1 Introduction, Orientation, and Rationale

1.1 Introduction

Ever since Kemp (1978) first described otoacoustic emissions (OAEs), there has been an interest in the use of these measures to develop another diagnostic tool to predict hearing ability objectively, non-invasively, and rapidly. One might ask why the development of *another* objective diagnostic tool should be investigated if so many technologically advanced audiological tests already exist. The field of audiology exploded in the 1970s with electrophysiological test procedures such as tympanometry, acoustic reflex, auditory brainstem response, and otoacoustic emissions. All of these procedures were recently incorporated into audiological test batteries and are currently used routinely (Northern, 1991). These test batteries are used quite effectively in site of lesion testing and to determine hearing ability across a wide range of populations (Robinette, 1994). To better understand the need for another diagnostic tool to predict hearing ability objectively, a short overview of objective diagnostic procedures will be given.

1.2 Overview of Objective Diagnostic Procedures in Audiology

For many decades, diagnostic audiology relied on behavioral testing procedures in which hearing thresholds were determined by studying the listener's motor responses (Yantis, 1994). The first behavioral audiology test battery was developed in 1920 when bone conductors and speech channels became a standard feature included in an

audiometer's capabilities (Brunt, 1994). For three decades, audiological tests were developed with only these basic features. Tests that were developed included the ABLB test for loudness growth to indicate cochlear pathology in the 1930s, the tone decay test to indicate retrocochlear pathology in the 1940s, and the SISI (Short Increment Sensitivity Index) for cochlear pathology in the 1950s (Brunt, 1994).

The first objective physiological procedure was developed in the 1970s. Progress in technology enabled audiologists to measure minimal changes in air pressure in the external meatus, which resulted in a completely new diagnostic tool, tympanometry. This allowed audiologists to obtain information not only about middle ear pressure and tympanic membrane movement but also about the stapedius reflex. This resulted in a variety of objective diagnostic functions, such as an indication of middle ear pathology, cochlear pathology when loudness recruitment is present, and retrocochlear pathology when reflex decay occurs. One application of the acoustic reflex, sensitivity prediction with the acoustic reflex (SPAR), was developed by Jerger in the 1970s to predict hearing ability (Northern & Gabbard, 1994). SPAR predicts hearing ability as normal, moderately impaired, or severely impaired. According to a study by Jerger in 1978 (cited in Northern & Gabbard, 1994), normal hearing ability was accurately predicted 100% of the time, severe hearing loss 85% of the time, and moderate hearing losses 54% of the time. However, SPAR is influenced by a number of variables, such as chronological age (children between 0 and 10 are most accurately predicted), minor middle ear abnormalities, and audiometric configuration. Even though prediction of moderate hearing levels is only slightly better than chance, in difficult-to-test populations SPAR can often offer a rapid,

economical, and objective estimate of hearing sensitivity and is also useful in screening (Northern & Gabbard, 1994).

Tympanometry allowed audiologists to verify results obtained with behavioral audiometry objectively, for the first time. Today, pure tone air conduction and bone conduction, speech audiometry, and tympanometry still form the basis of every test battery (Robinette, 1994).

The second development toward objective audiological measurements also occurred in the 1970s, when audiologists began to measure the electric potentials of the nervous system with surface electrodes. Auditory evoked potentials (AEPs) occur in different time intervals after stimulation and provide information about the cochlea, auditory nerve, and brainstem. AEPs are usually classified by their "latency epoch," the time domain within which the response occurs after stimulus onset (Ferraro & Durrant, 1994). AEPs occurring in the first 10–15 milliseconds are known as short latency responses (SLRs). SLRs include the auditory brainstem response (ABR) and components preceding the ABR that are recorded via cochleography (ECoghG). EcochG is used for a variety of applications, such as the enhancement of wave I in ABR testing, when test conditions are less than optimal or when a hearing loss is present. EcochG is also used to monitor Meniere's disease and to monitor cochlear and nerve functioning during surgical procedures that might permanently damage those structures. SLRs arise from the periphery and brainstem (Ruth, 1994).

Middle latency responses (MLRs), which refer to components in the latency epoch of 10–50 milliseconds, are generated in structures beyond the inferior colliculus (Kraus, Kileny & McGee, 1994). MLRs are clinically used to objectively determine hearing

ability in the lower frequencies. They are also used to assess the cochlear implant function and to localize auditory pathway lesions (Kraus et al., 1994). However, MLRs are affected by sleep and cannot be detected in certain phases of sleep. It is possible to monitor sleep phases with EEG measurements and to conduct MLR testing only in favorable sleep periods, but this requires much more expertise and expensive equipment. The fact that MLRs are affected by the subject's level of consciousness has limited their popularity as an objective diagnostic procedure (Ferraro & Durrant, 1994).

Components generated beyond 50–80 milliseconds post-stimulus onset are long latency responses (LLRs) and are cortically generated (Kraus et al., 1994). An example of an LLR measurement is the N_1-P_2 Complex, which was successfully used as an indicator of hearing sensitivity in difficult-to-test populations and also to detect lesions in the central auditory pathway (Ferraro & Durrant, 1994). Just like the MLR, the N_1-P_2 Complex is sensitive to the subject's state of consciousness. Another example of LLR is the $P_{300,}$ whose most common uses include studies of aging, dementia, and attention disorders (Ferraro & Durrant, 1994).

Auditory evoked potentials (AEPs) did not enjoy widespread acceptance or clinical application until the discovery of the auditory brainstem response (ABR). Although Sohmer and Feinmesser (1967) are generally recognized as the first to report recording auditory evoked responses from the eighth nerve, it was Jewett and Williston (1971) who labeled the seven waves and set the basis for ABR testing (cited in Robinette, 1994).

The ABR dominated clinical attention to AEPs for about a decade and is still a very popular test of auditory function for difficult-to-test populations (Ferraro & Durrant, 1994). Behavioral evaluation of very young infants relies on spontaneous responses such as eye and head movements. Even with some kind of reinforcement, these responses cannot be elicited near the threshold value. Presentation of stimuli is via loudspeakers, which does not provide information about hearing ability in separate ears. All these limitations of behavioral hearing testing made ABR the preferred objective audiologic technique for infants younger than 6 months (Weber, 1994). With ABR, stimuli are presented via earphones, making it possible to test the hearing status of the individual ears. ABR enables the audiologist to obtain responses to low stimulus intensity levels from sleeping infants. As Robinette (1994) stated, the ABR is popular in the evaluation of hearing when traditional behavioral tests are precluded or their results are equivocal.

