphone (ER-10B+ Low Noise Microphone) to the EMAV software (and the computer) for recording and storage.

3.5 CALIBRATION

Test signals were calibrated using a Bruel and Kjaer Type 2270 sound level meter (SLM) with an Artificial Ear Type 4153 2-cc coupler and the EMAV Tone Test. The 2-cc coupler was chosen to minimize saturation levels of DP output (Larson, Studebaker, & Cox, 1977). The EMAV software produced its own calibration tone, and it was listed as its own test within the software. The Tone Test produced a repeated 2-second, 1000-Hz pure-tone at 65 dB SPL. The SLM with coupler was connected separately to the left and right ER-2 insert earphones and measured 65 dB SPL for each earphone.

3.6 PRELIMINARY PROCEDURES

3.6.1 Otoscopy, Tympanometry, Audiometry

Otoscopy was performed in order to determine the presence of cerumen, or any outer-ear or tympanic-membrane anomaly that may have interfered with testing, specifically the measurement of the backward traveling waves in the ear canal (Shera & Guinan, 1999). Immittance screening (Welch Allyn GSI 33 Middle-Ear Analyzer) also was completed to identify any negative pressure or middle ear pathology that may have compromised the DPOAE testing (ANSI, 1987; Roup, Wiley, Safady, & Stoppenbach, 1998; Thompson, Henin, & Long, 2015).

An audiologic evaluation was performed to determine behavioral hearing thresholds for pure tones (GN Otometrics Madsen Itera audiometer; American Speech-Language-Hearing Association, 2005). All test ears had thresholds $\leq$10 dB HL for 250-8000 Hz at the octave frequencies. A narrow threshold range of normal hearing was needed as the 2f2-f1 component often provides smaller magnitude responses than the 2f1-f2 component (Bonfils *et al.*, 1988; Gorga *et al.*, 2000; Abdala & Dhar, 2010). Although responses in ears with less than exquisite sensitivity ultimately must be considered, the overriding need for the present study was to assure presence of both products in all subjects, leaving an examination of effects of sensitivity to be explored in future work. See Figure 6 for average audiometric results.

Six recruits were disqualified on the basis of hearing thresholds exceeding 10 dB HL in the right ear, the presence of fluid, or a significant otologic history (Gorga *et al.*, 2000; see Appendix A). Significant noise exposure was defined as exposure to long periods of loud music or industrial noise, firearm usage, and/or extended military combat. Any disqualified participants were given a complete audiologic evaluation and referred to the appropriate healthcare provider for follow-up, as needed. One participant was found to have mild-moderate, flat sensorineural hearing loss in both ears. This participant reported having failed hearing screenings previously, but was given a hearing test to determine her present hearing status. This participant was referred to an ENT to rule out medical cause of hearing loss and subsequently fitted with hearing aids for both ears. Not all participants who failed to qualify had hearing loss because of the strict hearing criterion for this study. Five of six rejected participants had hearing threshold levels poorer than 10 dB HL, but better than or equal to 20 dB HL, in their right ears (*i.e.*, threshold levels of 15 or 20 dB HL at one frequency or more).

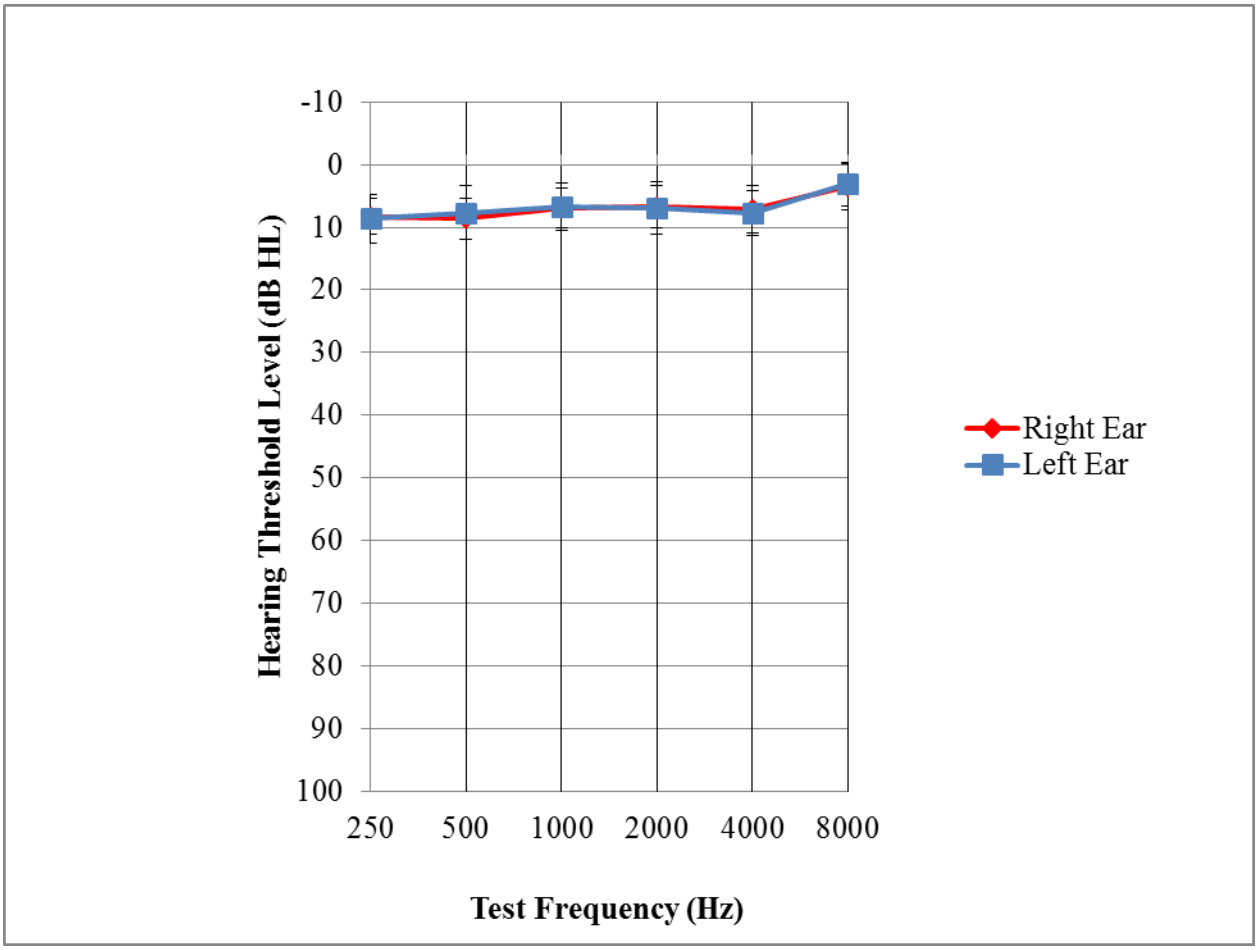


Figure 6. Average audiometric thresholds with standard deviations (SD), *n* = 24. Positive and negative SDs are included.

3.6.2 Screening 2f1-f2 DPOAEs

Preliminary testing also included a single DP-gram measured at L1/L2=65/55 dB SPL, f2/f1=1.22, for ½-octave frequencies from 500-8000 Hz. The purpose of this preliminary DP-gram was for comparison to other DPOAE research studies to ensure that this population had normal inner-ear function and represents the normal distortion process of the cochlear mechanism from the compiled participant data (Heitmann, Waldmann, Schnitzler, Plinkert, &

Zenner, 1998). The 2f1-f2 DP-grams were present in all participants' test ears with a signal-to-noise ratio (SNR) of approximately 10-25 dB. These SNR values are large, but they are not unreasonable given that participant hearing levels are ≤ 10 dB HL, participants had negative histories of excessive noise exposure or otologic issues, and the noise floors from the EMAV program were extremely low (see Abdala & Dhar, 2012). The preliminary mean DP-gram results may be seen in Figure 7. In addition, these SNRs are comparable to those from a hallmark study by Lonsbury-Martin and Martin published in 2007. The SNRs in Lonsbury-Martin and Martin were 0-25 dB. These results may be seen in Figure 8.

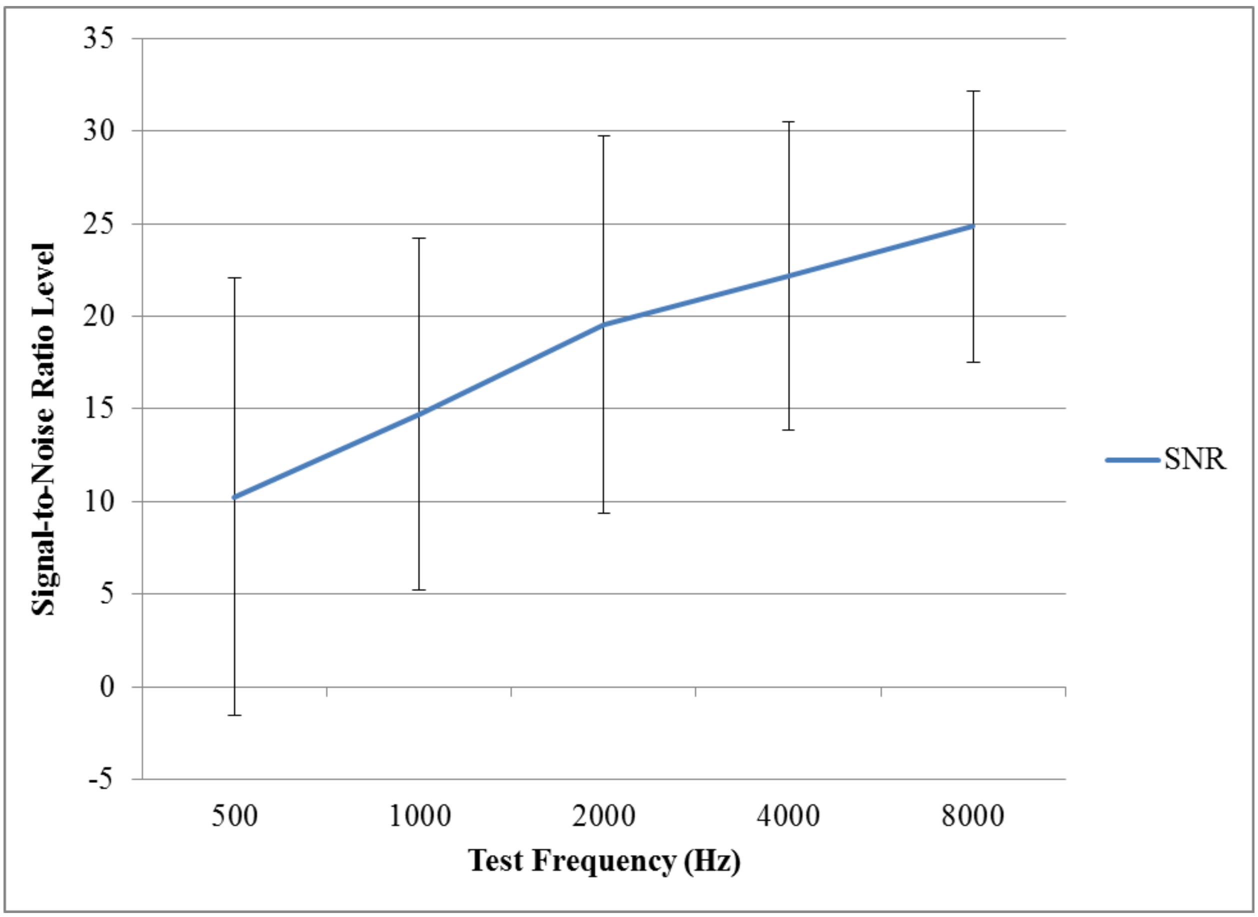


Figure 7. Average DP-gram response levels with standard deviations.

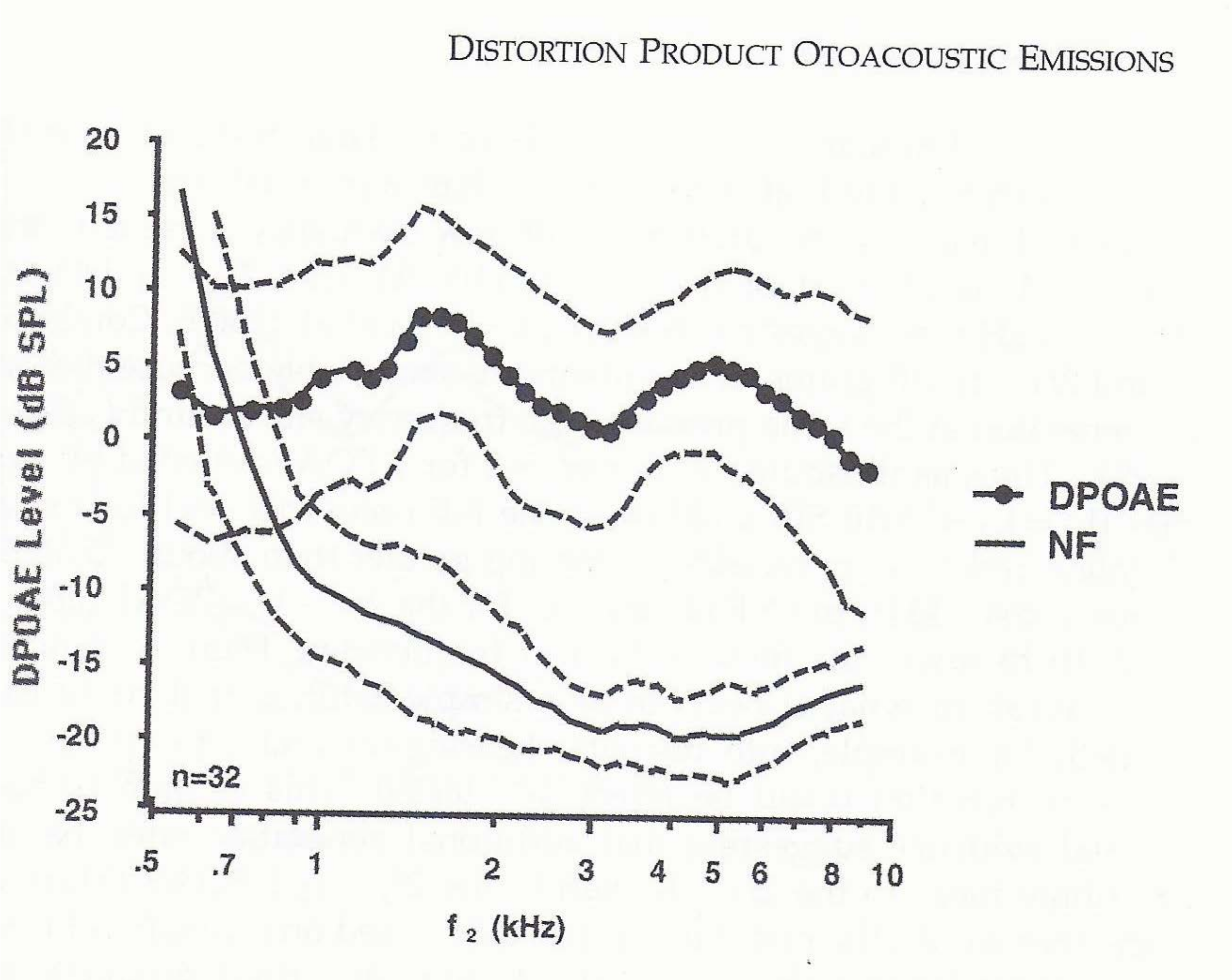


Figure 8. Mean DPOAE levels from Robinette and Glattke, <u>Otoacoustic Emissions: Clinical Application</u>, Chapter 5, written by Lonsbury-Martin and Martin. (Reprinted with permission from Robinette and Glattke. Copyright 2007, Thieme.)

3.7 EXPERIMENTAL PROCEDURES

An insert earphone with a plastic tip was placed snuggly within the ear canal of each participant's right ear. Earphone depth within the ear canal was adjusted in order to minimize standing waves within the ear canal. Minimization of standing waves was represented by a flat frequency response on the checkfit screen. After the earphone fit was checked, the earphone was calibrated within the ear canal then experimental procedures were implemented. The participants were asked to sit quietly but were allowed to read while the earphone was in place.

Experimental testing produced four fine-structure DP-grams recorded for all test ears. These fine structure DP-grams were recorded at L1/L2=65/55 with f2/f1=1.22 and L1/L2=65/65 with f2/f1=1.08 for f2=707-2000 Hz for both DPOAE components (see Table 8). The 2f1-f2 and 2f2-f1 components were recorded simultaneously (A and B, C and D). Test frequencies (f2) were chosen to optimize 2f2-f1 recording in consideration of signal and noise floor. The DPOAE signal data were measured by adding the A and B buffers (A+B) of the 2f1-f2 or the 2f2-f1 components, whereas the noise floor was measured by subtracting one buffer from the other (A-B). As the 2f1-f2 component has been documented extensively in the literature, it was examined in this study to provide validity to the study and to the observations made of the 2f2-f1 component.

Table 8. Parameters used to elicit DPOAE components across the 707-2000 Hz target stimuli.

A 2f1-f2 65/55 1.22	**B** 2f2-f1 65/55 1.22
C 2f1-f2 65/65 1.08	**D** 2f2-f1 65/65 1.08

The fine-structure step-size depended on the test frequency because the chosen software recorded frequency responses for every 1/64-octave. The DP averaging stopped after 32 seconds of quiet data collection or when the noise floor reached -25 dB SPL, whichever occurred first.

The order for starting f2 and parameter combination was counterbalanced across participants. All experimental data were collected within a single session of 45 minutes. Participants were given breaks as needed.

3.8 DATA ANALYSES

Several analyses were performed in order to answer the research questions posited. Four fine-structure DP-grams (Combinations A, B, C, and D above) were obtained from each participant. The fine-structure DP-grams were converted into Inverse Fast Fourier Transforms (IFFTs) and other graphical representations to determine the dominant source of each component to answer questions 1a and 1b. Separately, data analyses were performed on the raw data from each DP-gram to determine the fine-structure descriptors (*i.e.*, ripple spacing, ripple depth, and ripple prevalence) to answer questions 2a and 2b.

The analyses of the data were narrowly targeted due to the tremendous amount of data generated from the fine-structure DP-grams (Abdala *et al*., 2009). The analyses focused on the 1/3-octave bands centered on stimulus frequencies of 707, 1000, 1414, and 2000 Hz. This range of test frequencies encompassed lower-frequency stimuli known to enhance the 2f2-f1 component and mid-frequency stimuli known to enhance the 2f1-f2 component (Fitzgerald & Prieve, 2005; Gorga *et al.*, 2000).

3.8.1 Calculations of Ripple Characteristics

Ripple spacing, depth, and prevalence were derived from the definitions presented in section 2.8.3.2. Prior to applying the descriptions, each fine-structure DP-gram was measured for each value by hand. (No software programs that would perform these calculations automatically were known to the investigator.) Raw data were imported from EMAV into an Excel spreadsheet and then graphed (see Figure 9 for a representation of data from Combination A for one participant). As there was potential for human error during this process, one spectrum from each participant was reviewed by the second judge[1] (*i.e.*, 24 spectra out of 96 total). The reviewed spectra crossed all four stimulus combinations (A-D), but were not evenly selected from the four combinations (defined below). The second judge was then asked to calculate the response magnitudes for questions 1a and 1b and the ripple spacing, depth, and prevalence needed for questions 2a and 2b. When calculations occurred within 0.3 dB SPL or 3 Hz of the primary investigator's values, the values were accepted. When calculated results exceeded 0.3 dB SPL or 3 Hz, a discussion was held between the primary and secondary judge to determine where the difference occurred. No criteria regarding inter-judge agreement were found in the DPOAE literature, as such the above criteria were chosen as a reasonable expectation for difference in calculation by the primary and secondary judge. Often differences were attributed to calculation errors by the judges (*i.e.*, problems with addition or subtraction of magnitude values). There was 80% agreement between this investigator and the second judge on the first inspection of those 24 spectra, leading to discussion on 20% of the calculations. After calculations were re-checked on that 20%, any discrepancies that remained (namely, apropos 1 spectrum), any decision was

[1] The second judge is a veteran audiologist who evaluates DPOAEs in a clinical setting every day. She has experience reading standard DP-grams and was trained to read fine-structure DP-grams by the primary investigator.

weighted towards the investigator's choice as she had more experience with the spectra than the second judge.

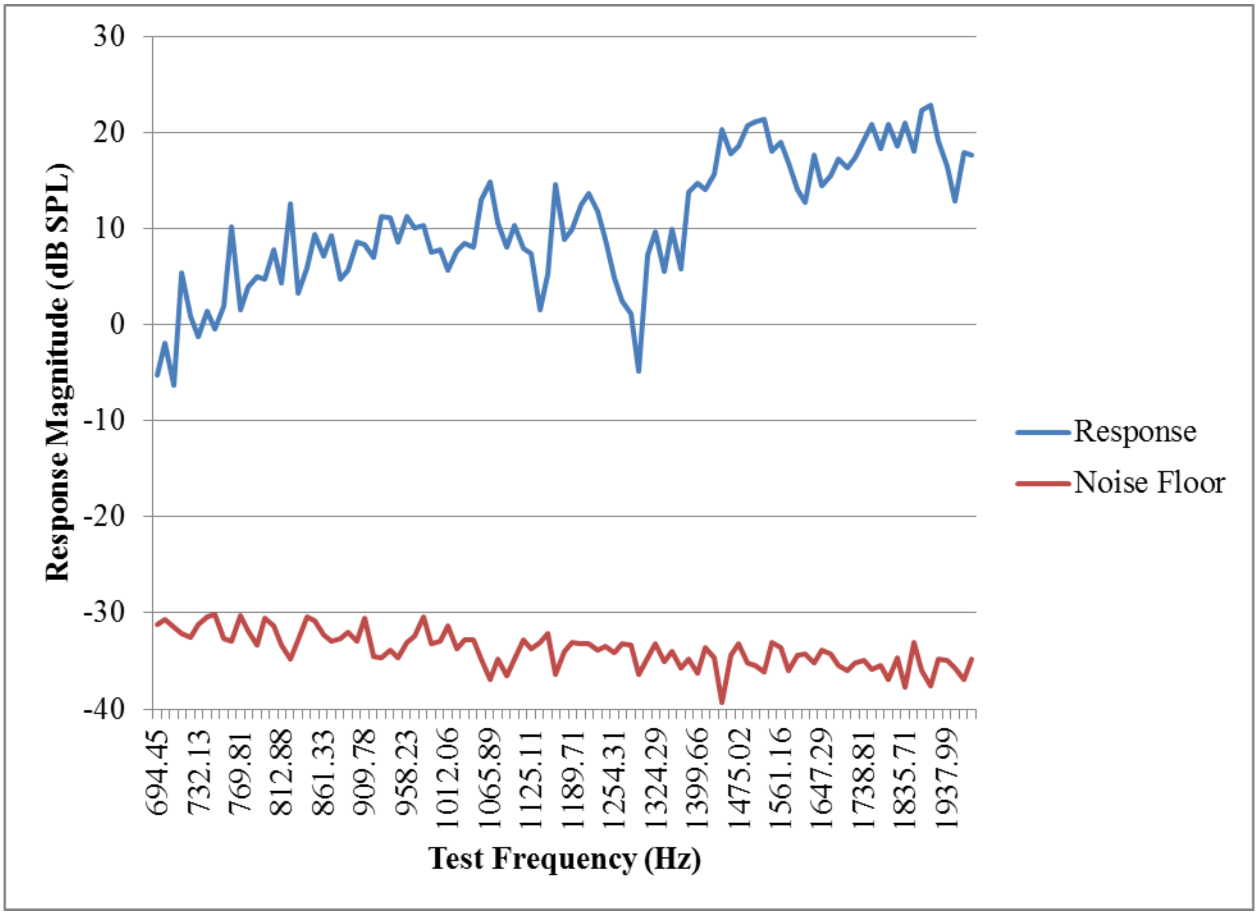


Figure 9. Example of a fine-structure graph generated in Microsoft Excel™ for one participant from the Combination A protocol (2f1-f2, 65/55 dB SPL, 1.22). The presence of the noise floor spectrum makes it difficult to appreciate the true peaks and valleys of the response spectrum.

The process by which ripple-characteristic data were calculated was complex and required multiple steps. First, ripple depth was measured by subtracting the trough from the maxima of each "spike" of the fine-structure DP-gram. For example, if the maxima equaled 22.9 dB SPL and the minima equaled 18 dB SPL, the depth was 4.9 dB (depth = 22.9 – 18 = 4.9 dB). The depth of each maximum was calculated and then separated into 1/3-octave bands for further statistical analyses. The ripple was considered authentic when it was larger than or equal to 3 dB. The 3-dB criterion was chosen because it is virtually a standard for many past DPOAE research studies and allows for comparison between this study and previous research (Reuter & Hammershoi, 2006; Whitehead *et al*., 1995b).

Ripple spacing was measured by determining the mean frequency of two maxima divided by the frequency difference of two maxima (Abdala *et al*., 2009). Again, this measurement occurred only for maxima that were $\geq$ 3 dB different or in "depth". The maxima represented by the values of 17.88 dB SPL and 22.9 dB SPL in Figure 9 are used to show an example of this process. Their corresponding frequencies were 1981.05 Hz and 1894.92 Hz, respectively.

$$\text{Spacing} = (\text{Frequency}_x + \text{Frequency}_y)/2 \text{ divided by } (\text{Frequency}_x - \text{Frequency}_y)$$

$$\text{Spacing} = (1981.05 + 1894.92)/2 \text{ divided by } (1981.05-1894.92) = 1937.985/86.13$$

$$\text{Spacing}_{(1981.05,\ 1894.92)} = 22.5$$

These measurements were implemented across the test frequency range. The ripple spacing results were then separated into 1/3-octave frequency bands for further statistical analyses.

Ripple prevalence was measured by counting the number of peaks (with depth larger than 3 dB) that occurred within a 1/3-octave band of 707, 1000, 1414, and 2000 Hz.

3.8.2 Nonlinear Impulse Phase Response (NIPR)

Distortion product magnitude and phase data, in the form of fine-structure DP-grams, were converted into the phase, level, and delay domains using a MATLAB-based algorithm developed by Dr. Carrick Talmadge (2007). Again, the DPOAE signal data were measured by adding the A and B buffers (A+B) of the 2f1-f2 or the 2f2-f1 components, whereas the noise floor was measured by subtracting one buffer from the other (A-B). The delay and level domains are explained in detail in Appendix B. The phase domain is useful in determining the dominant source of each spectrum as such it remains in this section.

On each spectrum there are four lines representing different aspects of the data. The Input data line (blue, solid thin line parallel to the abscissa) represented the original data collected in EMAV, the "Cleaned" data line (pink, dashed line) represented the input data with noise removed via complex algorithm, the Nonlinear line (green, thick solid line) represented the data acquired from the f2 place, and the Residual line (red, solid thin line sloping towards abscissa) represented data from the Fdp place.

The dominant source of each fine-structure DP-gram was determined by comparing the Input and "Cleaned" signals (*i.e.*, original data and filtered data signals, respectively) of a phase-by-frequency plot (Figures 10-12 as examples). When the Input data and "Cleaned" data lines were parallel to the Nonlinear component line the resulting pattern was considered to be consistent with a distortion source, as seen in Figure 10 for Combination A. When the Input data and "Cleaned" data lines were parallel to the Residual line the result was considered to be consistent with a reflection source as seen in Figure 11 for Combination D. Before determining the dominant source, each phase-by-frequency plot was printed out and labelled with its file number. File numbers did not contain any identifying information with regard to DP component or parameter combination. This allowed for the judges to be blinded to when determining the dominant source for each plot.

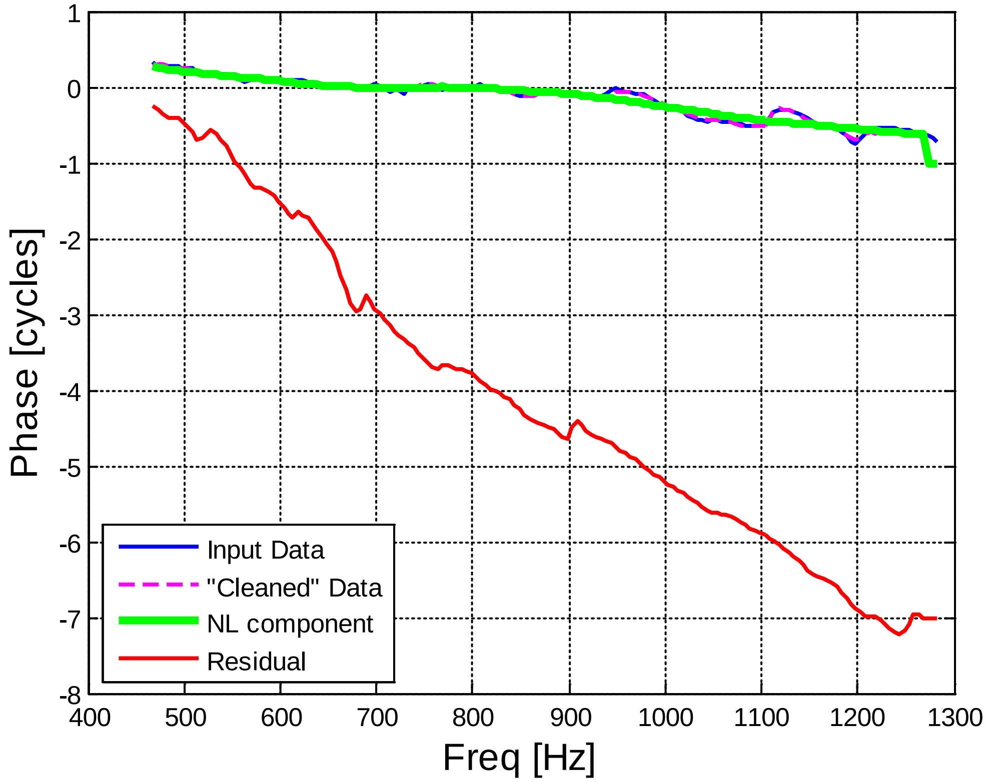


Figure 10. Example of a phase-by-frequency plot for 2f1-f2 DP component.

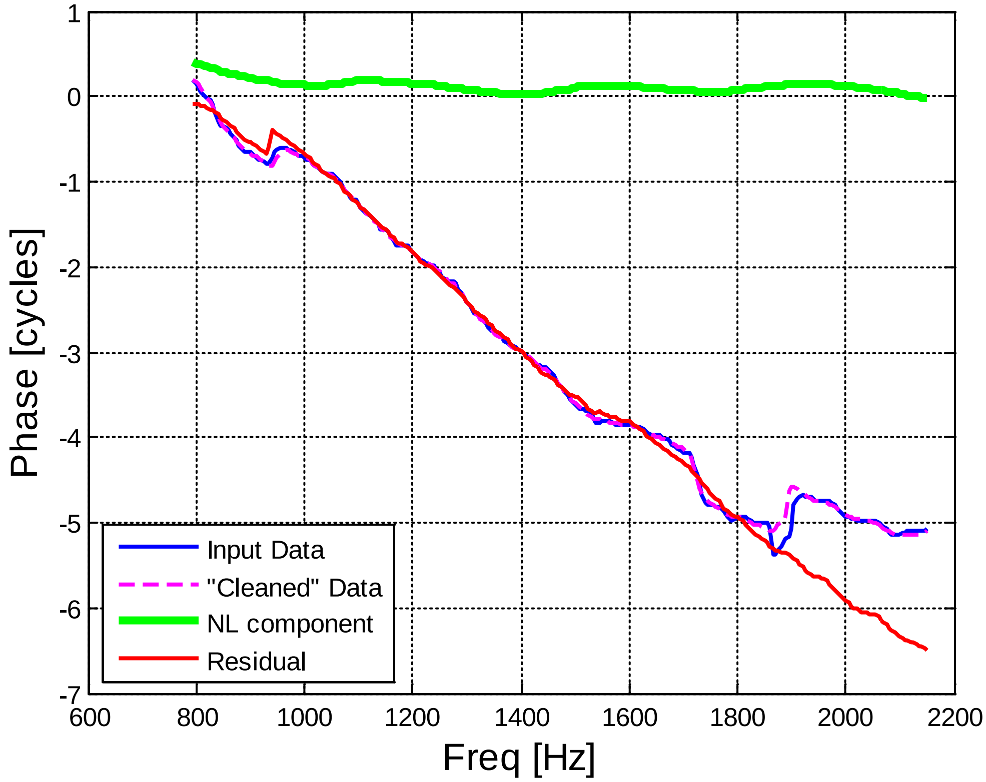


Figure 11. Example of a phase-by-frequency plot for 2f2-f1 DP component.

The 2f1-f2 and 2f2-f1 fine-structure spectra were separated into distortion-source or reflection-source categories by comparing the signals of the phase-by-frequency plots graph from the NIPR output. The optimized distortion-source-dominated response is represented with the Input and “Cleaned” data lines running parallel to the NL response (Figure 10). The optimized reflection-source-dominated response is represented with the Input and “Cleaned” data lines running parallel to the Residual response (Figure 11). Otherwise the phase of the optimized 2f2-f1 component has a steep slope, a characteristic known to occur with reflection-source dominance. Each spectrum was compared to determine to which lines the Input and “Cleaned” data were parallel. The flat phase associated with distortion-source dominance, and the sloped phase associated with reflection-source dominance, are the same guidelines as seen in other studies (*e.g.*, Abdala, Dhar, & Kalluri, 2011), but the samples represented by Figures 10 and 11 are idealized. As such, it was not always easy to determine unequivocally the dominant source of each graph (Figure 12). When it was difficult to determine the dominant source, the judges chose the source by observing to which line (NL component or Residual) the Input and "Cleaned" data lines seem mostly parallel, in Figure 12 the Input Data.

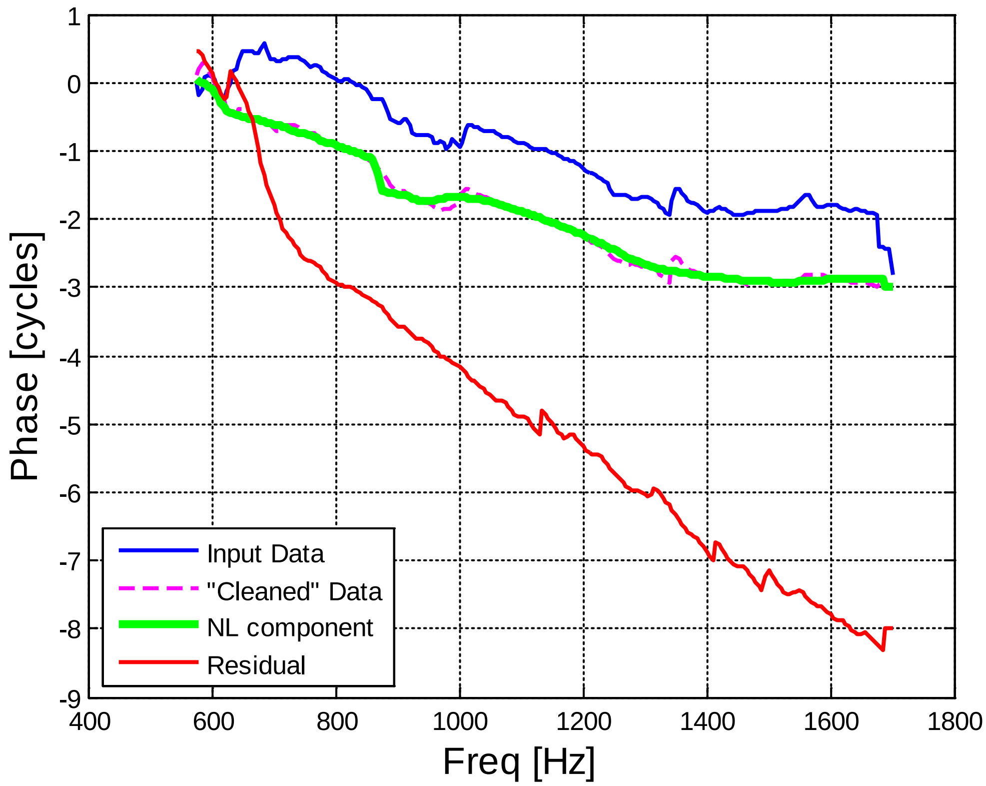


Figure 12. A realistic phase-by-frequency plot of a distortion-source response.

Both the investigator and a second judge performed the comparison of the phase-by-frequency plots to determine the dominant source of each graph. When there was a difference in opinion on the dominant source, the decision went to the investigator. There was 95% agreement (91/96 graphs) between the investigator and second judge on the first inspection. The five remaining graphs were compared again and discussed and 100% agreement was reached between the judges.

3.8.3 Analysis of Variance (ANOVA)

To examine research questions 1a and 1b, response magnitude was evaluated statistically using a two-way ANOVA (DP-combination x frequency) with repetition on two factors (DP-combination, frequency). Post-hoc t-tests were used as needed to address specific comparisons among the factors and interactions. The Bonferroni post-hoc correction was chosen as it minimizes the possibility of a Type I error (the incorrect rejection of a true null hypothesis) unlike other t-tests (*e.g.*, the Newman-Keuls test).