The ABR is, however, not without its own shortcomings. First, the frequency range in which hearing ability can be determined with ABR is limited. ABR testing with click stimuli provides only a one-point audiogram in the 2000–4000 Hz region. This is due to the type of stimuli needed to elicit an ABR—namely, abrupt onset acoustic clicks. The more abrupt the stimulus onset, the more neural fibers will respond in synchrony and the more clearly defined the ABR (Weber, 1994). The acoustic click has its greatest energy around 3000 Hz, therefore creating the stimulus range from 2000 to 4000 Hz.

Attempts to gain information about the low frequencies created a new set of problems. The use of low frequency tone bursts with abrupt stimulus onset resulted in high

frequency contamination. (An abrupt stimulus onset might stimulate broad areas of the basilar membrane.) Investigators have used several alternative techniques in an attempt to gain reliable and frequency-specific low frequency information such as masking techniques and filtering. Weber (1994) wrote that "the quest continues for a sensitive and robust electrophysiologic measure of low frequency hearing status that can be used with the sleeping child" (p. 382).

The second shortcoming of ABR testing is the amount of time the test requires. It can take more than 30 minutes to obtain a single ABR threshold for each ear (Weber, 1994).

The third weakness is the possibility of sedation. When testing of hearing ability close to the threshold is performed, it can be affected by patient movement artifacts. The child should therefore be as still as possible, preferably asleep. When infants younger than 6 months are tested, it can be assumed that there will be periods of sleep long enough for ABR testing. For older infants, it is often necessary to ensure adequate test conditions by giving the child some form of sedative, usually administered orally (Weber, 1994).

Lastly, ABR requires highly trained personnel and is a relatively expensive procedure (Musiek, Borenstein, Hall III & Schwaber, 1994).

At the end of the 1970s, another objective way to evaluate hearing ability was discovered by David Kemp (1978), who called it otoacoustic emissions—that is, sounds generated from a normal cochlea either spontaneously or in the presence of

acoustic stimulation. It appeared that normal cochleae emitted these responses, whereas ears with a hearing loss >35 dB HL did not.

Kemp's (1978) original reports were greeted rather skeptically, and much early research only replicated his study to confirm the presence of otoacoustic emissions. After two decades of intensive research, however, there is much excitement among researchers, since certain types of otoacoustic emissions prove to be highly applicable in the areas of hearing screening and even diagnostic audiology (Kummer, Janssen & Arnold, 1998; Martin, Probst & Lonsbury-Martin, 1990; Stach, Wolf & Bland, 1993; Stover, Gorga & Neely, 1996a). Many researchers hope that this relatively new field in audiology will prove to be the long-awaited objective, rapid, and accurate test of auditory function to aid in the assessment of difficult-to-test populations.

Otoacoustic measurement will certainly never replace pure tone audiometry, immittance, or ABR, but OAEs offer diagnostic information regarding the auditory system that is not available from any other test. This new objective procedure will be discussed below in more detail.

1.3 Otoacoustic Emissions

Otoacoustic emissions are low intensity acoustic signals generated by the outer hair cells (OHC) in the organ of Corti on the basilar membrane either spontaneously or in the presence of acoustic stimulation. Brownell (1990) describes the outer hair cell motility as a lengthening or shortening of the outer hair cells in response to acoustic stimulation. This active biological mechanism in the outer hair cells causes a vibration

of the basilar membrane in an attempt to enhance the ear's sharpness and sensitivity (Attias, Furst, Furman, Haran, Horowitz & Breslof, 1995). The vibration of certain areas of the basilar membrane amplifies the basilar membrane's response to low level sound (Lonsbury-Martin, McCoy, Whitehead & Martin, 1992). This vibration, called an otoacoustic emission, can be recorded using a very sensitive microphone placed in the ear canal.

The primary value of otoacoustic emissions is that their presence indicates that the preneural cochlear mechanism (and middle ear as well) can respond to sound in a normal manner. A large area of the basilar membrane is stimulated, and the measured emissions are frequency-specific and frequency selective, so it is possible to gain information about different areas of the cochlea simultaneously. "No other clinical test," wrote Kemp, Ryan, and Bray (1990), "specifically tests cochlear biomechanisms or combines the operational speed, non-invasivity, objectivity, sensitivity, frequency selectivity, and noise immunity of otoacoustic emission testing" (p. 94).

Kemp (1978) described two main classes of otoacoustic emissions: spontaneous otoacoustic emissions (SOAEs) and evoked otoacoustic emissions (EOAEs), which will be described below.

1.3.1 Spontaneous Otoacoustic Emissions (SOAEs)

SOAEs are tonal or narrowband low level signals that can be recorded in the absence of any auditory stimulation in only 50% of all persons with hearing levels <20 dB HL

and in 60% of persons with hearing levels <30 dB HL (Lonsbury-Martin, 1994). Because of this low incidence of SOAEs, they are not viewed as a suitable clinical indicator of the mechanical activity of the cochlea (Lonsbury-Martin, 1994; Norton & Stover, 1994). After Kemp (1978) reported the existence of SOAEs, many clinicians hoped that they would be the objective basis for tinnitus. It has been proved, however, that most people are unaware of their spontaneous otoacoustic emissions, and only a very small percentage of people with tinnitus have recordable SOAEs that can be linked to their tinnitus (Norton, Schmidt, & Stover, 1990). Spontaneous otoacoustic emissions can therefore only be used as a complementary technique for evoked otoacoustic emissions (Bonfils, Avan, Francois, Marie, Trotoux & Narcy, 1990).

Several types of evoked OAEs exist, depending on the type of stimulus used during the measurement. Evoked emission types include stimulus frequency emissions, transient evoked otoacoustic emissions, and distortion product otoacoustic emissions.

1.3.2 Stimulus Frequency Otoacoustic Emissions (SFEs)

A stimulus frequency otoacoustic emission (SFE) is the most frequency-specific of all emission types, but it is also probably the least clinically applicable (Norton & Stover, 1994). SFEs reflect the response of the cochlea at a certain pure tone, occurring simultaneously with and at the same frequency as the stimulus presented. When a tone is presented to the ear, the sound pressure measured in the ear canal is the sum of the sound pressure of the stimulus and the response. In the case of other evoked emission types, the stimulus sound pressure level is separated from the response either spectrally (as in the case of distortion product otoacoustic emissions) or temporally

(as in the case of transient evoked otoacoustic emissions). Due to the lack of temporal or spectral separation techniques in measuring SFEs, more sophisticated equipment and processing of data are required, and therefore SFEs are not currently practical for clinical use (Lonsbury-Martin & Martin, 1990; Norton & Stover, 1994). Lonsbury-Martin, (1994) described this phenomenon quite effectively: "SFEs are technically difficult to measure, due to the complexities of separating the in-going acoustic stimulus from the out-going emitted response. Thus, to date, little information has accumulated concerning either their basic nature or their clinical utility" (p. 2).