To examine research questions 2a and 2b, separate mixed model ANOVAs were applied to the data derived from the four fine-structure DP-grams. The dependent measures (ripple space, ripple depth, and ripple prevalence) were nested under center frequency and DP-combination for two 3-way ANOVAs. Individual participants were entered into the model to account for individual variability across the repeated measures. This type of model allowed for the investigation of ripple characteristic, center frequency, and fine-structure parameter set interactions. This model addressed the specific comparisons needed to answer the experimental questions under 2a and 2b, but post-hoc ANOVAs and subsequent t-tests were used as needed to assess interactions. The alpha was controlled at the .05 level for each ANOVA and the post-hoc analyses were controlled as needed with Bonferroni corrections.

3.8.4 Coefficients of Variation

The coefficient of variation is a statistic used to compare two tests of differing values or a method by which variability of two measures may be compared (Lloyd, 2008; Reh & Scheffler, 1996). The coefficient is a ratio calculated by dividing the standard deviation by the mean ($SD/\bar{X}$) of a particular data set. Whereas standard deviation is a measure relative to the mean of a data set, the coefficient of variation normalizes this measure of variance to the mean so as to place standard deviations of measure substantially different means or different measure per se on a common numerical scale. This measure was attractive to expectations that these measures would differ substantially numerically, such as response values of 24.38 for ripple spacing versus 4.69 for ripple prevalence.

4.0 RESULTS

As mentioned in the Methods section, the data were analyzed using ANOVA and post-hoc testing to determine the significance of effects and interactions between the combinations and their characteristics. Prior to the analyses needed to answer questions 1 and 2, basic information on the four DPOAE combinations were examined and summarized in Table 9. These data were not essential to addressing the experimental questions per se but they provided a fundamental understanding of the source dominance found in this study and allowed for comparison to other studies.

Table 9. Number and percentages of ears producing distortion-source or reflection-source dominance. Dominant source is highlighted by asterisk.

A 2f1-f2 65/55 1.22 Distortion: 24/24 (100%)* Reflection: 0/24 (0%)	**B** 2f2-f1 65/55 1.22 Distortion: 8/24 (33%) Reflection: 16/24 (67%)*
C 2f1-f2 65/65 1.08 Distortion: 8/24 (33%) Reflection: 16/24 (67%)*	**D** 2f2-f1 65/65 1.08 Distortion: 0/24 (0%) Reflection: 24/24 (100%)*

Combinations A and D represented components with maximum source dominance. Combination A was 100% distortion-source dominated, whereas Combination C was 100% reflection-source dominated. These results were in agreement with predictions made for this study based on previous research and provided assurance of the validity of the study measures. Combinations B and C, the “mismatched” pairs, represented the individual variations of the distortion and reflection processes of the cochlea and seemed to follow the predictions postulated and represented in Table 7. The results reveal the less-than-complete dominance of the reflection source. These outcomes and the results of statistical analyses applied to the various measures are presented in the context of each research question in the following sections.

4.1 QUESTION 1A

Question 1a asked whether there is a significant difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f1-f2 (Combinations A vs. B).

Response magnitudes are summarized in Figure 13 below. To address this question a two-way ANOVA with repetition on two measures (DP-combination, frequency) was applied to the response-magnitude data from Combinations A and B with the magnitude means and standard deviations shown in Appendices C and D, and ANOVA results shown in Table 10.

Table 10. ANOVA results for comparing response magnitudes from Combinations A and B.

Source	*df*	*Mean Square*	F^1	*Effect Size*	*p*
DP-combination (DP)	1.000	177.164	11.796	.339	.002*
Error	23.000	15.019			
Frequency (F)	2.407	144.458	41.076	.641	.0009*
Error	55.355	3.517			
DP x F	1.748	319.985	37.143	.618	.0009*
Error	40.202	8.615			

Note: [1] Greenhouse-Geisser correction was used for all sources as effect size was smaller than .75 per Mauchly's test of sphericity.

*$p \leq .05$

The response magnitudes were significantly larger for Combination A than Combination B overall (mean difference = 1.921, standard error = .559), but the significant interaction suggested that the DP-combination difference varied by frequency. A significant frequency effect also was found, as expected. To determine the influence of test frequency on response magnitudes for Combinations A and B, an interaction plot was created to show the magnitude patterns per frequency for each of the DP-combinations (Figure 13).

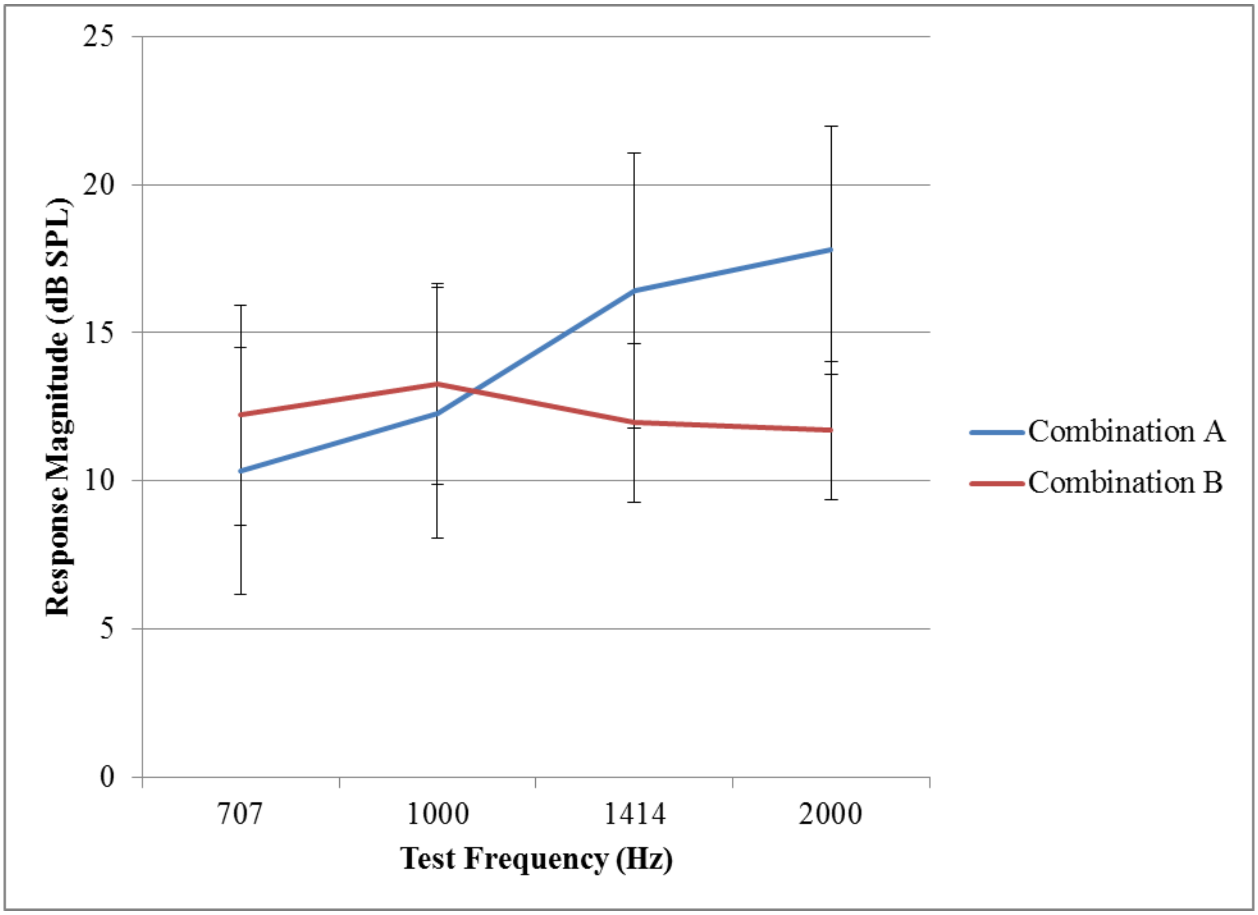


Figure 13. Interaction plot of response magnitudes for Combinations A and B. (Error bars reflect +/- 1 SD).

To further examine the DP-combination difference and the source of the DP-combination by frequency interaction, t-tests were used to compare Combinations A and B at each test frequency. The results of these analyses are shown in Table 11. Combination A was significantly larger than Combination B for test frequencies 1414 and 2000 Hz, but they did not differ at 707 and 1000 Hz. In general, the largest response magnitudes were produced with Combination A and for the higher test frequencies (*i.e.*, 1414 and 2000 Hz), which also were the frequencies associated with a significant difference between combinations.

Table 11. Post-hoc analyses of response magnitudes for Combinations A and B by test frequency.

Frequency Pairs	*Means (A, B)*	*SDs (A, B)*	*df*	*t*	*p*
A707 B707	10.344, 12.221	4.170, 3.707	23	-2.248	.034
A1000 B1000	12.291, 13.270	4.220, 3.391	23	-1.340	.193
A1414 B1414	16.435, 11.965	4.634, 2.685	23	2.157	.0009*
A2000 B2000	17.788, 11.714	4.197, 1.327	23	8.424	.0009*

$^*p \leq .0125$.

4.2 QUESTION 1B

Question 1b asked whether there is a significant difference in response magnitude between the distortion and reflection sources when using parameters that best elicit 2f2-f1 (Combinations C vs. D).

The response magnitudes used to address Questions 1b were analyzed in the same manner as for Question 1a, and are illustrated in Figure 14 below. The ANOVA results are presented in Table 12. See Appendices C and D for magnitude values.

Table 12. ANOVA results for comparing response magnitudes from Combinations C and D.

Source	*df*	*Mean Square*	F^1	*Effect Size*	*p*
DP-combination (DP)	1.000	313.301	82.915	.783	.0009*
Error	23.000	3.779			
Frequency (F)	1.868	56.122	5.408	.190	.009*

Table 12 continued.

	Error	42.966	10.377			
DP x F		2.307	63.254	12.186	.346	.0009*
	Error	53.060	5.191			

Note: [1] Greenhouse-Geisser correction was used for all sources as effect size was smaller than .75 per Mauchly's test of sphericity.

*$p \leq .05$

The two-way ANOVA detected significant differences in response magnitudes between the C and D Combinations. Combination D produced DPs of greater magnitude than Combination C (mean difference = 2.555, standard error = .281) and as expected a frequency effect was found with the ANOVA. The frequency effect was evaluated and shown in Table 13.

Table 13. Post-hoc comparisons for test frequency pairs from Combinations C and D.

Frequency Pair		*Mean Difference*	*Standard Error*	*p*
707	1000	-1.843	.441	.002*
	1414	-1.619	.646	.118
	2000	-.691	.570	1.000
1000	1414	.224	.531	1.000
	2000	1.152	.569	.328
1414	2000	.928	.271	.014

$p \leq .0125$

Post-hoc analyses of frequency effect showed a significant difference between 707 and 1000 Hz, but no difference between the other frequency pairs. It was expected that the 707-Hz test frequency would provide a larger magnitude response than the 1000-Hz test frequency, but that was not confirmed. Yet, Combination D at the lower test frequencies created responses that were larger in magnitude than at the higher test frequencies. A significant DP-combination by frequency interaction also was observed and is depicted in Figure 14.

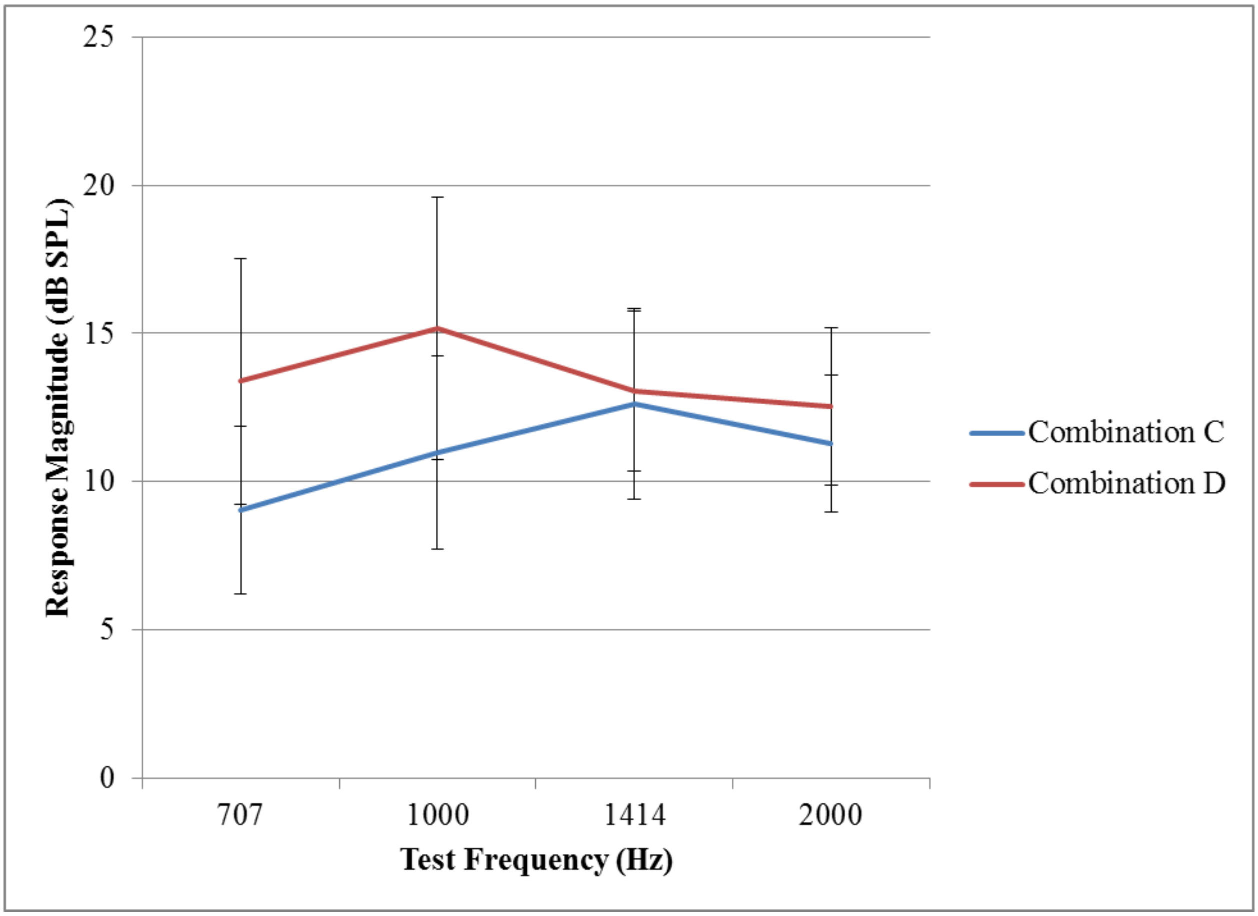


Figure 14. Interaction plot of response magnitudes for Combinations C and D. The error bars reflect +/- 1 SD.

The interaction was further examined with paired t-tests; with the results displayed in Table 14. Given an overall alpha of $p \leq .05$ (Bonferroni corrected), Combination D was significantly larger than Combination C at 707, 1000, and 2000 Hz but there was no difference between the combinations at 1414 Hz. The Combination D protocol evaluated the 2f2-f1 component with parameters known to enhance it. Combination D showed larger magnitude responses than Combination C, especially for the lower test frequencies, when using parameters thought to elicit the most robust 2f2-f1 component.

Table 14. Post-hoc analyses of response magnitudes for Combinations C and D by test frequency.

Frequency Pairs	*Means (C, D)*	*SDs (C, D)*	*df*	*t*	*p*
C707 D707	9.060, 13.399	2.823, 4.147	23	-5.591	.0009*
C1000 D1000	10.968, 15.177	3.259, 4.412	23	-6.732	.0009*
C1414 D1414	12.633, 13.064	3.204, 2.696	23	-.997	.329
C2000 D2000	11.300, 12.541	2.314, 2.649	23	-3.401	.002*

*$p \leq .0125$

4.3 QUESTION 2A

Questions 2a addressed whether there is an effect on fine-structure descriptors (ripple spacing, ripple depth, and ripple prevalence) when 2f1-f2 components are measured with differing parameter combinations (Combinations A and C).

In Section 2.8.3.2, three criteria were listed for the ripple characteristics of the 2f1-f2 fine-structure DP-gram to be accepted for analyses. Those criteria were: Ripple spacing $\leq$ 25, ripple depth $\geq$ 2.5 dB, and ripple prevalence of 1.5-3 maxima per 1/3-octave band (Abdala & Dhar, 2010; Abdala *et al.*, 2009; Reuter & Hammershoi, 2006). A three-way mixed model ANOVA was applied to the ripple-characteristic data with the results presented in Table 15.

Table 15. ANOVA results comparing ripple characteristics of the 2f1-f2 DP component (Combinations A and C).

Source	*df*	*Mean Square*	*F*[1]	*Effect Size*	*p*
DP-combination (DP)	1.000	76.810	4.330	.158	.049*
Error	23.000	17.739			
Frequency (F)	2.783	122.826	11.519	.334	.0009*
Error	64.005	10.663			
Ripple Charac. (R)	1.481	30265.629	1465.915	.985	.0009*
Error	34.134	20.892			
DP x F	2.513	20.254	1.240	.051	.302
Error	57.799	16.334			
DP x R	1.440	96.662	4.953	.177	.022*
Error	33.123	19.515			
F x R	3.231	292.262	13.023	.362	.0009*
Error	74.303	22.441			
DP x F x R	2.671	41.777	1.405	.058	.252
Error	61.436	29.735			

Note: [1] Greenhouse-Geisser correction used for all sources as effect size was less than .75 per Mauchly's test of sphericity.

*$p \leq .05$

A significant DP-combination effect was found, and there were significant differences for all of the ripple characteristics along with significant interactions. Greater values were found for Combination C than for Combination A. These results were not expected as Combination A was concluded (from results in the literature) to be representative of the most robust DP component (*i.e.*, 2f1-f2) measured with its optimized parameters (f2/f1 = 1.22 and 65/55 dB SPL).

4.3.1 Ripple Spacing

Individual ripple characteristics thus were analyzed since there were significant differences found between Combinations A and C. These characteristics were analyzed by a secondary two-way mixed-model ANOVA (Table 16). See Appendices E and G for ripple-spacing values.

Table 16. Two-way mixed-model ANOVA for ripple spacing.

Source	*df*	*Mean Square*	*F*[1]	*Effect Size*	*p*
Combination (DP)	1.000	29.540	.793	.033	.320
Error	23.000	37.234			
Frequency (F)	2.826	436.718	16.010	.410	.0009*
Error	64.995	27.277			
DP x F	2.254	34.479	.809	.034	.464
Error	51.836	42.611			

*$p \leq 0.05$

The ANOVA showed no DP-combination effect and no interaction between DP-combination and frequency (Figure 15), although a significant frequency effect was confirmed for ripple spacing (mean= -.730, standard error = .351, p = .049). To determine the direction of the effect, post-hoc testing was applied to the data. The post-hoc t-tests indicated significant differences in ripple spacing across the test frequencies for Combinations A and C (Table 17).

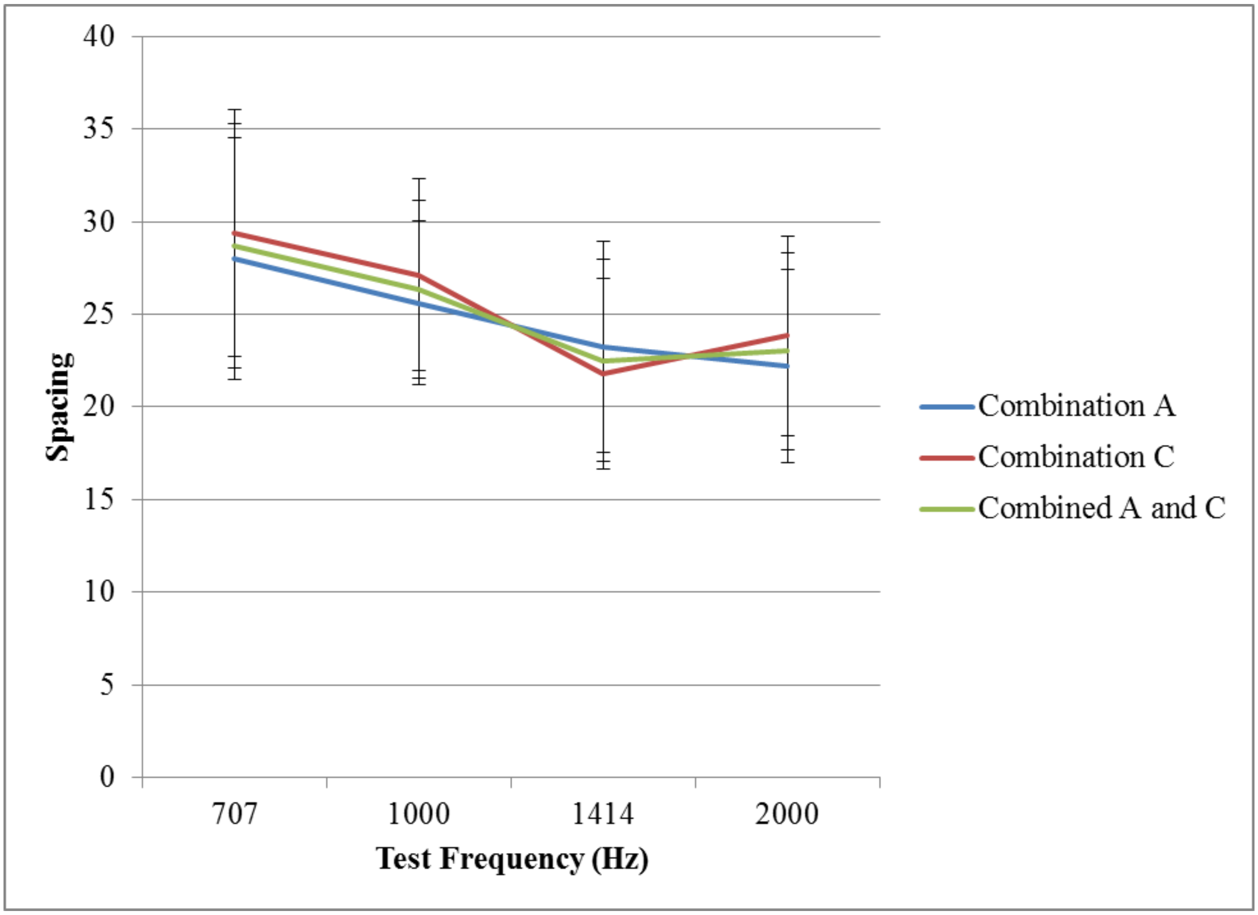


Figure 15. Ripple spacing across all test frequencies for Combinations A, C, and A and C combined. The errors reflect +/- 1 SD.

Table 17. Post-hoc comparisons for ripple spacing at each test frequency.

Frequency (Hz)	*Mean*	*SD*	*df*	*t*	*p*
707	28.708	6.559	47	30.325	.0009*
1000	26.378	4.828	47	37.856	.0009*
1414	22.508	5.427	47	28.736	.0009*
2000	23.015	5.309	47	30.032	.0009*

*$p \leq .0125$

4.3.2 Ripple Depth

The ripple-depth characteristics of Combinations A and C were further analyzed with a secondary mixed-model ANOVA. The initial ANOVA (Table 15) had not provided detailed analyses on this particular characteristic. The results of the two-way ANOVA are shown in Table 18. See Appendices F and H for ripple-depth values.

Table 18. Two-way mixed-model ANOVA for ripple depth.

Source	*df*	*Mean Square*	*F*[1]	*Effect Size*	*p*
Combination (DP)	1.000	174.477	26.977	.540	.0009*
Error	23.000	6.468			
Frequency (F)	2.064	1.926	.196	.008	.829
Error	47.478	9.819			
DP x F	1.916	34.949	3.420	.129	.044*
Error	44.059	10.219			

*$p \leq 0.05$

The two-way ANOVA confirmed a significant difference in ripple depth between Combinations A and C (Table 18; mean difference = -1.907, standard error = .367). A significant difference also was seen for the combination by frequency interaction. No effect for the frequency was observed.

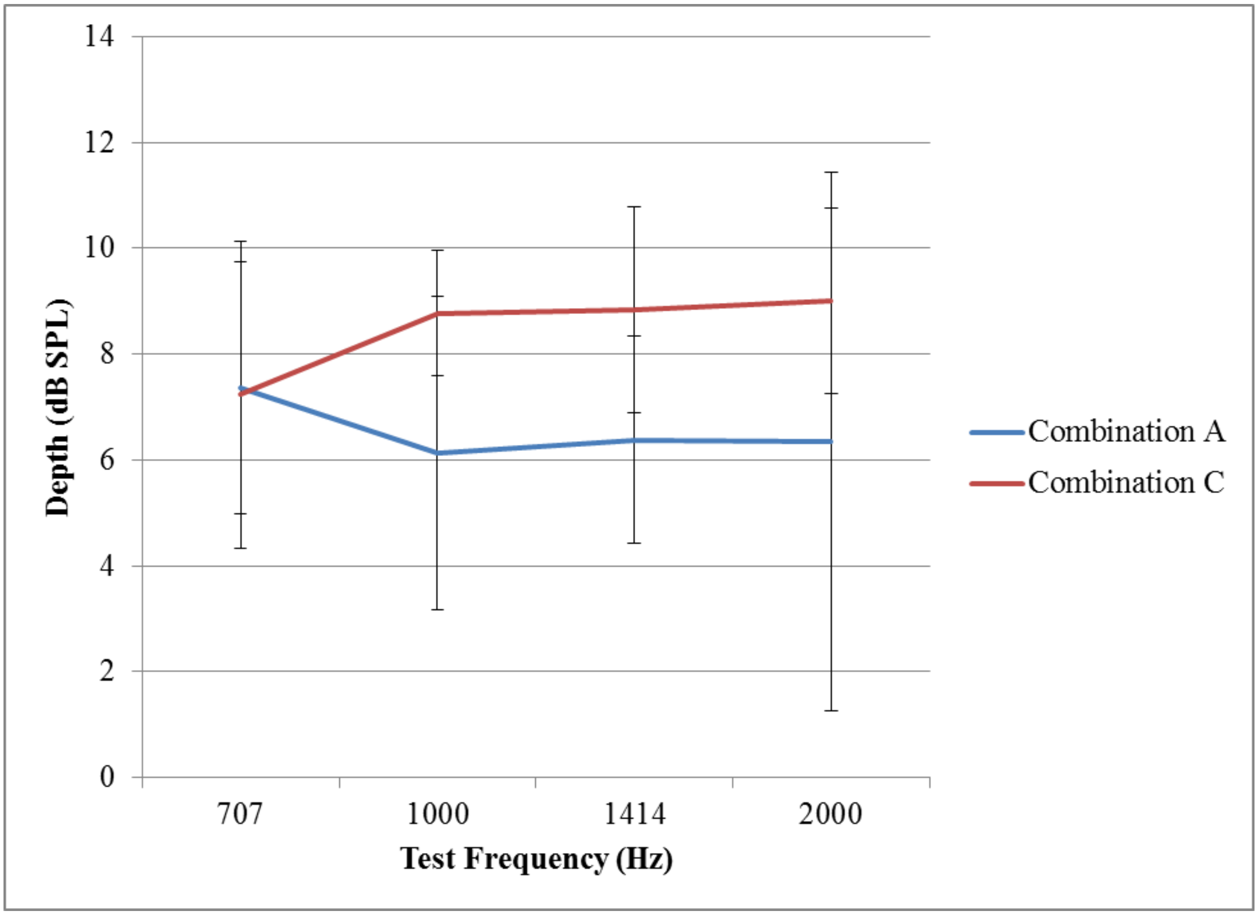


Figure 16. Interaction plot for ripple depth for all test frequencies (Combinations A and C). The error bars reflect +/- 1 SD.

The interaction between DP-combination and frequency is illustrated in the above interaction plot (Figure 16) and post-hoc t-tests were run to further examine it. Significant differences in ripple depth were seen with the 1000 and 1414 Hz test frequencies, with Combination C showing deeper ripples than Combination A (Table 19). However, no differences were found for the 707 and 2000 Hz test frequencies. This was not surprising as the 707 Hz mean values were similar and the error bars overlapped substantially for 2000 Hz.

Table 19. Post-hoc comparisons for ripple depth of Combinations A and C at each test frequency.

Pair	*Means (A, C)*	*SDs (A, C)*	*df*	*t*	*p*
A707 C707	7.234, 7.369	2.9, 2.382	23	.257	.799
A1000 C1000	8.774, 6.135	1.176, 2.964	23	-3.998	.001*
A1414 C1414	8.833, 6.374	1.94, 1.954	23	-4.536	.0009*
A2000 C2000	9.007, 6.344	1.75, 5.093	23	-2.464	.022

*$p \leq .0125$

4.3.3 Ripple Prevalence

Table 20. Two-way mixed-model ANOVA for ripple prevalence.

Source	*df*	*Mean Square*	*F*[1]	*Effect Size*	*p*
Combination (DP)	1.000	12.000	5.604	.196	.027*
Error	23.000	2.141			
Frequency (F)	2.429	19.720	9.937	.302	.0009*
Error	55.863	1.984			
DP x F	2.139	8.339	3.665	.137	.30
Error	49.189	2.275			

*$p \leq .05$

Ripple prevalence data were further analyzed with a two-way mixed-model ANOVA to determine if there existed significant differences between Combinations A and C (Table 20). The results confirmed a significant difference in ripple prevalence between Combinations A and C (mean difference = .500 standard error = .211), and a frequency effect, but no DP-combination by frequency interaction was observed. The significant difference in ripple prevalence between Combinations A and C can be seen in Figure 17, with the frequency effects examined with paired t-tests (Table 21). The only frequency difference was between 707 and 1000 Hz. See Appendices F and I for ripple prevalence values.

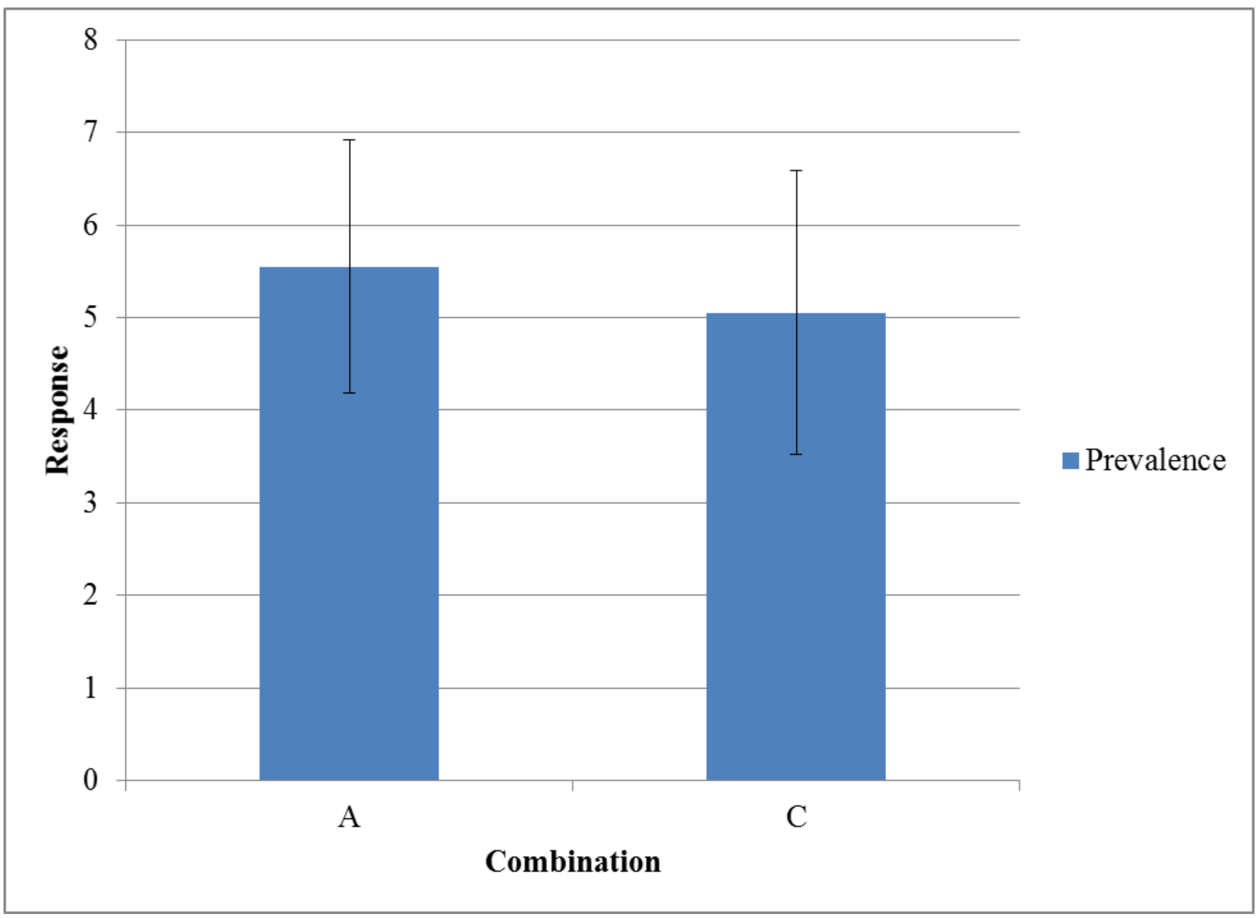


Figure 17. Ripple prevalence values for Combinations A and C without frequency effects.

Table 21. Post-hoc comparisons for ripple prevalence for test frequency pairs.

Frequency Pair		*Mean Difference*	*Standard Error*	*p*
707	1000	-1.333	.249	.0009*
	1414	-.833	.255	.020
	2000	-.375	.271	1.000
1000	1414	.500	.289	.580
	2000	.958	.293	.020
1414	2000	.458	.178	.101

$p \leq .0125$

4.4 QUESTION 2B

Question 2b asked whether there is an effect on fine-structure descriptors (ripple spacing, ripple depth, and ripple prevalence) when 2f2-f1 components are measured with differing parameter combinations (Combinations B vs. D).

All ripple-characteristic criteria described in section 4.3 were examined in this section. As in Section 4.3, the ripple data were initially examined using a three-way mixed-model ANOVA. The results of the ANOVA for Combinations B and D are shown in Table 22.

Table 22. ANOVA results comparing ripple characteristics of the 2f2-f1 DP component (Combinations B and D).

Source	*df*	*Mean Square*	F^1	*Effect Size*	*p*
DP-combination (DP)	1.000	2.034	.283	.012	.600
Error	23.000	7.179			
Frequency (F)	2.812	21.917	1.272	.052	.291
Error	64.677	17.229			
Ripple Charac. (R)	1.057	33779.516	348.185	.938	.0009*
Error	24.309	97.016			
DP x F	2.488	12.905	.643	.027	.562
Error	57.234	20.077			
DP x R	1.371	21.802	1.405	.058	.255
Error	31.532	15.521			
F x R	3.431	77.101	3.435	.130	.016*
Error	78.915	22.443			
DP x F x R	3.346	39.551	1.523	.062	.211
Error	76.967	25.971			

Note: [1] Greenhouse-Geisser correction used for all sources.

$^*p \leq .05$

Unlike the previous comparisons, Combinations B and D did not differ, nor was there a DP-combination by frequency interaction, but a significant ripple characteristic effect was found, and there was a significant test-frequency-by-ripple-characteristic interaction.

4.4.1 Frequency-Ripple Characteristic Interaction (FxR)

The test frequency by ripple characteristic interaction found was further examined with a two-way mixed-model ANOVA with the results shown in Table 23. The ANOVA confirmed a significant ripple characteristic effect and a significant frequency by characteristic interaction. No frequency effect was observed.

Table 23. Two-way mixed-model ANOVA for frequency-characteristic interaction.

Source	*df*	*Mean Square*	F^1	*Effect Size*	*p*
Frequency (F)	2.720	22.657	1.262	.026	.290
Error	127.851	17.954			
Characteristic (R)	1.114	32042.011	583.110	.925	.0009*
Error	52.368	54.950			
F x R	3.485	75.901	3.186	.063	.020*
Error	163.811	23.822			

*$p \leq .05$

Post-hoc testing results comparing ripple characteristics are shown below (Table 24, Figure 18) and revealed, not surprisingly, that each ripple characteristic is significantly different from the other when analyzed without the influence of DP-combination or test frequency. Figure 18 is the representation of the significant ripple-characteristic effect from Table 24 plotted by test frequency without the effect of DP-combination.

Table 24. Post-hoc comparisons of ripple characteristics.