1.3.3 Transient Evoked Otoacoustic Emissions (TEOAEs)

TEOAEs are responses that follow a brief acoustic stimulus such as a click or a tone burst. TEOAEs can be recorded in nearly all persons with normal hearing (hearing levels < 20 dB from 500 Hz to 4000 Hz) and are absent in all ears with a hearing loss 30–40 dB HL. (Hearing loss > 40 dB HL according to Glattke, Pafitis, Cummiskey, & Herer, 1995; hearing loss > 35dB according to Robinette, 1992; or hearing loss > 30 dB according to Kemp et al., 1990.)

In measuring a TEOAE, a probe is inserted into the ear canal, containing a miniature sound source for delivering the stimulus and a very sensitive microphone for detecting the response. TEOAEs are obtained by using synchronous time-domain averaging techniques. Responses to several stimuli (e.g., 500–2000 clicks) are averaged to improve the signal-to-noise ratio and make the response distinguishable from the noise floor (Glattke et al., 1995). The ear canal sound pressure is amplified, filtered, and then digitized, and the first 2.5 seconds of the response are eliminated to remove

the stimulus (Norton & Stover, 1994). This process is presented schematically in Figure 1.1.

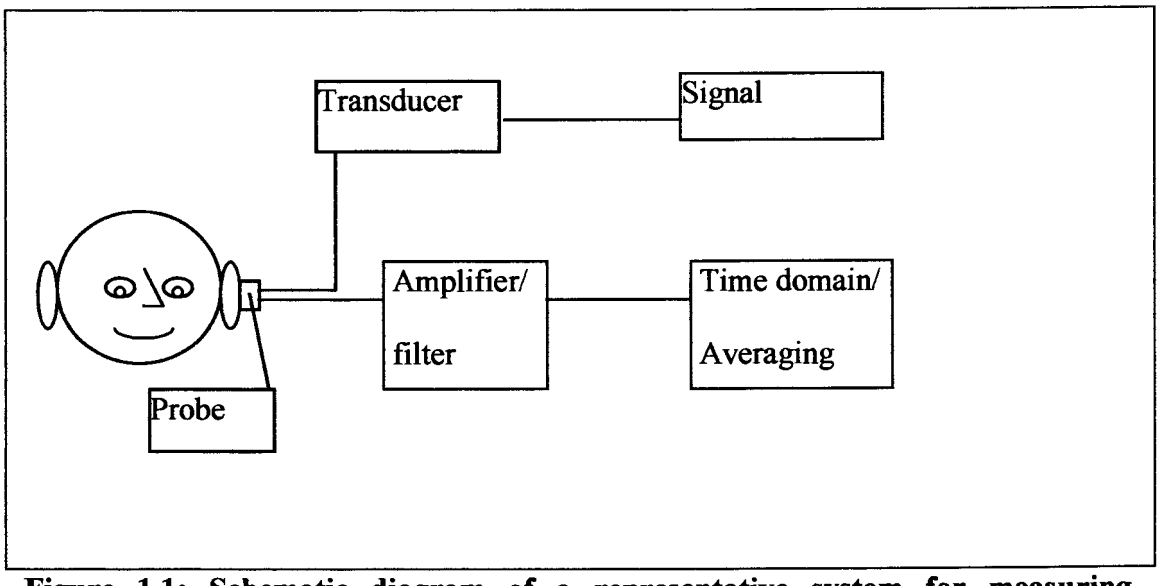

Figure 1.1: Schematic diagram of a representative system for measuring TEOAEs (Norton & Stover, 1994:450)

Another characteristic aspect of TEOAEs is that they are frequency dispersive: high frequencies coded basally on the basilar membrane have a shorter latency (4 ms for 5000 Hz) than low frequencies, coded apically on the basilar membrane (20 ms for 500 Hz). According to Kemp et al. (1990), this provides for temporal separation of the stimulus's and response's sound pressure level, both measured in the ear canal.

The frequency specificity of TEOAEs is determined by the bandwidth of the stimuli being used to elicit a response. Emissions can be evoked at most frequencies in the normal cochlea. The broader the stimulus spectrum, the broader the emission spectrum (Norton & Stover, 1994). Broadband clicks are usually used for measuring TEOAEs, which allows for simultaneous multifrequency testing (Kemp & Ryan, 1993). TEOAEs provide simultaneous information regarding the functioning of the outer hair cells on the basilar membrane for a very broad region of frequencies (Kemp et al., 1990; Norton & Stover, 1994). Some frequency-specific information can be gained by analyzing the spectral distribution. Kemp et al. (1990) successfully used TEOAEs to identify frequency ranges of normal hearing in pathological ears. In a case with a high frequency hearing loss, they obtained emissions up to the frequency of the hearing loss and no emissions for the pathological frequencies. It should be noted, however, that no information regarding the thresholds of the pathological frequencies could be obtained. Many other researchers have also had difficulty in making comparisons between frequency-specific audiometric thresholds and frequency information provided by TEOAEs (Bonfils et al., 1990; Lee, Kimberley & Brown, 1993; Lonsbury-Martin & Martin, 1990). The fact that no emissions can be obtained when the hearing loss exceeds 30–40 dB HL has proven TEOAEs to be more applicable in the area of hearing screening than diagnostic audiology (Harris & Probst, 1991; Lee et al., 1993).

TEOAEs were the first method to be tried and recommended for neonatal hearing screening and are currently the most widely used OAE method for screening (Kemp & Ryan, 1993). TEOAEs can be measured very effectively in newborns. Both ears can be screened in a sleeping infant in about 10 minutes, compared to about 20

minutes with screening ABR (Norton & Stover, 1994). Another advantage of TEOAEs is that a broader frequency spectrum is being evaluated than with ABR, they do not require highly trained personnel, and they are objective and non-invasive (Lonsbury-Martin et al., 1992; Stevens et al., 1990).

TEOAEs do, however, have limitations. The first is that they are only recordable in normal and near-normal ears (30–35 dB HL). TEOAE data cannot be translated into "threshold data." An ear with a hearing loss of 65 dB will have the same absent response as an ear with a hearing threshold of 40 dB (Kemp et al., 1990). Although TEOAEs function as a wonderful screening procedure (Stevens et al., 1990), no information regarding hearing status can be obtained once the emission is absent, as in the case of mild and moderate hearing losses.