Characteristic Pair		*Mean Difference*	*Standard Error*	*p*
Spacing	Depth	15.255	.741	.0009*
	Prevalence	17.844	.591	.0009*
Depth	Prevalence	2.589	.243	.0009*

*p<.05

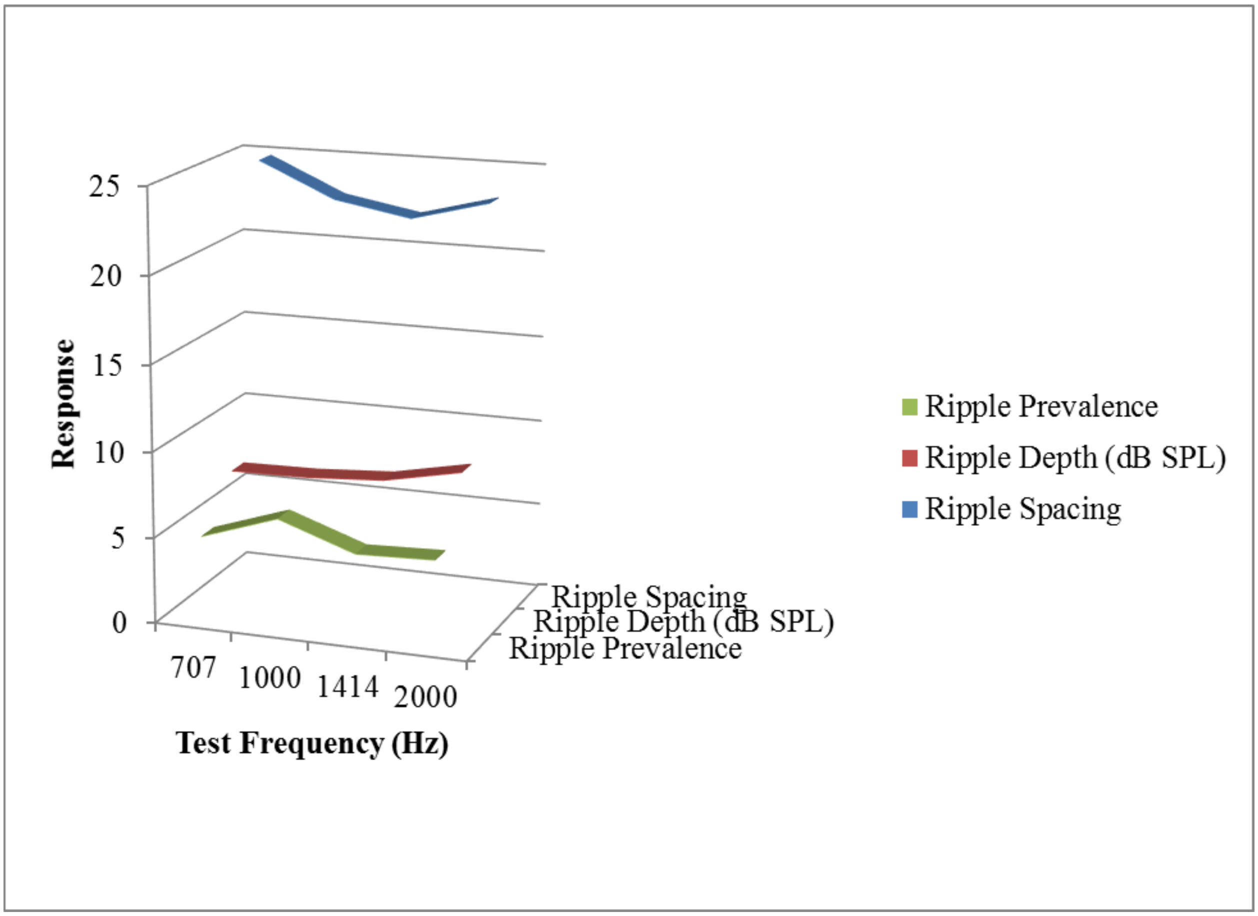


Figure 18. Frequency-by-ripple characteristic graphic.

Figure 18 shows the averaged values of each ripple characteristic plotted by frequency. As the ripple characteristics from Table 24 were significantly different from each other, further post-hoc testing was completed on each characteristic within the frequency domain (Tables 25-27).

Table 25. Post-hoc comparisons of ripple spacing for test frequency pairs.

Frequency Pair		*Mean Difference*	*Standard Error*	*p*
707	1000	1.984	1.007	.366
	1414	2.775	1.330	.289
	2000	1.603	1.284	1.000
1000	1414	.791	1.088	1.000
	2000	-.381	1.141	1.000
1414	2000	-1.172	1.167	1.000

$p \leq .0083$

Table 26. Post-hoc comparisons of ripple depth for test frequency pairs.

Frequency Pair		*Mean Difference*	*Standard Error*	*p*
707	1000	-.077	.421	1.000
	1414	-.367	.490	1.000
	2000	-1.287	.650	.359
1000	1414	-.290	.484	1.000
	2000	-1.211	.553	.233
1414	2000	-.921	.579	.753

$p \leq .0083$

Table 27. Post-hoc comparisons of ripple prevalence for test frequency pairs.

Frequency Pair		*Mean Difference*	*Standard Error*	*p*
707	1000	-1.521	.249	.0009*
	1414	.021	.256	1.000
	2000	-.146	.277	1.000
1000	1414	1.542	.287	.0009*
	2000	1.375	.297	.001*
1414	2000	.167	.291	1.000

$p \leq .0083$

Bonferroni corrections were applied to the test frequency data for ripple spacing, depth, and prevalence. There were no significant differences between frequency pairs for ripple spacing and depth (Tables 25-26). However, significant differences exist for ripple prevalence (Table 27). For $p \leq .0083$, the 707-1000 Hz, 1000-1414 Hz, and 1000-2000 Hz pairs showed significant differences. Essentially, the difference between each test frequency had a significant effect on ripple prevalence.

4.5 COEFFICIENTS OF VARIATION

As described in Section 3.8.4 the coefficient of variation is a standardized measure of variability. In this case, the variable of measurement was response magnitude. A two-way ANOVA (DP-combination x frequency) was run to determine effects and interactions that could occur between the combination and frequency (Table 28). The coefficients were calculated within Excel and compared across DP-combination per frequency using the Statistical Package for Social Sciences (SPSS™).

Table 28. Two-way ANOVA for coefficients of variation.

Source	*df*	*Mean Square*	*F*	*Effect Size*	*p*
DP-combination (DP)	2.187	.250	14.527	.387	.0009*
Error	50.307	.017			
Frequency (F)	1.264	.110	2.351	.093	.130
Error	29.079	.047			
DP x F	2.106	.120	2.191	.087	.120
Error	48.439	.055			

*$p \leq .05$

Table 29. Average coefficients of variation for the four combinations and test frequencies (f2) for n = 24.

DP-Gram	Test Frequency (Hz, f2)			
	707	1000	1414	2000
A	32.7	29.1	25.2	21.7
B	34.4	32.4	35.3	34.5
C	45.3	35.3	35.1	34.1
D	31.0	29.6	30.9	34.0

Table 30. Post hoc comparisons of coefficient of variation for combinations.

Combination Pairs		*Mean Difference*	*Standard Error*	*p*
A	B	-.070	.014	.0009*
	C	-.103	.015	.0009*
	D	-.042	.017	.141
B	C	-.033	.016	.277
	D	.028	.012	.182
C	D	.061	.021	.052

*$p \leq .0083$.

The two-way ANOVA (Table 28) showed significant differences between combinations, but no frequency effect or interaction were evident. The Bonferroni-corrected post-hoc testing compared the combinations and showed significant differences for Combinations A and B and A and C (mean difference = -.070 for Combinations A and B; mean difference = -.103 for Combinations A and C), respectively. Combination A was the least variant of the combinations followed by Combination D, then B and C.

5.0 DISCUSSION

The results of this study confirmed and expanded on what is known about the 2f1-f2 and 2f2-f1 DPOAE components and their dominant source(s). Briefly, the results from this study affirmed that the 2f1-f2 component may be dominated by either the distortion or reflection source depending on the chosen parameters and that the 2f1-f2 component has a larger magnitude response with mid-range test frequencies (*i.e.*, 1414 and 2000 Hz), whereas the 2f2-f1 component has a larger magnitude response with lower test frequencies (*i.e.*, 707 and 1000 Hz). Similar results have been revealed by other research studies, thus by comparison serving to validate the present study and its findings. More importantly, the current study expanded what is known about the 2f2-f1 component, extent of its domination by the reflection source, and thus by what type of mechanism(s) it is created.

The new data reinforced the two-source/two-mechanism model developed by Shera and Guinan (1999) in general concept in that the 2f1-f2 component was dominated by the distortion source in certain conditions with the distortion source occurring near the f2 place and the reflection source near the Fdp place. Yet, these workers did not include the 2f2-f1 component. Wilson and Lutman (2006) developed an expansion of Shera and Guinan's model, included the 2f2-f1 component, and suggested that this component may derive from two sources like the 2f1-f2 component. However, their data did not settle the issue of 2f2-f1 sources, so further study was needed. The current study expanded upon these two models by determining what parameters allowed for one source (and mechanism) to dominate the 2f2-f1 component. From the results of the current study it is believed that the 2f2-f1 component is entirely reflection-source dominated, but also requires refinement of the model to accommodate such results and conclusion.

5.1 TEST COMBINATIONS AND SOURCE DOMINANCE

It was predicted that the 2f1-f2 component measured with the parameters in Combination A would be distortion-source dominated as the result of the nonlinear mechanism of the cochlear partition, whereas the 2f1-f2 and 2f2-f2 components measured with the parameters in Combinations B, C, and D were predicted to be reflection-source dominated as the result of the linear mechanism (*i.e*., reflected waves, Table 8). These predictions proved to be essentially true. Combinations A and D showed 100% distortion-source and reflection-source dominance, respectively, whereas Combinations B and C demonstrated only 67% reflection-source dominance (Table 9).

Combination A represents the 2f1-f2 DPOAE component used in many research laboratories and as the default stimulus parameter combination in clinical settings. The decision to use this parameter combination to optimize presumably the 2f1-f2 component, was based on results of other researchers (e.g., Harris *et al*., 1989; Kummer *et al*., 1998). Previous studies of 2f1-f2 fine structure have shown 100% distortion-source dominance as was measured in this study (Shera & Guinan, 1999; Wilson & Lutman, 2006). As Combination A results were similar to the results of previous studies it is possible to extrapolate that the mechanism that produced these results was the same mechanism as seen in Shera and Guinan’s and Wilson and Lutman’s studies. To clarify, the 2f1-f2 component with the parameter combination A resulted from the mixing of the backward traveling waves arising from the f2 and Fdp places on the cochlear partition resulting in the dominance of the distortion source.

The 2f1-f2 DP with Combination A showed its largest response magnitudes at the higher test frequencies used in the study (1414 and 2000 Hz). This result was expected as the 2f1-f2 DP component is strongest in the mid-frequency range (Keefe, 2007). The response magnitudes of 2f2-f1 component with Combination B at 707 and 1000 Hz were larger, though not significantly, than those measured for 2f1-f2 with Combination A. The complete success in recording 2f2-f1 in this study was thanks to enhanced magnitudes of the 2f2-f1 component under Combination B (given optimal/near optimal parameters) and better extraction techniques for signals (Gorga *et al.*, 2000). The 2f1-f2 and 2f2-f1 components measured with Combinations A and B, respectively, thus reflect, per most broadly accepted theories presently, different physiological-acoustic mechanisms of the cochlear partition (nonlinear and linear mechanisms, respectively). At the higher test frequencies (*i.e.*, 1414 and 2000 Hz), there was a significant difference in response magnitude between the distortion and reflection sources when using parameters that best elicit the 2f1-f2 component supporting the alternative hypothesis presented with Question 1a.

For measuring the 2f2-f1 component, parameters of Combination D were chosen to represent the putative "ideal" or "optimal" 2f2-f1 test parameters based on far more limited numbers of previous research studies, and in particular in deference to the results of Erminy *et al.*, 1998, Fitzgerald & Prieve, 2005, and Horn *et al.*, 2008. The 2f2-f1 component measured with this combination has larger magnitude responses than the 2f1-f2 component measured using Combination A at 707 and 1000 Hz. This result shows that the 2f2-f1 component can have larger magnitude responses than the 2f1-f2 component due to the improved recording of 2f2-f1 at low test frequencies, making the 2f2-f1 component ideal for clinical interest (Gorga *et al*., 2000). Indeed, the larger response-magnitude of 2f2-f1 using Combination D over the 2f1-f2 component using Combination C at all test frequencies indicated that the 2f2-f1 component can be more robust than the 2f1-f2 component. Therefore, the results of this study suggested that there is an ideal or nearly ideal parameter combination for the 2f2-f1 DP component, as in the case of 2f1-f2, but it differs from that of the 2f1-f2 component. Likely the 2f2-f1 component benefitted from the occurrence of the cochlear inhomogeneities before the nonlinear distortion mechanism and the close proximity and overlap of the two primary tones due to the use of the smaller 1.08 frequency ratio. However, as both Combinations C and D are dominated by the reflection source (and derived from the linear mechanism), a difference in response magnitude did not exist between distortion and reflection sources. As such, the null hypothesis of Question 1b cannot be rejected.

However, the predictions of source dominance for 2f2-f1 versus 2f1-f2 using Combinations B and C, respectively, were not as compelling, showing only 67% reflection-source dominance. Reasons for incomplete reflection-source dominance of these combinations may relate to several issues including individual variance and non-optimized frequency ratios. Although the literature suggested idealized expectations for complete reflection-dominance of 2f2-f1 and 2f2-f1 using Combinations B and C (respectively), human research reflects a realistic outcome in which there are variances within each participant and external factors that may affect the dominance of a particular source. There may be variance in outer and middle ear anatomy that affects stimulus presentation or recording and/or variance in inner ear anatomy and physiology that affect the generation and the multi-path-like effects of the backward traveling waves and, therefore, the dominant source of the DP.

Regarding effects of non-optimized frequency ratios, the natural variability of the human cochlear partition raises the quandary of whether a frequency-ratio tuning function should be plotted for each test frequency for each participant. Harris *et al.* (1989) found that the 1.22 frequency ratio was ideal for recording DPOAEs and this parameter was then adopted into clinical practice. However, frequency-ratio tuning-function studies have shown variability in this parameter (Harris *et al*., 1989). Vento, Durrant, Sabo, and Boston (2004) tested young adults aged 18-25 years and found maxima of the frequency ratios of 1.203-1.248 depending on test frequency. Their adults had hearing < 15 dB HL, similar to participants in the current study.

Even the 1.08 frequency ratio may not be precisely optimal for all participants from whom the 2f2-f1 component was recorded. The study from Horn *et al.* (2008) showed ratios of 1.04 and 1.08 were equally beneficial for eliciting 2f2-f1 data though the 1.08 frequency ratio has greater precedence in research, and thus adopted in this investigation. In order to choose optimized parameters for the 2f2-f1 component, a frequency-ratio tuning function would need to be assessed for each participant and perhaps with even higher numerical precision. In any event, this is a time-consuming process requiring further study.

Another issue is the need of (apropos the program employed in this study) calculation of these characteristics by hand, in turn potentially vulnerable to errors, although addressed here by way of having a secondary judge review a substantial subset of the data. Thus, further development of the software might have been beneficial and, in any event if made commercially available, could be useful in research and clinical work alike for the objective assessment of ripple characteristics.

These then were possible limitations of the present study. Nevertheless, participants, test parameters, test equipment, and software were selected from the methodology of more experienced researchers within the field of DPOAEs. Despite possible limitations on 2f2-f1 and 2f1-f2 components using Combinations B and C (respectively), the effective dominance of the linear mechanism and the reflection source exists, as well reflected in the results using these methods.

5.2 RIPPLE CHARACTERISTICS

When comparing the 2f1-f2 component using parameter Combinations A and C (respectively), 2f1-f2 with Combination C showed peaks with wider spacing and greater depth, but not greater prevalence. The ripple characteristics should be more prominent with 2f1-f2 using Combination C as it is a set of parameters promoting reflection source dominance presumably deriving from inhomogeneities, eliciting backward traveling waves. The resulting DPs are thus expected to be inherently more sensitive to changes in phase, thus creating ripples seen in a fine-structure recording. So, the test combination most affected by the reflection source, due to inhomogeneities and rapid phase changes should dominate all of the descriptors (*i.e.*, the ripple characteristics) of the fine-structure recording. However, the effects of using Combination A showed significantly greater ripple prevalence than using Combination C. Likely the increased prevalence from Combination A was due to the robustness of the nonlinear mechanism within the cochlear partition. Another possible explanation comes from Johnson and colleagues (Johnson, Neely, Kopun & Gorga, 2006) who measured 2f1-f2 fine structure in seven participants with excellent hearing (thresholds ≤10 dB HL) at 2000 and 4000 Hz test frequencies. They found greater prevalence of fine structure at 2000 Hz than 4000 Hz. Extrapolating from their data it could be assumed that the fine structure prevalence, and therefore ripple prevalence, would increase with even lower test frequencies (*i.e.*, 1414 Hz). The 2f1-f2 component showed more robust responses at 1414 and 2000 Hz, increasing the likelihood of greater prevalence, and thereby supporting the results of the current study.

Although the three ripple characteristics are needed to describe comprehensively a fine-structure DP-gram, it may be argued that the most important ripple characteristic is depth. Ripple depth is one way to determine if the cochlear partition has been compromised because it becomes shallower due to any number of anatomical deformities or physiological dysfunctions. This effect is suggested by two studies about Connexin-26 (Cx26) mutations from Engel-Yeger and colleagues (2002, 2003). In brief review, a Cx26 mutation results in the inability of cells within the inner ear to communicate to each other in the form of preventing gap junctions from occurring. The intercellular miscommunication prevents the redistribution of potassium throughout the inner ear. It is hypothesized that Cx26-mediated gap junctions, when normally functioning, redistribute potassium so that the sensory hair cells do not lose sensitivity (Bruzzone, White, & Paul, 1996b; Forge *et al*., 2002; Forge & Wright, 2002).

Engel-Yeger *et al*. (2002) studied a large population of people with Cx26-related hearing loss and carrier status in an isolated Israeli Arab village in the Galilee. They tested 56 individuals (age 10-80 years) from families with deaf individuals. The participants were divided into carrier, non-carrier, and affected groups. All participants had behavioral threshold testing (octaves from 250-8000 Hz) and DPOAE testing (f2=1000-10000 Hz, L1=L2=65 dB SPL, f2/f1=1.22). The individuals in the affected group almost always had profound hearing loss. Carriers and non-carriers had similar behavioral thresholds according to the authors. The DPOAEs were absent in the affected individuals as expected by the presence of profound hearing loss. The authors noted a significant difference in DPOAE response levels between carriers and non-carriers. Non-carriers had best responses between test frequencies of 1000 and 7000 Hz. Carriers had best responses between 1000 and 4000 Hz. The mean age of non-carriers was 27 years and the mean age of carriers was 38 years. The authors contended that age did not have a significant effect on DPOAE response levels, but carrier status did result in decreased response amplitudes and frequency response. They proposed that the reduced amplitude DPOAEs may signal the possibility of earlier deterioration of hearing in carriers, but the data supporting their hypothesis was weak.

In the 2003 study, Engel-Yeger and colleagues returned to the same Israeli Arab village. This time they tested 128 people (aged 3-80 years) from families with deaf individuals. The participants were split into three groups – carriers (n=65), non-carriers (n=24), and affected (n=39). All of the participants were tested for behavioral thresholds (for octaves 250-8000 Hz), speech recognition testing, DPOAEs (1000 to 10000 Hz, 65/55 dB SPL, 1.22). Once again carriers and non-carriers had similar behavioral thresholds within normal limits. However, DPOAE response levels were reduced in carriers as compared to non-carriers.