Another weakness of TEOAEs is that even in cases where the TEOAE response is present, this test can still not predict frequency-specific hearing levels from the emission spectrum (Lee et al., 1993). Hurley and Musiek (1994) indicated that TEOAEs are affected by small changes in cochlear physiology that do not result in comparable changes in auditory threshold. In other words, they found considerable TEOAE variability among ears with similar hearing sensitivity. TEOAEs could only classify hearing levels as normal (<20 dB HL) or abnormal (>20 dB HL).

Finally, it seems that TEOAE amplitude and occurrence are negatively affected by increasing age. Norton and Widen (1990) reported a statistically significant decrease in TEOAE amplitude with increasing age even in a carefully screened sample. Kemp et al. (1990) also indicated stronger responses as well as responses at more

frequencies for neonates than adults. It is still unclear whether the age-associated changes are due to normal developmental changes in the middle ear or to progressively impaired cochlear function.

All the emission types previously discussed—namely, SOAEs, SFEs, and TEOAEs—all have one limitation in common. None of these emission types can function as an objective test of hearing where pure tones can be predicted given only the otoacoustic emissions (Bonfils et al., 1990; Hurley & Musiek, 1994; Lee et al., 1993; Lonsbury-Martin, 1994). The requirement for an emission type to be able to potentially predict pure tone thresholds given only the otoacoustic emissions is that the emission type should be present in normal and hearing impaired ears (Kimberley, Hernadi, Lee & Brown, 1994). It should also be frequency-specific and easily compared to the frequencies of the behavioral thresholds (Lee et al., 1993). There is one emission type that might prove to be clinically applicable in the prediction of behavioral pure tone thresholds—namely, distortion product otoacoustic emissions (Lee et al., 1993; Lonsbury-Martin & Martin, 1990).

1.3.4 Distortion Product Otoacoustic Emissions (DPOAEs)

DPOAEs can be recorded in virtually all normal hearing ears (100% according to Lee et al., 1993; and 95% according to Kimberley et al., 1994). DPOAEs can also be measured in ears with a mild to moderate sensorineural hearing loss. The second advantage of DPOAE measurement over the measurement of TEOAEs is the frequency specificity of the stimuli used. With DPOAEs, pure tone stimuli are used. The location of stimulation on the basilar membrane can be pinpointed quite

accurately. Very specific information regarding outer hair cell function at any chosen location on the basilar membrane can be obtained with DPOAEs (Lonsbury-Martin & Martin, 1990). The facts that specific input frequencies can be selected and that responses are measured at certain frequencies make it easier to make comparisons between DPOAE results and conventional pure tone thresholds. This feature of DPOAE measurement makes it the best-suited emission type to relate to behavioral thresholds (Lee et al., 1993). Lastly, DPOAEs are the only otoacoustic emission type that can be recorded in the presence of a hearing loss. TEOAEs can only classify a person's hearing as normal or abnormal (Bonfils, Piron, Uziel & Pujol, 1988). DPOAEs can classify hearing ability as normal, slightly impaired, mildly impaired, moderately impaired, or severely impaired (in cases where no emissions can be measured) (Durrant, 1992; Gaskill & Brown, 1990; Lee et al., 1993). This advantage of DPOAEs allows emission testing of a much larger population with varying hearing sensitivity, making this one of the best reasons to develop DPOAEs as an additional objective test of hearing.

The distortion product with all its characteristics and complexities will be discussed in detail in Chapter 2.

1.4 Rationale for This Study

This overview of the development of objective diagnostic procedures clearly indicates the profound improvement in the ability to measure hearing equity since the 1920s. Progress in modern technology enabled audiologists to measure the exact degree, configuration, and site of hearing loss and to confirm these findings with a series of

objective electrophysiologic procedures, such as tympanometry, the acoustic reflex, ABR, and otoacoustic emissions. It is, however, evident that there are some weaknesses in current objective diagnostic procedures. In the evaluation of special populations such as neonates from birth to 6 months, the crucially ill, and malingerers, audiologists often have to rely heavily on the objective electrophysiological procedures to determine hearing ability. To determine hearing thresholds with electrophysiological procedures are often costly, require a large amount of time and highly trained and specialized personnel, and may require sedation. Above all, current objective physiologic procedures, such as ABR, have a limited frequency area in which hearing ability can be determined accurately. There is therefore a definite need for an objective, reliable, rapid, and economic test of hearing that evaluates hearing ability across a range of frequencies to aid in the assessment of difficult-to-test populations.

The rationale for this study is to investigate one type of emission, the distortion product otoacoustic emission (DPOAE), as a possible new objective test of hearing. Such a test will be an objective, rapid, non-invasive, inexpensive, and accurate measurement of hearing that will have a profound implication for the field of Audiology as we know it (Kimberley et al., 1994). First, the objectivity of the measurement will make it an ideal testing procedure for difficult-to-test populations such as newborns, infants, the crucially ill, foreign speakers, the multiply handicapped, and malingerers (Elberling, Parbo, Johnsen & Bagi, 1985; Lonsbury-Martin, 1994). When combined with other tests such as pure tone audiometry, speech audiometry, acoustic immittance, ABR, or electrocochleography, this new procedure will greatly improve the differential diagnosis of hearing pathology. The primary site

of lesion will be determined accurately as sensory or neural, or as a central auditory dysfunction (Lonsbury-Martin, 1994; Robinette, 1992). This test will vastly improve the assessment of the peripheral ear.

Chapter 2 will discuss the distortion product in more detail.

2 Distortion Product Otoacoustic Emissions

2.1 Introduction to Distortion Product Otoacoustic Emissions

Distortion product otoacoustic emissions are different from the other emission types in a number of ways. First, DPOAEs are elicited by the simultaneous presentation of two pure tones and the emission is an internally produced frequency different from the two stimuli, in frequency and amplitude. Second, in contrast to other emission types such as TEOAEs, SOAEs and SFEs, the distortion product can very easily be measured in many common vertebrate laboratory animals (Mills, 1997). Research on laboratory animals allows experimental control of certain factors which contributes to a better understanding of the characteristics of distortion product emissions and OAEs in general (Zhang & Abbas, 1997). DPOAEs have even been measured in the ear of a grasshopper with a completely different morphology. The hearing organ of a grasshopper does not have any sensory hair cells, but the dendrites of the ciliated receptor cells are responsible for generation of distortion (Kossl & Boyan, 1998). Distortion product otoacoustic emissions have therefore been proven useful in both clinical and research settings. Third, DPOAEs can be measured in hearing impaired ears with elevated threshold levels of up to 65dB HL (Moulin, Bera & Collet, 1994). This feature enables DPOAEs to provide more than just hearing screening information.