Although the researchers of these two studies did not use fine-structure DP-grams or measure ripple characteristics, the studies suggest reduced amplitude responses occur even in a population with normal hearing thresholds. It was described in the literature review that some damage to the cochlear partition may not affect greatly physiological function and contributes to the appearance of cochlear fine structure. However, too much damage to the cochlear partition could result in significantly reduced amplitude resulting in further reduction of ripple depth, and damage to the cochlear partition as may be gleaned from the Engel-Yeger studies, thereby making it the most important of the three characteristics from the perspective of the current study.

5.3 FURTHER REVISION OF THE MODEL OF DPOAE GENERATION

A new model was developed to describe the process by which both 2f1-f2 and 2f2-f1 components are created within the cochlear partition when elicited by selected primary tones (f1, f2; Figure 19). This new model included the generating mechanisms and places of generation for both the 2f1-f2 and 2f2-f1 components. To reiterate briefly, Shera and Guinan's model only considers the formation of the 2f1-f2 component. Wilson and Lutman's model considers the formation of the 2f2-f1 component and the inhomogeneities found on the cochlear partition. The proposed model incorporates all of these considerations while further emphasizing the tonotopic organization of the cochlear partition. It should be noted that the three models reflect both time and place domains with respect to the place-frequency mechanism, that is, a reminder that the energy of the sound is delivered ultimately by propagated waves and thus not instantaneously to all places accounting for timing differences between the distortion and reflection sources.

In this proposed model of DPOAE generation, the two stimuli (f2, f1) enter the outer and middle ears (represented by the rectangle), and enter the inner ear. The stimuli encounter the inhomogeneities (I) of the cochlear partition. The inhomogeneities add boundary conditions potentially adding to the linear mechanism of the cochlear partition contributing to the collective formation of the reflection source. From the reflection source, the energy from the two stimuli travels to the 2f2-f1 Fdp (R_{2f2}), and then travels apicalward to the 2f2-f1 f2 region (D_{2f2}). The energy from the 2f2-f1 distortion area (D_{2f2}) travels apicalward to the 2f1-f2 distortion area (D_{2f1}) and basalward to the oval window. The energy from the D_{2f1} region (*i.e.*, the f2 place on the cochlear partition) moves apicalward to the R_{2f1} Fdp region and basalward to the oval window as well. The basalward energy from R_{2f2}, D_{2f2}, D_{2f1}, and R_{2f1} mixes in the ear canal and can be measured with an ear-level probe.

In the proposed model, the reflection source at the 2f2-f1 Fdp (R_{2f2}) on the cochlear partition is encountered before the f2 place (D_{2f2}) for the 2f2-f1 DPOAE, based on tonotopic organization. As such, a greater amount of energy from the primary tones passes through the 2f2-f1 reflection (R_{2f2}) site thereby making the reflection source (and linear mechanism) the stronger of the two sources (mechanisms) for this DP component. This is unlike the Wilson and Lutman model in which the sources and mechanisms of both components occur in the same location of the cochlear partition. In addition, the point of maximal excitation for both primary tones (f1, f2) overlaps more in the 2f2-f1 region of the cochlear partition than in the 2f1-f2 region (R_{2f1}) especially with the use of smaller frequency ratios. These are two reasons for improved measurement of the 2f2-f1 component in the current study.

As for the 2f1-f2 component, it remains robust and distortion-source dominated (as described by the two previous models) for parameters including 65/55 dB SPL and f2/f1=1.22. One issue to consider is whether the f2 place of the 2f2-f1 component (D_{2f2}) contributes to the formation of the 2f1-f2 component. In keeping with both Shera and Guinan's and Wilson and Lutman's models, the distortion-source energy continues to move apicalward. If the energy from the D_{2f2} place moves apicalward then the possibility of its enhancing the energy at the D_{2f1} place must be considered.

See Table 31 for further comparison of the distinguishing characteristics of the Shera and Guinan (1999), Wilson and Lutman (2006), and the proposed model.

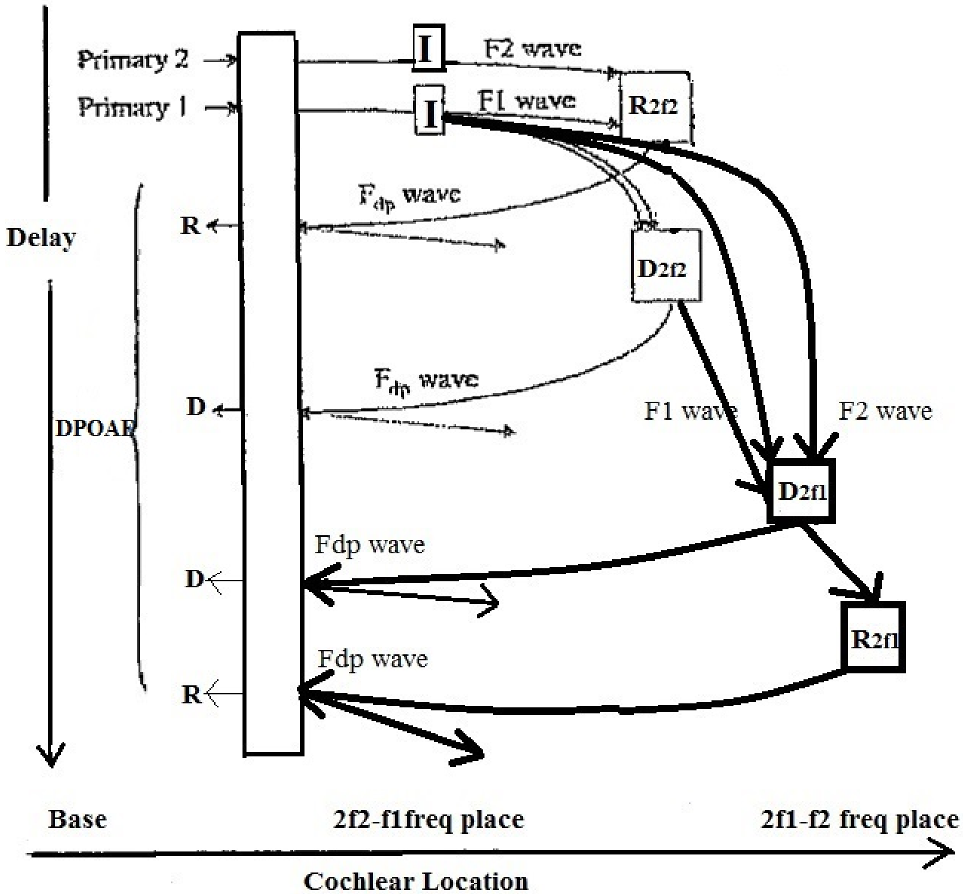


Figure 19. Model proposed by Horn. (I = inhomogeneities, R = reflection source, D = distortion source, Fdp = frequency of the distortion product).

Table 31. Comparison of DP generation models.

Characteristics	Model		
	Shera & Guinan (1999)	**Wilson & Lutman (2006)**	**Horn (2015)**
Stimulus input	2 traveling waves (f1, f2)	2 traveling waves	2 traveling waves
Accounted for cochlear inhomogeneities	No	Yes	Yes
1st mechanism (source)	Nonlinear distortion (D)	Nonlinear Distortion (D)	Linear reflection (R_{2f2})
Direction Fdp wave traveled	Forward and backward	Forward and backward	Backward
2nd mechanism (source)	Linear reflection (R)	Linear reflection (R)	Nonlinear distortion (D_{2f2})
Direction Fdp wave traveled	Backward	Backward	Forward and backward
3rd mechanism (source)			Nonlinear distortion (D_{2f1})
Direction Fdp wave traveled			Forward and backward
4th mechanism (source)			Linear reflection (R_{2f1})
Direction Fdp wave traveled			Backward
DP examined	2f1-f2	2f1-f2 2f2-f1	2f1-f2 2f2-f1
Notes	Did not account for 2f2-f1 DP	Did not account for tonotopic organization	Accounts for tonotopic organization

5.4 HOW DO THE DATA RELATE TO THE PROPOSED MODEL

Previous research focused primarily on how to maximize the 2f2-f1 component and its likely source (Fitzgerald & Prieve, 2005; Horn *et al*., 2008; Wilson & Lutman, 2006). However, no prior study had offered a comprehensive model that represented the formation of this component in the inner ear. It is contended that the author is the first to offer a comprehensive model, namely inclusive of the actual formation of the 2f1-f2 component in the inner ear. The data collected and analyzed for this study were consistent with the previous two models, yet revealed incomplete reflection-source dominance, unexpected in the test conditions. Differences seen between the Wilson and Lutman and the current model are attributed to the complete dominance of the distortion and reflections sources for parameter Combinations A and D. Therefore, the description of the linear mechanism (reflection source) occurring before the nonlinear mechanism (distortion source) in the proposed model is correct. This occurrence is attributed to tonotopic organization of the cochlear partition, i.e. events again happening in both time and space. A review of the three models and how the data support them is found in Table 32.

Table 32. Do the data support Shera & Guinan (1999), Wilson & Lutman (2006), and proposed models?

<table>
<tr><td rowspan="2">Question</td><td colspan="6">Model</td></tr>
<tr><td>Shera & Guinan (1999)</td><td>Wilson & Lutman (2006)</td><td colspan="4">Proposed Model (2015)</td></tr>
<tr><td>Does data support model?</td><td>Yes</td><td>Yes</td><td colspan="4">Yes</td></tr>
<tr><td>How?</td><td>Energy from backward traveling waves generated from the f2 place dominates the 2f1-f2 component.</td><td>Energy from backward traveling waves generated from the f2 place dominates both the 2f1-f2 and 2f2-f1 components. Addition of inhomogeneities helped to form linear mechanism.</td><td colspan="4">Energy from backward traveling waves generated from the f2 place dominates the 2f1-f2 component. Energy from backward traveling waves generated from the DP place dominates the 2f2-f1 component. Addition of inhomogeneities helped to form the linear mechanism. Placing 2f2-f1 reflection source first enhanced the 2f2-f1 DP responses.</td></tr>
<tr><td rowspan="2">Does data support proposed alternate hypotheses of the current study?</td><td rowspan="2">N/A</td><td rowspan="2">N/A</td><td>A</td><td>B</td><td>C</td><td>D</td></tr>
<tr><td>Y</td><td>N/Y*</td><td>N/Y*</td><td>Y</td></tr>
<tr><td rowspan="2">Does data support proposed questions of the current study?</td><td rowspan="2">N/A</td><td rowspan="2">N/A</td><td>A</td><td>B</td><td>C</td><td>D</td></tr>
<tr><td>1a/2a</td><td>1a/2b*</td><td>1b/2a*</td><td>1b/2b</td></tr>
</table>

* Respectively.

Other evidence to support the proposed model includes inhomogeneities on the cochlear partition by inference. Inhomogeneities were considered by Wilson and Lutman's in their model, but not by Shera and Guinan. Likely effects of such inhomogeneities may be observed in the Residual line of the NIPR graph (Appendix B; the level by frequency plot). That line is virtually a map of the inhomogeneities of an individual's cochlear partition. The peaks and troughs observed in the fine structure recording of the cochlear partition are indicative of their presence and the need for their inclusion in any model of the cochlea.

Although the exact locations of 2f2-f1 generation sites cannot be determined without invasive procedures, it is possible to determine that this component comes from a different location on the cochlear partition and dominance(s) different than that of 2f1-f2, hence different parameters needed to provide optimal response. As the 2f1-f2 and 2f2-f1 components arise from different locations on the cochlear partition, they provide information about different areas of the cochlear partition.

5.5 CONCLUSIONS

The consistency of results across the three DPOAE generation models encourages the acceptance of the proposed model. From a perspective of elaboration, rather than contradiction, the current model accounts better for the generation process of upper sideband DPOAEs, such as 2f2-f1, accounting for their presence and the mechanisms by which they are generated. The proposed model may be tested further through more in-depth study in humans, particularly by way of frequency-ratio tuning functions.

The 2f1-f2 component remains the most robust and least variable when measured with a frequency ratio of 1.22 and stimulus levels of 65/55 dB SPL, but 2f2-f1 DPOAE components were found to be a worthy measure of cochlear-partition function at low test frequencies and provides information regarding aspects of the cochlear partition not measured by 2f1-f2 components. As the 2f1-f2 and 2f2-f1 components can be measured simultaneously and 2f2-f1 is recorded with superior SNRs to that of the 2f1-f2, they should be considered equally necessary for answering questions regarding cochlear anatomy, function, and health. The 2f2-f1 component may be useful especially in people with normal hearing in the low-frequency range with precipitously sloping sensory hearing loss in the higher frequencies.

Lastly, the results are taken to warrant future studies of 2f2-f1. (1) Are the 2f1-f2 and 2f2-f1 components equally susceptible to damage to the inner ear? (2) Does the etiology of this damage affect the components differently, *e.g.*, ototoxic drugs vs. genetic anomalies? (3) If sensitive down to defects at the molecular genetic level, might the 2f2-f1 component show a reduced amplitude response, for example, in Cx26 carriers as is seen with the 2f1-f2 component or show more-or-less sensitive response to the 2f1-f2 component?

APPENDIX A

PERSONAL INFORMATION SHEET

Participant ID: ____

Participant's Name: ____

Address: ____

Phone Number: ____

Email Address: ____

Date of Birth: ____

****

Do you have a history of middle ear infections? **Yes** **No**

Do or did you have pressure equalization tubes? **Yes** **No**

Do you have a history of other ear surgeries? **Yes** **No**

If yes, please list: ____

Have you had a hearing screening before (through school or a doctor)?

Yes **No**

What was the outcome of that screening? ________________________________

****

Do you have a history of noise exposure? **Yes** **No**

If yes, please list types of noise: ________________________________

(Examples of noise exposure include: Music, construction, shooting, factory work.)

APPENDIX B

THE NIPR PROCESS

After recording the 2f1-f2 and 2f2-f1 components, the DPOAE levels and phases from the frequency data were converted into the time domain using the IFFT. First, the test frequencies were zeroed out so that the 707-2000 Hz test range for this study became 0-1293 Hz. Then phase was ‘unwrapped’ by “adding or subtracting multiples of 360 degrees as to minimize adjacent phase steps” (Knight & Kemp, 2000, p. 461; Parazzini *et al.*, 2005, p.71-72). Essentially the unwrapping process allowed for less extreme jumps between neighboring frequencies. The unwrapping occurred in small frequency windows of 150 Hz with a 50 Hz overlap. The width of 150 Hz was chosen for each analysis window to countermand irregular spacing of DPOAE frequencies combined with a round-off error resulting in the introduction of a substantial amount of phase noise. Lastly, the frequency data were scaled or “linearized” because the cochlear frequency scale interferes with the time domain if a logarithmic frequency scale is not used to diminish its effects. As described by Knight and Kemp (2001) “an exponential frequency spacing was adopted in order to linearize the underlying curve in the phase versus frequency relationship of the [reflection source] DPOAE” (p. 1515). The result of this linearization process is multiple peaks in the time domain instead of the distortion and reflection peaks appearing as part of one large peak.

The NIPR program then stacks those multiple peaks and returns the data to the frequency domain with an FFT conversion so that level and phase were plotted. These processes result in the graphs as seen in Figures 20-21 – Frequency-by-delay and level-by-frequency.

The NIPR program then stacks those multiple peaks and returns the data to the frequency domain with an FFT conversion so that level and phase were plotted. These processes result in the graphs as seen in Figures 20-21 – Frequency-by-delay and level-by-frequency.

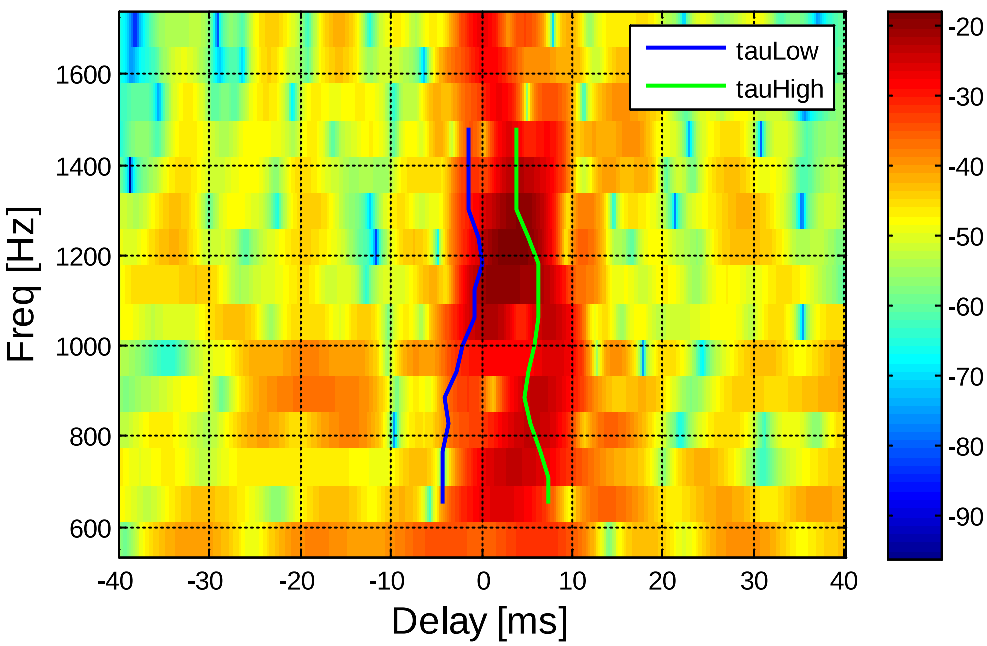


Figure 20. Frequency-by-delay plot.

In Figure 20 is, in effect, three-dimensional, wherein delay is represented by color in this two-dimensional display. The red (or darker) “band” in the center of the plot is representative of the maximum phase delay. The length of that delay is expressed on a color scale with red signifying shorter delays moving to blues signifying longer delays. The tauLow and tauHigh lines represent the filter settings, which may be adjusted to narrow the search band to account for step-size differences within these data. These settings were most commonly used to filter out the Nonlinear (NL) aspect of the source and results in the "Cleaned" or filtered data represented by the pink line (dashed line) in Figures 11-13. All fine-structure spectra were analyzed first using the default tau = $\pm$0.004 seconds. Those spectra that did not result in obvious source dominance were analyzed again using tau = $\pm$0.002 seconds to provide clarification of source dominance. Twenty-one of 96 (21.9%) spectra were re-analyzed using the $\pm$0.002 seconds parameter.

Figure 21 represents a "zeroed out" DP-gram using data from a participant with poor response magnitudes. Zeroing out a DP-gram takes the actual test frequencies of 707-2000 Hz and converts them, again, into relative frequencies of 0-1293 Hz. The DP-gram below shows the input data, the filtered input data, the NL or distortion source, and the linear or reflection source. Most remarkable is the smoothness of the nonlinear source. The reflection source is created partially by the inhomogeneities of the cochlear partition lending to the rippled manner of the fine-structure DP-gram.