These interesting differences between DPOAEs and other emission types led to an extensive investigation of DPOAEs to determine the clinical applicability of DPOAEs (Bonfils & Uziel, 1989). This clinical interest in DPOAEs is twofold. The first interest

lies in the development of an objective test of auditory function. The second interest is to develop a test uniquely sensitive to the functioning of the outer hair cells, and therefore a useful tool in differential diagnostic testing (Durrant, 1992). This research project focuses on the first interest: To develop an objective, noninvasive test of auditory function with distortion product otoacoustic emissions.

To better understand the nature of the distortion product, its definition will now be discussed.

2.2 Definition of DPOAE

DPOAEs are elicited by the simultaneous presentation of two different pure tones, f1 and f2, where f1<f2. The distortion product response is a third tone of frequency, produced internally and in a frequency region different from the two primary frequencies. Responses can be expected at several different distortion product frequencies such as 2f1-f2, 3f1-2f2, 4f1-3f2, etcetera. Of all the distortion products, the cubic distortion product is the most prominent in humans and occurs at 2f1-f2 (Nielsen, Popelka, Rasmussen & Osterhammel, 1993).

The normal cubic distortion product is typically 60dB lower than the overall level of the primaries (Nielsen, et al., 1993). The relationship of the distortion product (2f1-f2) and the two primary frequencies (f1 and f2) can very clearly be seen in the spectrum of the ear canal sound pressure of normal hearing subjects undergoing DPOAE testing. This relationship is illustrated in Figure 2.1.

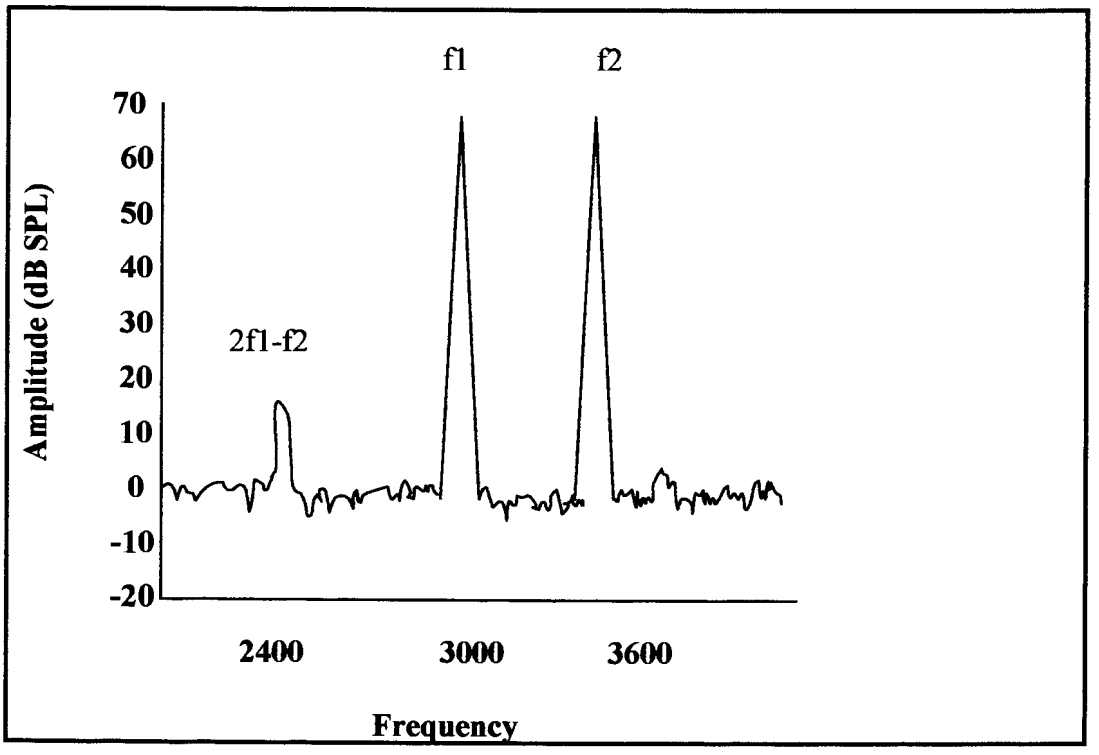

Figure 2.1: The spectrum of the ear canal sound pressure of a normal hearing adult undergoing DPOAE testing. f1 and f2 are the stimuli and 2f1-f2 is the response (from Norton & Stover, 1994:457).

The acoustic distortion product can be measured in the ear canals of animals and humans. The next section will discuss the measurement procedures and instrumentation necessary to elicit a distortion product otoacoustic emission.

2.3 Measurement Procedures and Instrumentation for DPOAEs.

For the measurement of a distortion product otoacoustic emission, two separate channels for stimulus generation and attenuation are necessary. These two channels should be electrically isolated to prevent distortion. The signals are presented to the

ear canal via a probe microphone assembly with two delivery ports. Probe microphone systems for DPOAEs consist of a miniature sound source and a very sensitive microphone built into a unit small enough to fit snugly into a human ear canal (Siegel, 1995). Figure 2.2 represents such a probe microphone system schematically.

After the two signals are presented to the ear canal, the ear canal sound pressure is averaged to reduce the noise floor and then spectrally analyzed for the levels of the primaries (f1 and f2) and the response (2f1-f2). Figure 2.1 shows the spectrum of the sound pressure measured in the ear canal, depicting the two primary stimuli f1 and f2, as well as the response, 2f1-f2.

A complete DPOAE system is presented schematically in Figure 2.3.

There are several different stimulus parameters that influence the emission amplitude or threshold (lowest level where an emission can be elicited above the noise floor). These stimulus parameters will be discussed in the following section.