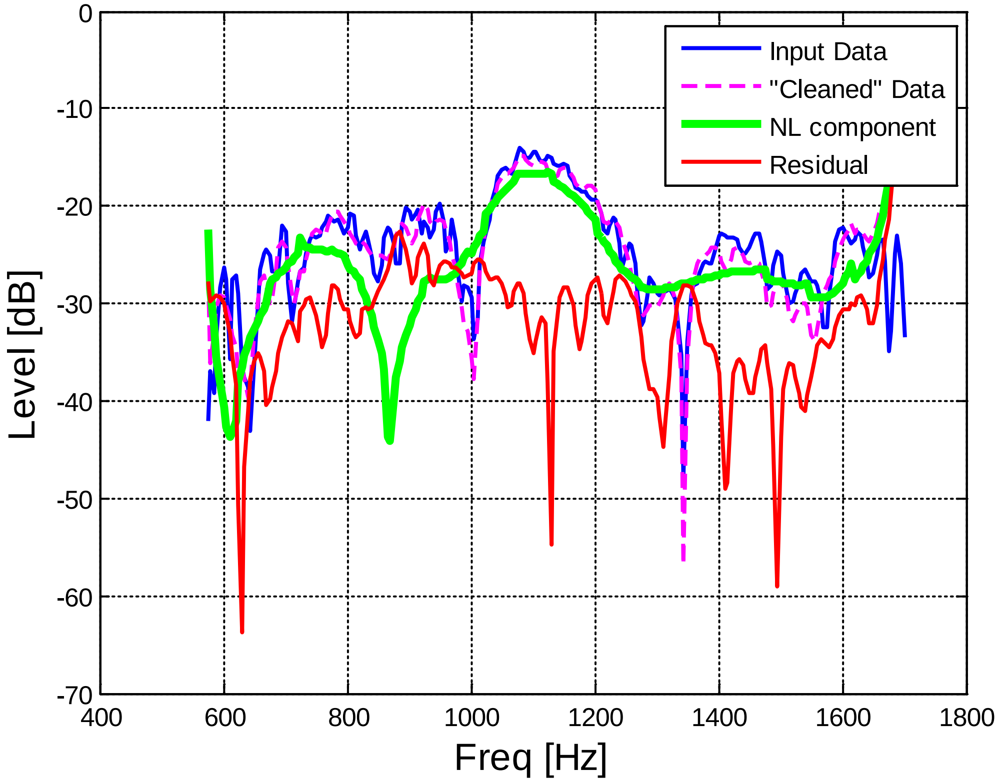


Figure 21. Level by frequency plot (a "zeroed out" DP-gram) for 2f1-f2 with 65/55 dB SPL and f2/f1=1.22.

Once the data has been zeroed out (as such), a third graph may be utilized to determine the dominant source for each spectrum within each combination, as seen in Figures 10-12.

APPENDIX C

AVERAGED RESPONSE MAGNITUDE MEANS AND STANDARD DEVIATIONS FOR EACH COMBINATION IN 1/3-OCTAVE FREQUENCY RANGE

Combo A	Means				SDs			
	Frequency				Frequency			
Participant	2000	1414	1000	707	2000	1414	1000	707
1	12.92	11.51	11.73	9.35	3.14	3.24	3.05	2.53
2	19.21	18.21	13.32	9.72	2.74	2.51	3.59	3.15
3	16.96	12.45	8.46	4.69	3.96	6.35	2.94	4.80
4	16.01	10.89	6.26	5.80	4.89	6.04	3.74	5.08
5	13.55	11.46	6.63	6.62	4.05	3.30	2.43	1.89
6	11.83	8.21	5.60	5.49	4.03	3.28	1.92	1.77
7	11.11	14.16	11.60	9.19	4.72	3.72	3.84	2.84
8	20.00	19.38	13.86	13.47	3.28	2.56	2.47	2.33
9	14.18	11.14	8.04	7.27	4.25	3.83	3.14	2.25
10	19.94	19.23	13.95	12.09	2.85	3.77	2.63	2.36
11	19.69	21.18	14.08	8.49	3.00	1.99	4.35	3.06
12	21.85	20.81	17.89	15.15	2.11	2.72	2.89	2.82
13	14.94	13.51	10.77	7.40	3.35	2.28	3.26	3.18
14	20.37	19.86	14.68	8.02	3.08	2.82	4.88	2.79
15	24.38	22.08	17.16	10.88	3.53	2.32	4.05	3.90
16	18.11	13.13	12.21	15.73	3.55	4.96	3.82	2.24
17	20.16	19.25	16.84	14.91	4.41	4.12	2.40	2.82
18	23.93	21.94	15.88	12.24	2.86	4.50	3.69	2.65
19	17.39	13.26	8.78	8.12	3.84	4.78	2.40	2.57
20	19.58	18.38	16.76	18.34	3.64	5.04	2.87	1.99
21	14.97	14.75	7.32	7.37	3.36	4.21	2.79	3.10
22	27.25	26.86	21.10	20.47	2.62	2.99	2.45	1.61
23	16.28	18.58	14.15	10.36	3.23	3.49	5.03	2.63
24	12.31	14.21	7.92	7.11	4.84	4.11	3.08	2.46

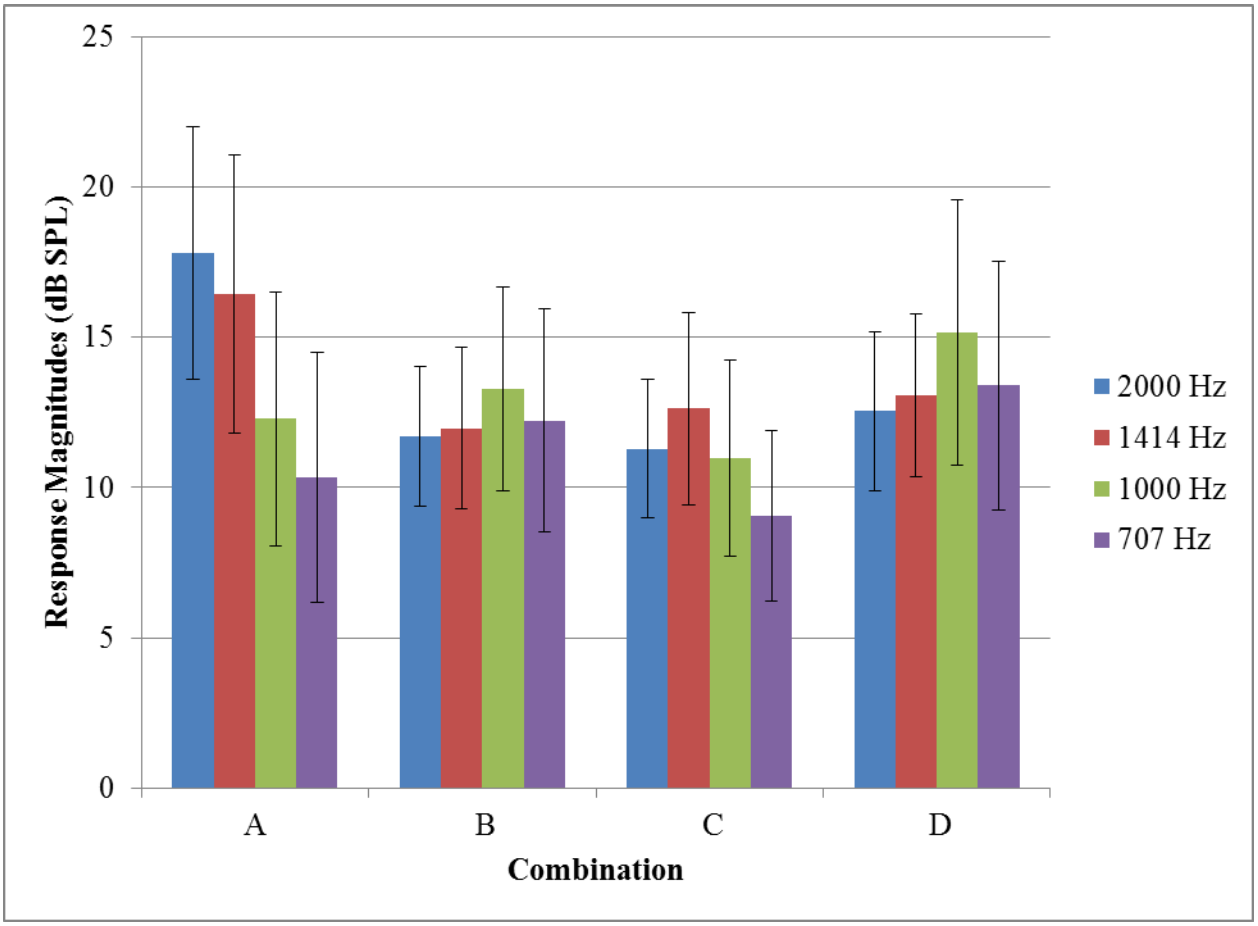
Combo B	Means				SDs			
	Frequency				Frequency			
Participant	2000	1414	1000	707	2000	1414	1000	707
1	12.58	12.34	12.94	10.32	3.54	3.55	4.11	2.97
2	12.15	12.70	14.43	10.16	3.53	2.84	4.55	3.51
3	10.89	9.63	13.19	9.77	4.37	6.01	5.86	4.99
4	10.02	9.47	12.16	7.56	4.35	5.54	5.96	5.92
5	8.61	9.55	9.82	8.75	3.03	3.29	4.51	3.57
6	11.02	10.75	10.75	8.03	3.36	3.71	3.21	2.59
7	10.86	9.36	9.61	8.21	3.99	3.24	3.63	3.22
8	10.34	10.89	13.16	14.85	3.41	3.49	4.67	3.92
9	11.54	12.78	13.50	9.19	4.13	4.25	4.62	4.79
10	10.53	12.16	13.99	15.00	3.89	4.59	4.82	3.40
11	13.08	11.40	11.23	16.19	5.67	4.80	5.18	3.60
12	9.43	8.97	8.77	14.99	3.82	3.84	3.78	4.29
13	12.61	12.02	13.02	11.87	4.21	3.76	3.00	3.70
14	10.83	10.91	18.30	14.57	4.05	4.46	4.27	4.67
15	19.10	21.52	20.12	15.97	5.00	2.80	3.46	3.94
16	12.25	13.67	12.39	7.65	4.02	4.26	4.34	2.66
17	15.04	15.76	14.95	15.38	3.88	4.93	5.45	6.59
18	13.39	11.91	15.61	21.62	5.26	4.46	5.59	1.43
19	9.83	10.41	14.18	10.34	3.86	4.37	4.54	3.87
20	10.32	10.99	11.32	10.37	3.81	3.72	3.29	2.50
21	11.78	12.50	9.80	10.25	4.44	4.24	4.03	3.70
22	15.55	15.54	22.52	17.58	4.65	3.64	3.34	8.69
23	9.47	11.02	14.13	14.46	4.11	4.76	3.78	3.03
24	9.91	10.92	8.72	10.22	3.58	2.84	2.64	2.90

Combo C	Means				SDs			
	Frequency				Frequency			
Participant	2000	1414	1000	707	2000	1414	1000	707
1	13.16	12.38	6.20	5.65	3.43	3.11	2.13	1.92
2	13.92	13.96	10.21	12.04	3.72	4.73	3.70	4.02
3	10.65	13.53	10.33	4.79	5.40	6.07	3.62	5.83
4	8.78	11.23	10.59	3.85	5.07	6.76	2.31	7.69
5	8.74	8.71	7.47	6.28	2.64	3.38	2.76	2.14
6	10.24	8.87	7.31	6.68	2.86	2.27	3.33	2.46
7	8.79	8.48	5.95	7.80	3.02	2.86	2.28	3.18
8	11.90	13.08	12.21	11.31	3.07	3.54	3.56	2.38
9	8.48	11.13	7.31	7.94	2.44	4.40	2.90	2.36
10	12.65	13.20	12.84	11.77	4.47	5.20	3.02	2.68
11	12.27	15.31	15.72	9.98	3.97	4.98	4.64	4.54
12	10.87	13.04	12.65	9.57	3.52	3.93	5.46	4.08
13	9.62	11.47	7.35	6.82	3.09	4.08	4.16	2.46
14	14.80	18.38	9.81	8.17	4.62	5.60	5.32	2.77
15	14.44	15.81	13.28	9.17	4.48	5.84	3.51	4.35
16	12.62	13.69	10.32	9.06	3.14	3.35	4.81	3.04
17	13.76	12.48	17.61	12.62	4.68	4.57	4.08	2.84
18	11.83	13.72	15.99	11.08	4.13	5.10	5.74	3.76
19	9.92	13.81	10.78	8.58	4.80	5.53	3.21	3.35
20	8.55	12.21	13.74	16.48	2.93	5.14	5.25	3.29
21	8.48	8.21	9.33	8.85	2.77	2.29	3.15	2.61
22	16.15	21.46	14.96	12.05	5.36	6.37	4.97	4.02
23	11.85	11.72	12.84	8.64	4.23	3.79	3.40	4.47
24	8.73	7.33	8.44	8.25	3.32	2.97	2.57	3.51

Combo D	Means				SDs			
	Frequency				Frequency			
Participant	2000	1414	1000	707	2000	1414	1000	707
1	14.49	14.37	12.65	10.03	3.65	3.91	3.59	2.91
2	13.39	16.77	14.73	11.03	4.30	3.76	4.16	3.81
3	9.49	11.48	15.71	12.04	5.52	4.87	5.90	3.28
4	8.97	11.30	15.19	12.63	5.11	4.06	5.54	3.55
5	9.03	9.66	12.13	8.98	3.62	4.19	4.17	3.84
6	11.92	13.29	8.71	8.18	4.17	3.89	2.69	2.89
7	11.35	10.86	10.16	10.16	3.77	3.19	3.42	2.63
8	11.13	12.69	17.10	16.90	4.22	4.22	3.50	3.41
9	13.06	13.13	12.47	9.16	3.93	2.89	5.22	3.73
10	13.33	14.10	13.94	15.75	3.39	4.30	3.05	2.67
11	13.90	12.30	20.80	19.93	4.25	4.93	3.35	5.09
12	10.03	12.10	17.84	14.65	3.99	3.85	3.21	4.13
13	14.51	10.51	14.44	12.04	4.77	3.81	4.62	4.07
14	12.53	16.32	21.15	12.56	3.33	4.84	5.75	5.00
15	18.40	17.63	19.68	18.20	4.03	5.65	4.47	4.18
16	14.21	15.93	11.60	9.99	4.43	2.69	2.96	3.18
17	15.50	15.71	20.87	23.30	4.61	4.80	6.19	3.37
18	13.90	11.75	21.27	21.08	5.30	3.62	4.40	5.96
19	10.51	11.26	16.05	12.55	2.94	3.15	4.52	3.35
20	11.03	11.66	11.40	13.20	3.26	3.61	3.83	3.91
21	10.91	10.14	10.94	12.13	4.31	3.50	4.67	4.99
22	18.19	18.76	24.23	12.47	4.67	3.55	6.85	7.38
23	12.78	13.79	13.57	16.71	4.06	3.41	4.16	3.16
24	8.42	8.04	7.62	7.89	3.03	3.31	3.20	3.33

APPENDIX D

AVERAGE SIGNAL-TO-NOISE RATIOS ACROSS ALL COMBINATIONS



APPENDIX E

AVERAGED RIPPLE SPACING

Combo A	Frequency			
Participants	2000	1414	1000	707
1	20.19	17.68	18.07	18.98
2	16.96	30.12	26.58	23.19
3	18.32	21.53	28.13	31.83
4	16.80	26.13	28.34	29.83
5	23.62	26.50	35.49	27.04
6	22.97	22.06	27.37	32.87
7	26.68	25.29	25.53	21.21
8	26.87	17.83	21.56	22.47
9	21.56	24.25	28.10	26.57
10	24.54	18.20	24.45	38.52
11	17.31	18.42	23.31	19.39
12	23.82	18.05	27.88	26.13
13	15.34	14.64	32.78	43.06
14	27.99	25.27	28.14	26.89
15	25.27	24.65	24.19	22.51
16	34.16	26.34	29.35	20.22
17	20.89	24.73	21.44	30.96
18	7.72	14.47	17.52	23.55
19	22.07	33.41	22.26	26.96
20	17.66	33.92	20.52	25.77
21	24.36	23.02	29.08	41.01
22	24.98	22.11	13.63	30.98
23	24.80	21.79	27.46	26.07
24	27.73	26.73	33.58	36.42

Combo B	Frequency			
Participants	2000	1414	1000	707
1	17.70	22.92	25.83	27.45
2	29.83	18.41	22.55	34.84
3	17.48	12.45	8.10	16.88
4	24.59	13.16	13.23	22.10
5	27.42	29.28	26.09	22.02
6	19.80	14.47	18.32	26.41
7	22.01	22.42	29.43	28.31
8	23.09	23.46	24.76	7.09
9	20.57	22.85	24.65	20.43
10	27.21	27.08	20.85	29.60
11	9.39	20.54	21.63	20.69
12	24.77	17.24	13.44	17.57
13	17.92	25.37	22.00	13.08
14	30.68	28.51	26.95	32.31
15	7.45	13.26	23.93	25.52
16	23.57	33.79	38.00	33.96
17	25.06	26.35	10.93	29.45
18	28.02	23.35	19.27	11.29
19	31.11	28.57	14.83	24.53
20	23.66	26.40	30.51	27.45
21	35.37	23.37	33.55	31.97
22	18.14	19.26	18.18	14.85
23	33.26	21.94	24.28	13.09
24	32.03	22.59	26.68	26.31

Combo C	Frequency			
Participants	2000	1414	1000	707
1	17.85	27.33	32.96	37.84
2	19.95	28.38	23.67	36.30
3	23.04	14.56	26.85	32.47
4	24.62	15.96	21.44	17.72
5	23.81	30.02	29.82	22.53
6	15.74	20.88	29.48	24.39
7	30.42	22.75	27.43	30.92
8	31.19	19.01	21.39	35.24
9	27.96	25.64	32.90	26.32
10	24.35	18.44	29.53	24.17
11	20.61	27.24	20.58	37.96
12	21.77	28.66	27.95	34.63
13	32.44	26.02	31.40	21.43
14	20.49	12.18	34.26	33.95
15	24.42	17.06	21.47	23.15
16	30.89	27.13	27.40	33.03
17	26.44	12.57	29.64	25.76
18	15.91	19.40	27.30	39.46
19	30.69	21.71	30.14	26.85
20	20.26	21.69	18.41	28.38
21	28.96	17.85	28.74	16.14
22	14.62	15.78	21.33	30.45
23	22.68	21.07	30.09	32.01
24	22.99	31.89	27.18	34.47