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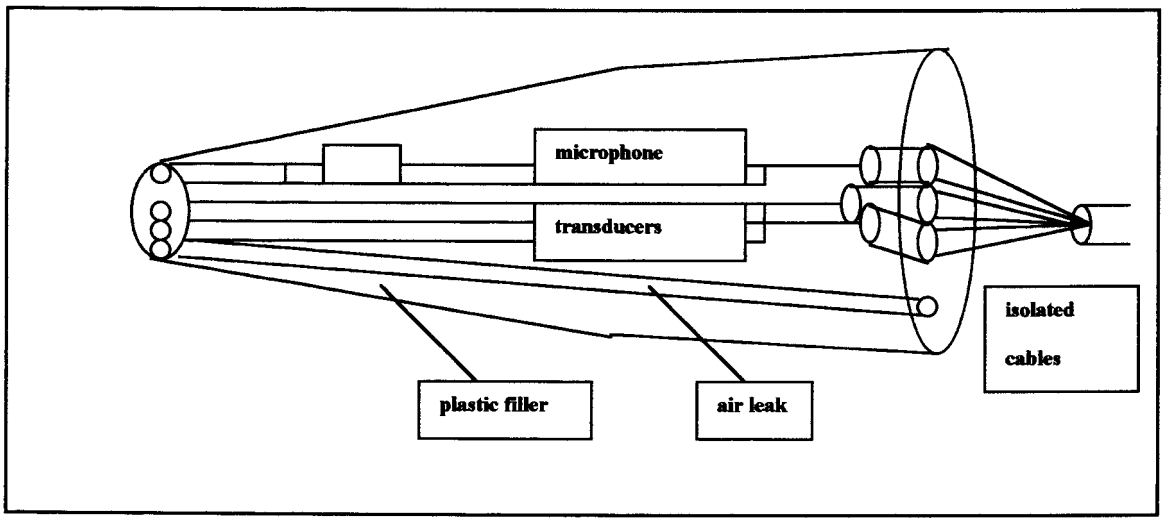

Figure 2.2: Probe microphone system for distortion product otoacoustic emissions (Kemp, Ryan & Bray, 1990).

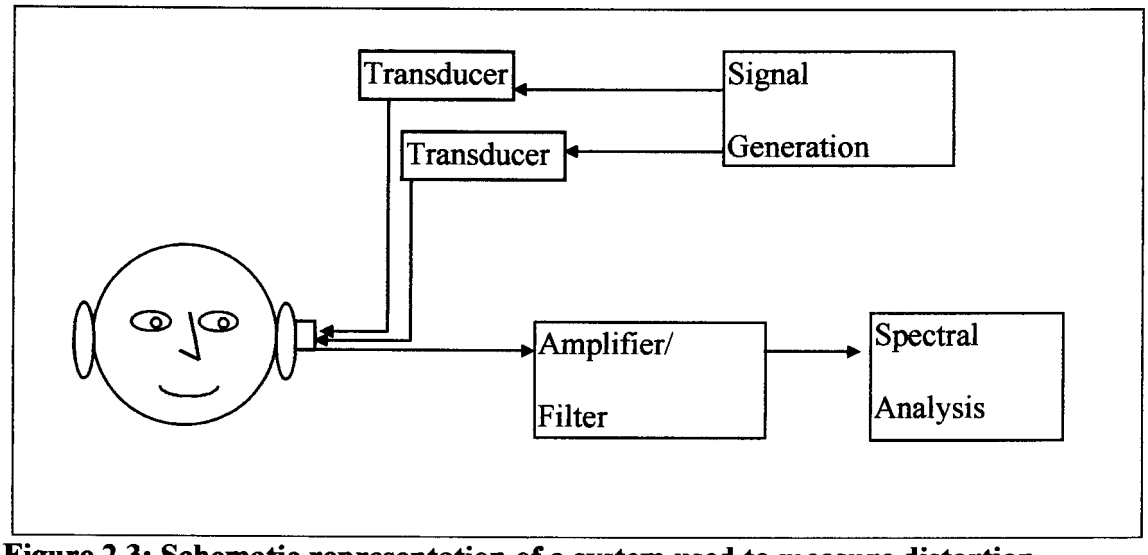

Figure 2.3: Schematic representation of a system used to measure distortion product otoacoustic emissions (Norton & Stover, 1994:456).

2.4 Stimulus Parameters of DPOAEs

There are a number of critical factors or variables involved in the generation of the stimuli necessary to elicit a DPOAE. The distortion product 2f1-f2 is highly influenced by the primary frequencies f1 and f2, the intensities of both stimuli, L1 and L2, the frequency ratio of the primary frequencies (f2/f1) and the loudness ratio of f1 and f2 (L1/L2). David Mills (1997:414) rightly commented on this four-dimensional space over which cochlear space can be explored: "In practice, this aspect may have led to more confusion than understanding." Either the frequencies are changed and the loudness level kept constant (this is sometimes referred to as a "distortion product audiogram") or the frequencies are being kept constant while the loudness level is changed (an input/output function is obtained). It should be noted that the "distortion product audiogram" does not include the concept of threshold, as does the conventional audiogram in this case.

A study by Harris, Lonsbury-Martin, Stagner, Coats and Martin (1989) investigated which f2/f1 ratio yielded the maximal DPOAE amplitude. They used stimulus frequencies and level ranges that were representative of clinical audiograms and found that on the average, a ratio of 1.22 elicited the largest acoustic distortion products for emissions between 1kHz and 4kHz.

Nielsen et al. (1993) measured the cubic distortion product at six probe tone frequency ratios varying between 1.15 and 1.40 using equilevel primaries of 75dB SPL. The results showed that a frequency ratio between 1.20 and 1.25 optimizes the

amplitude of the distortion product and is also most applicable to the standard frequencies used in pure tone audiometry.

Other studies that described the optimum frequency ratio included f1/f2 = 1.225 (Gaskill & Brown, 1990), f1/f2 = 1.23 (Avan & Bonfils, 1993) and f1/f2 = 1.3 (Stover, Gorga & Neely, 1996a).

It would therefore seem that a frequency ratio of f1/f2 = 1.2 to 1.3 yields the best DPOAE amplitudes (Avan & Bonfils, 1993; Gaskill & Brown, 1990; Harris et al., 1989, Nielsen, et al., 1993; Stover et al., 1996a).

Another factor that influences DPOAE amplitude, apart from the frequency ratio, is the loudness level ratio of the primaries, namely L1 and L2.

Mills (1997) studied the effect of the loudness levels of the primaries on the distortion product. The author concluded that the cubic distortion emission amplitude is not symmetric, so that given the same L1, higher emission amplitudes can occur for L2 > L1 compared to L1 = L2. Authors such as Stover et al., (1996a) found maximal DPOAE amplitudes when L2 > L1 by 10dB and Gorga, Neely, Bergman and Beauchaine, (1993) found maximal DPOAE amplitudes when L2 > L1 by 15 dB.

"Recently, there has been emerging consensus on recommendations for using L1/L2 ratios in the range of 10-15dB" (Mills, 1997:414).

It is very important to choose the right frequency and loudness level ratios that yield maximum DPOAE amplitudes. These variables should be chosen in such a manner that the stimulus levels and frequency ranges are representative of clinical audiograms, to enable comparisons between the DPOAEs and pure tone thresholds (Moulin, et al., 1994). Once the optimal parameters are determined, experiments can be conducted to study DPOAEs in persons with normal or impaired hearing (Harris et al., 1989).

Apart from all the parameters that should be specified, there are also two different ways to construct DPOAE testing, namely, to obtain a distortion product audiogram (DP Gram) or an input/output function (I/O function). The differences between these two options will be reviewed in the next section.

2.5 DP Gram versus I/O Function

The distortion product can be measured and displayed in two forms.

2.5.1 The DP Gram

The first form, namely the DP Gram, depicts DPOAE amplitude as a function of stimulus frequency at a fixed loudness level (Lonsbury-Martin & Martin, 1990). In other words, the loudness level is kept constant and the frequencies are changed. In this manner, a test cochlea can be evaluated over a large frequency range by comparing the evoked DPOAE amplitudes to average amplitudes determined from a population of normal hearing individuals (Lonsbury-Martin, 1994). Figure 2.4

represents a DP Gram of a normal hearing person. The DP Gram is analyzed by comparing DPOAE amplitudes with average amplitudes obtained from normal hearing persons. It does not obtain "threshold" information, as does the conventional pure tone audiogram.

2.5.2 The I/O Function

The second form of DPOAE measurement, namely the I/O function, can be used to determine the dynamic range of the distortion generation process (Lonsbury-Martin & Martin, 1990). This procedure described the growth of DPOAE amplitude at a constant frequency (Lonsbury-Martin, 1994). An I/O function can be obtained when the frequencies of the primaries are kept constant and the loudness levels are being changed (Norton & Stover, 1994).

The threshold of a DPOAE depends almost entirely on the noise floor and the sensitivity of the measuring equipment whereas the DPOAE amplitude is greatly influenced by the frequency ratio and decibel ratio of the primaries (Martin et al., 1990b; Norton & Stover, 1994).

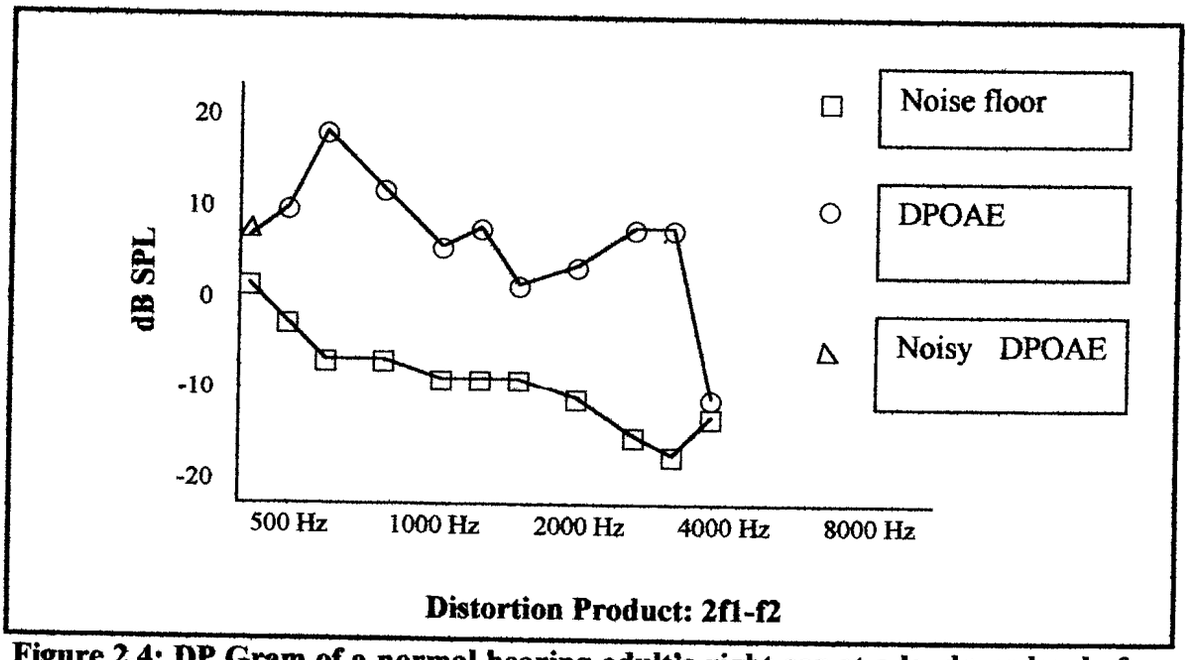

Figure 2.4: DP Gram of a normal hearing adult's right ear at a loudness level of L1=65 dB SPL, L2=55 dB SPL, in the frequency region of 2f1-f2 from 406 Hz to 4031 Hz.

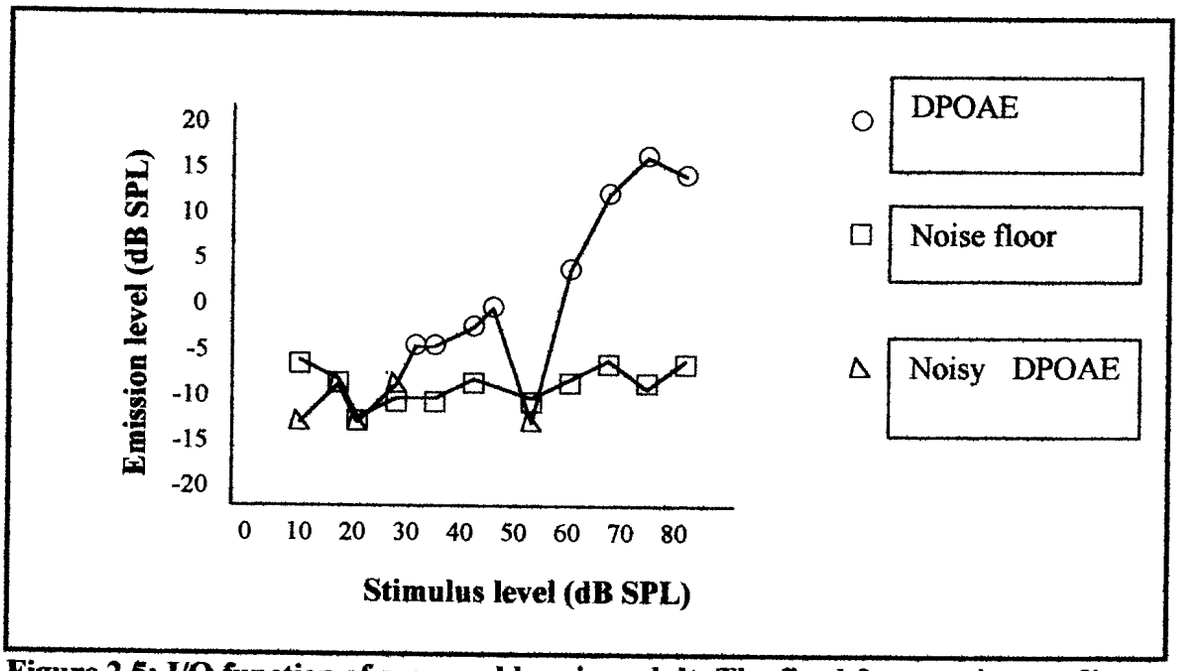

Figure 2.5: I/O function of a normal hearing adult. The fixed frequencies are f1= 1660Hz, f2= 2000 Hz and the loudness levels vary from 10 dB to 80dB SPL (Norton & Stover, 1994:457).