Combo D	Frequency			
Participants	2000	1414	1000	707
1	24.28	26.43	20.06	33.70
2	22.35	21.00	24.27	20.52
3	18.87	19.10	6.35	11.88
4	24.88	11.12	23.07	28.85
5	25.00	21.99	27.44	15.62
6	24.01	25.72	23.17	25.60
7	10.77	21.16	27.82	39.36
8	25.98	20.41	23.21	31.56
9	15.57	10.28	29.59	31.00
10	23.70	19.73	26.30	34.76
11	24.93	21.88	5.59	14.89
12	30.79	19.04	27.11	27.27
13	21.86	27.67	16.13	22.13
14	22.11	32.39	30.80	25.29
15	16.04	17.26	19.32	12.61
16	31.95	22.25	22.68	37.17
17	17.08	31.80	26.04	26.59
18	20.73	17.22	23.59	25.79
19	18.56	3.10	31.40	32.61
20	23.07	27.82	24.19	28.96
21	32.21	23.94	26.54	31.58
22	14.25	21.66	24.02	12.36
23	23.21	24.39	18.14	26.58
24	30.35	32.01	29.57	35.75

APPENDIX F

AVERAGED RIPPLE DEPTH AND PREVALENCE

Combo A	Depth				Prevalence			
	Frequency				Frequency			
Participants	2000	1414	1000	707	2000	1414	1000	707
1	6.24	7.70	8.03	6.77	3	6	4	4
2	7.43	5.61	5.56	9.23	3	4	8	5
3	5.32	9.18	6.38	7.71	4	6	5	6
4	7.94	9.54	6.81	8.21	4	6	9	7
5	7.92	6.63	8.89	14.19	5	6	10	5
6	7.53	12.50	6.55	6.50	6	6	7	5
7	8.45	5.18	6.96	13.70	6	7	7	5
8	4.79	4.93	4.46	5.37	7	5	5	4
9	6.77	6.93	8.11	7.96	5	6	8	5
10	5.28	8.09	4.96	4.51	5	6	6	4
11	5.45	4.93	6.68	10.12	5	5	5	5
12	5.75	5.15	5.86	7.31	4	6	6	5
13	9.20	4.52	4.91	6.93	4	4	8	8
14	4.99	5.10	7.57	7.92	6	7	7	5
15	5.23	4.44	4.53	7.50	5	5	8	5
16	3.76	5.27	5.83	4.37	9	7	7	3
17	8.00	7.78	5.05	5.39	4	5	6	6
18	4.48	5.53	6.06	4.20	2	3	4	4
19	6.37	6.83	6.52	12.87	5	7	7	7
20	6.64	5.05	5.35	4.47	4	7	5	4
21	4.04	5.89	5.29	6.79	5	6	8	6
22	3.77	5.76	5.06	4.41	4	5	3	3
23	6.56	4.75	5.51	4.65	6	5	7	5
24	10.37	5.72	6.35	5.77	5	6	8	7

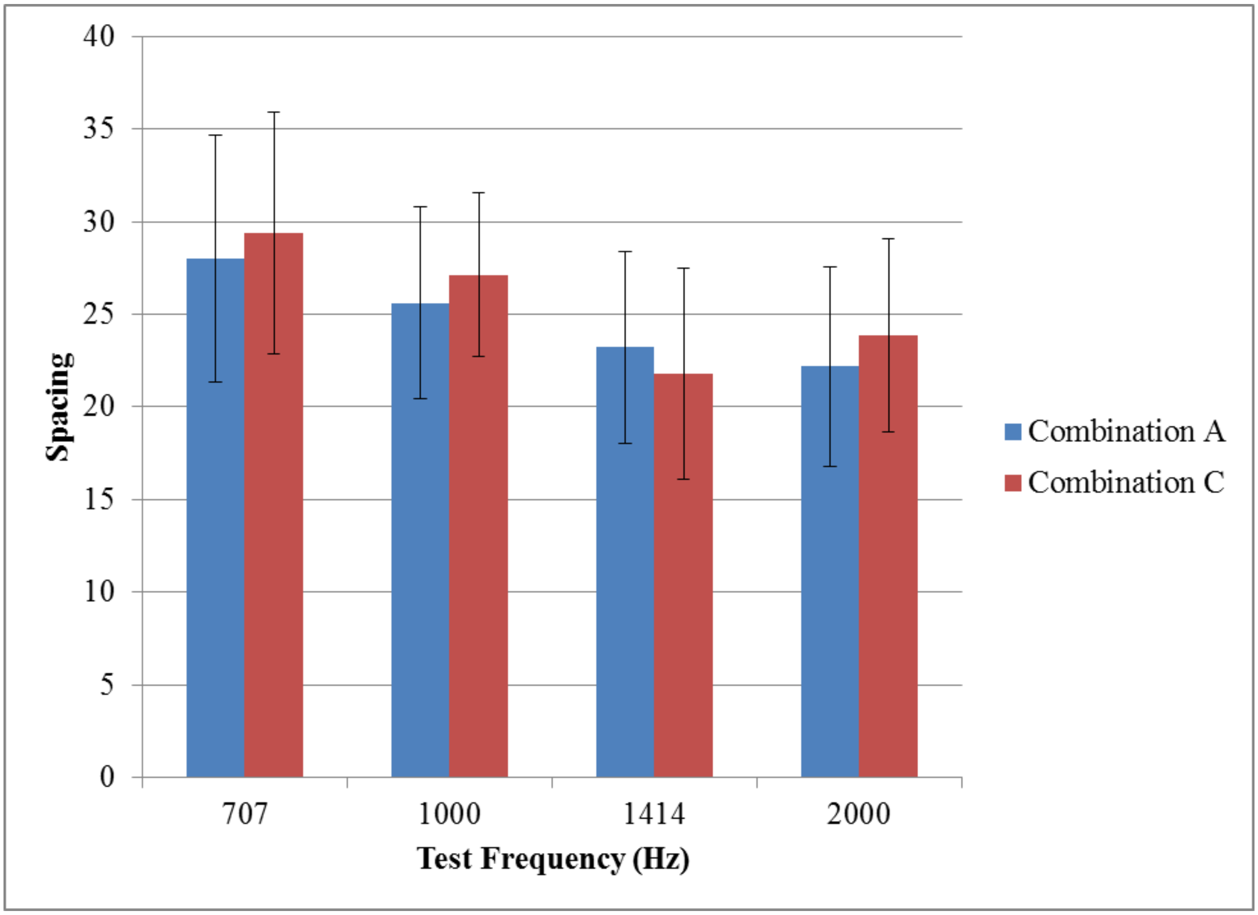
Combo B	Depth				Prevalence			
	Frequency				Frequency			
Participants	2000	1414	1000	707	2000	1414	1000	707
1	9.29	5.87	6.56	5.54	3	4	8	5
2	7.54	9.67	7.56	6.29	7	5	5	5
3	7.25	10.59	15.05	11.52	5	3	2	2
4	6.30	11.19	12.29	11.39	4	4	3	5
5	5.33	9.28	7.37	10.96	5	7	8	4
6	4.79	10.27	8.77	7.75	4	4	6	5
7	13.26	10.07	7.74	7.03	4	5	4	6
8	6.36	9.86	8.41	9.95	6	6	5	2
9	7.87	7.23	7.68	8.28	5	5	6	4
10	6.91	7.39	9.53	4.45	6	6	6	3
11	25.81	12.10	4.97	7.05	2	5	4	3
12	8.45	7.65	10.39	8.89	7	6	4	4
13	10.95	12.26	11.37	9.02	5	4	5	2
14	6.91	7.43	7.62	5.73	7	6	6	6
15	5.14	6.65	7.06	5.62	2	3	6	6
16	5.56	5.28	4.24	5.50	5	8	9	6
17	20.60	7.33	12.02	6.90	6	6	4	5
18	15.04	9.19	6.42	3.77	4	5	4	2
19	7.69	8.23	14.88	10.34	7	6	5	5
20	6.51	7.82	8.10	3.72	6	8	6	5
21	5.63	10.13	5.61	7.55	7	6	9	6
22	9.96	6.69	5.40	5.67	5	5	4	3
23	5.91	11.43	8.88	4.09	6	6	4	3
24	7.13	8.40	12.66	6.64	8	5	7	4

Combo C	Depth				Prevalence			
	Frequency				Frequency			
Participants	2000	1414	1000	707	2000	1414	1000	707
1	11.02	8.27	7.68	7.71	5	6	10	7
2	9.44	8.51	4.58	4.04	4	6	6	4
3	8.24	10.52	4.76	8.06	6	3	7	8
4	6.83	11.19	4.79	17.64	5	3	7	3
5	6.25	10.94	7.92	7.70	5	7	9	4
6	13.31	8.87	10.73	11.51	5	4	8	4
7	7.61	5.15	7.48	7.45	5	7	7	5
8	6.96	8.84	5.13	2.87	6	4	5	5
9	10.11	8.33	12.21	11.78	4	5	9	5
10	14.33	11.52	4.20	3.97	5	5	6	2
11	7.24	5.94	8.57	9.01	6	5	6	8
12	8.41	6.57	6.76	11.27	6	7	8	6
13	8.16	8.83	7.68	14.78	7	6	8	5
14	7.94	6.75	7.24	5.13	6	3	9	7
15	7.73	7.89	6.17	7.18	4	3	7	5
16	6.66	5.57	8.11	5.25	7	6	8	5
17	7.54	7.86	4.80	5.98	5	3	8	5
18	20.01	6.86	7.98	4.56	5	4	6	4
19	9.72	8.10	6.81	6.75	7	5	8	6
20	6.80	5.86	8.42	4.96	5	6	4	6
21	4.77	9.61	7.31	6.95	5	4	8	3
22	12.54	3.44	9.79	6.65	3	2	5	4
23	9.17	5.73	5.27	8.53	4	5	8	5
24	6.08	10.65	12.94	10.22	5	9	8	7

Combo D	Depth				Prevalence			
	Frequency				Frequency			
Participants	2000	1414	1000	707	2000	1414	1000	707
1	5.12	8.17	9.68	6.14	4	7	4	7
2	8.07	6.31	6.01	10.06	5	4	6	4
3	10.75	7.04	16.34	10.02	6	4	2	2
4	10.63	6.60	8.52	7.27	6	3	6	5
5	8.01	10.14	8.41	8.46	4	4	5	3
6	7.12	10.94	5.32	8.36	6	5	6	6
7	10.25	7.66	10.32	5.72	3	4	7	6
8	7.34	7.89	5.86	5.20	6	5	5	3
9	11.52	4.84	7.77	5.65	4	3	7	7
10	5.44	7.51	6.56	4.52	6	5	5	3
11	6.68	11.43	5.53	7.60	6	5	2	3
12	7.89	7.53	7.67	9.12	7	6	8	6
13	8.41	6.82	10.86	8.53	4	6	4	5
14	8.15	4.02	5.94	8.61	4	6	6	5
15	5.94	9.25	5.73	6.33	4	5	6	3
16	6.27	5.18	6.21	8.15	6	5	6	6
17	7.12	7.38	6.62	4.88	3	7	6	5
18	12.81	10.76	3.54	6.96	4	4	7	5
19	11.50	8.60	10.14	6.82	4	1	6	5
20	10.26	7.00	6.77	4.56	3	5	6	6
21	8.31	9.28	7.99	6.77	8	6	7	6
22	10.13	5.71	10.75	6.99	4	4	4	2
23	11.06	6.81	7.37	5.68	5	5	6	5
24	6.41	9.23	6.74	7.98	7	9	8	6

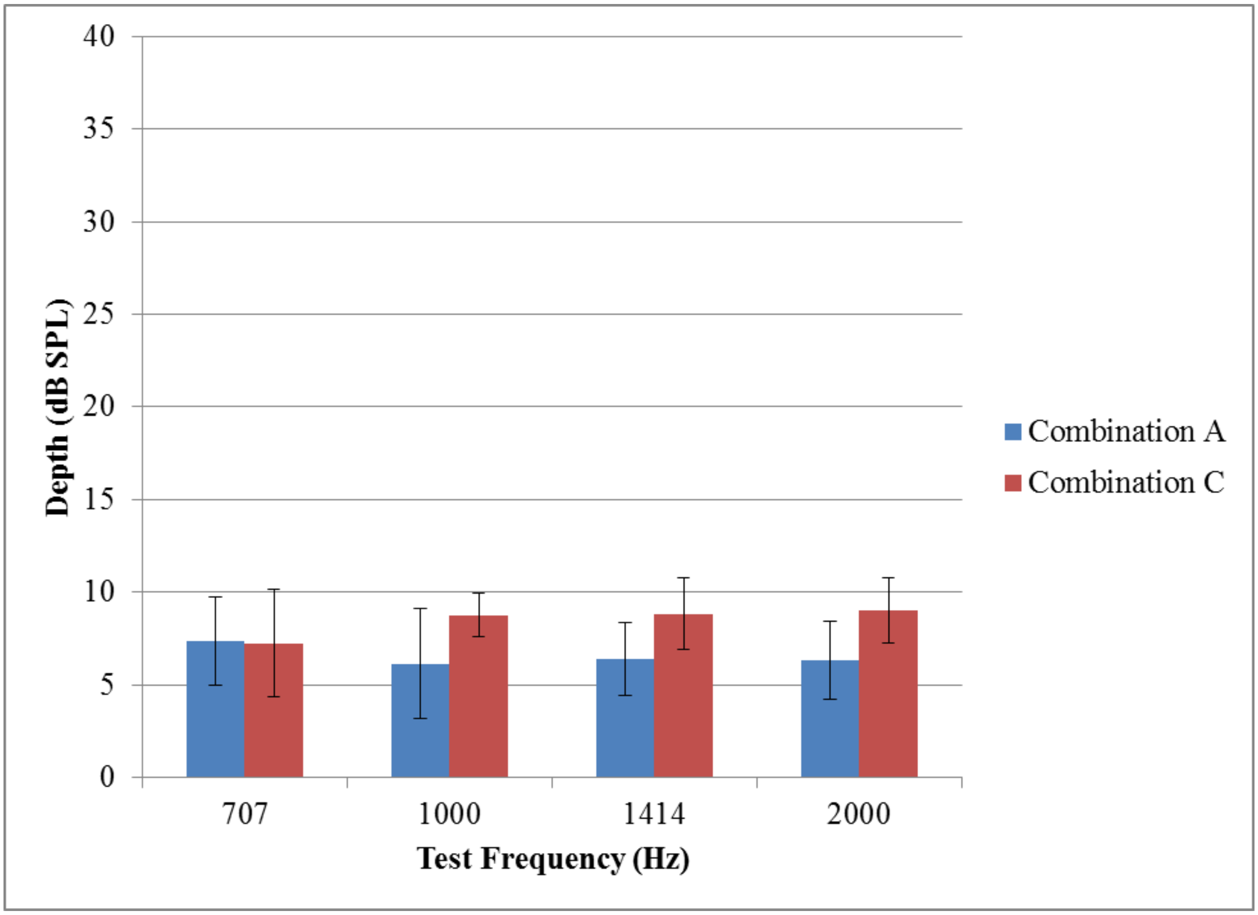
APPENDIX G

COMPARISON OF RIPPLE SPACING FOR COMBINATIONS A AND C



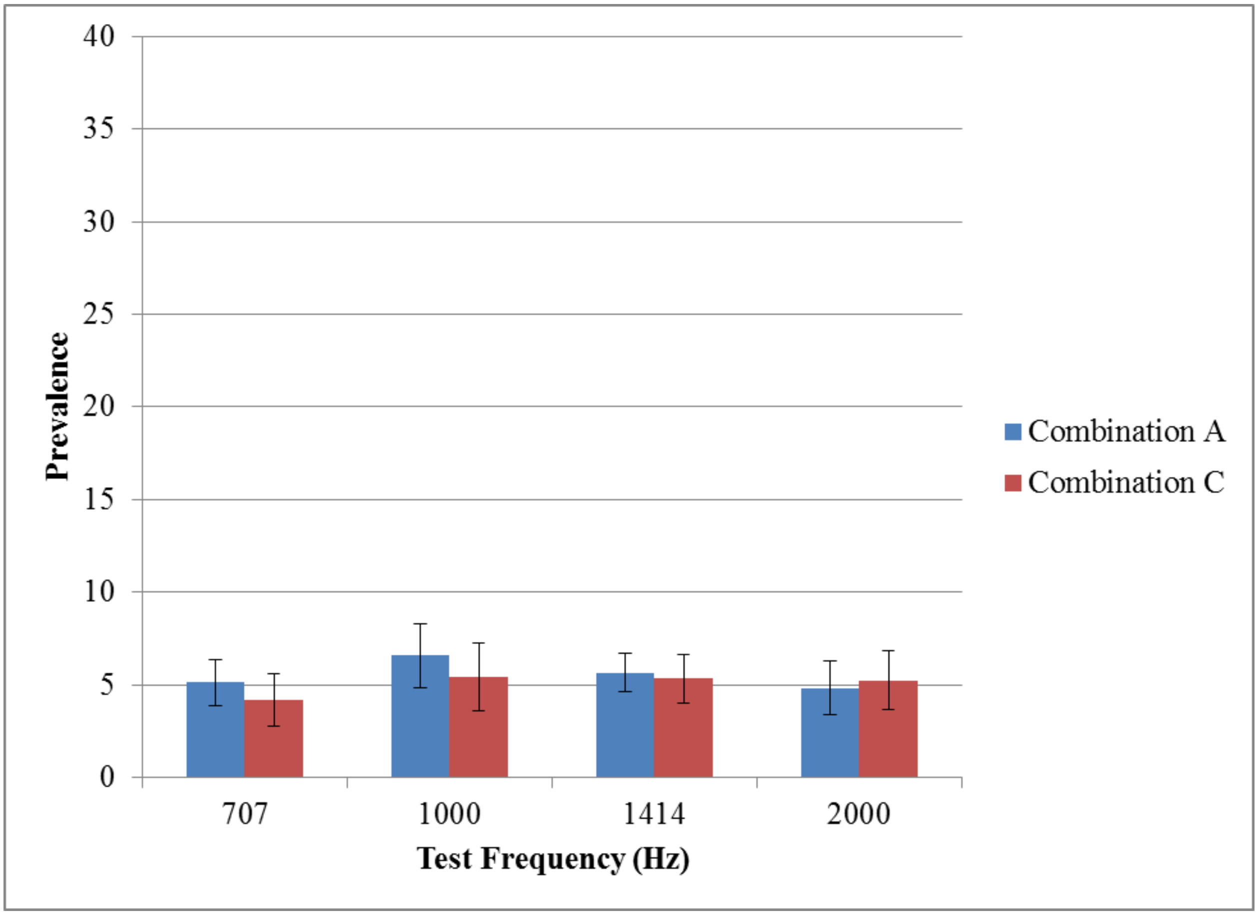
APPENDIX H

COMPARISON OF RIPPLE DEPTH FOR COMBINATIONS A AND C



APPENDIX I

COMPARISON OF RIPPLE PREVALENCE FOR COMBINATIONS A AND C



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