To determine the normalcy of an I/O function, the detection threshold (i.e. the stimulus level where the DPOAE reaches a pre-determined criterion level, for example 3 dB, above the noise floor) is compared to average detection thresholds of normal hearing individuals (Lonsbury-Martin & Martin, 1990). Figure 2.5 illustrates an I/O function for a normal hearing adult. The DPOAE threshold should not be confused with the pure tone audiogram threshold, and can not be directly compared (Norton & Stover, 1994).

There is not yet clear consensus on the best testing procedure to identify normal and impaired ears. Gorga, Stover, Neely and Montoya (1996) conducted a study to determine critical values and levels of confidence for clinical DPOAE measurement and used only I/O functions where DPOAE thresholds were determined. Gorga, et al. (1993), on the other hand, used only DP Grams to investigate DPOAE responses in normal hearing and hearing impaired subjects.

Most researchers, however, use a combination of the two procedures or perform both procedures separately. Martin, Ohlms, Franklin, Harris and Lonsbury-Martin (1990), Spektor et al., (1991) and Smurzynski, Leonard, Kim, Lafreniere, Marjorie and Jung, (1990) performed both procedures in their studies separately, while Moulin et al. (1994), and Kimberley and Nelson (1989) combined the two procedures in an interesting way. Moulin et al. (1994), conducted several DP Grams but at different loudness levels in 10 dB steps, therefore gaining almost the same information as performing both procedures. Kimberley and Nelson (1989), on the other hand, measured several I/O functions but at eight different frequencies.

"Thus it remains unclear which test protocol is more diagnostically effective and whether DPOAE amplitude or DPOAE threshold is the better indicator of cochlear status" (Stover et al., 1996a: 957). Not knowing which procedure is currently the most applicable in the areas of diagnostic effectivity, it seems plausible to gain as much information as possible by combining the two procedures or performing both separately (Kimberley & Nelson, 1989; Martin, et al., 1990a; Smurzynski et al., 1990).

Now that the distortion product with all its complex parameters, instrumentation and measurement procedures is fully understood, other issues such as prevalence, age and gender effects, frequency specificity and their relation to auditory sensitivity can be discussed.

2.6 Prevalence of DPOAEs in Normal Hearing and Hearing Impaired Populations

Many studies provided comprehensive descriptions of the prevalence of DPOAEs in normal hearing and hearing impaired subjects. There is growing evidence that DPOAEs can be measured in essentially all normal hearing subjects (Gorga et al., 1996; Kimberley & Nelson, 1989; Kimberley et al., 1994; Lonsbury-Martin et al., 1990; Smurzynski et al., 1990; Spektor, et al., 1991). However, optimal stimulus parameters are required for optimal measuring procedures. Gorga, et al. (1993) for example, indicated the prevalence of DPOAEs in normal hearing subjects to be 95%, but used equilevel primary frequencies of 75 dB SPL. When primary frequencies with a frequency ratio of 1.22 and loudness levels of L1>L2 by 10-15 dB are used, it can

be expected to measure recordable DPOAE responses in 99-100% of normal hearing subjects with pure tone levels 0-10 dB HL (Martin et al., 1990b; Moulin et al., 1994; Vinck, Vel, Xu & Van Cauwenberge, 1995).

Popelka, Karzon and Arjmand (1995) investigated prevalence of DPOAEs for low level stimuli in premature normal hearing neonates and concluded that DPOAE I/O functions for low level stimuli produced the same results as those reported for adults. These results have important implications for developing the use of DPOAEs to accurately estimate cochlear function in this population.

In humans, DPOAE levels typically vary from –20 dB SPL to +20 dB SPL and are typically 40-60 dB below the level of the eliciting stimuli (Kimberley & Nelson, 1989). Probst and Hauser (1990) found DPOAE levels to be 60-70 dB below the level of the stimuli but used only one high level of input stimuli namely L1 = 73 dB and L2 = 67 dB. Kimberley and Nelson (1989), on the other hand, tested DPOAEs over a range of 50 dB from 30 dB to 80 dB and therefore could elicit DPOAEs at lower levels.

In some cases, the DPOAE level may be only 10-20 dB less than the primaries. This interesting phenomenon can be observed when the DPOAE frequency corresponds with a spontaneous otoacoustic emission (Moulin et al., 1994). When a normal hearing ear exhibits a spontaneous otoacoustic emission and DPOAEs are measured in that ear close to the SOAE (within 50 Hz), the distortion product may be enhanced (Probst & Hauser, 1990).

In contrast to other emission types, the distortion product is the only emission type that has been measured in hearing impaired ears (Lee et al., 1993). In human pathology, however, considerable variation in DPOAE prevalence has been found. This variation is partly due to the numerous different stimulus parameters used in many of the studies, making a comparison between studies somewhat difficult (Gorga et al., 1996). When low intensity primaries are used, the distortion product can be measured in ears with a hearing loss of up to 30 dB (Avan & Bonfils, 1993). With high level intensities of the primaries (>60 dB), DPOAEs have been measured in ears with a hearing loss of up to 65 dB HL (Moulin et al., 1994). Many researchers agree that the distortion product can be measured in hearing impaired ears with pure tone thresholds between 50-60 dB HL (Lonsbury-Martin & Martin, 1990; Moulin et al., 1994; Ohlms, Lonsbury-Martin & Martin, 1990; Spektor, et al., 1991).

It should be noted that this hearing impairment should be of a sensorineural nature (Zhang & Abbas, 1997). The distortion product depends on optimal transmission through the middle ear (Osterhammel, Nielsen & Rasmussen, 1993). DPOAEs have to perform a "twofold pass" through the middle ear. This means that the stimulus sound coming to the cochlea is highly dependent on the forward transfer function of the middle ear mechanism. Middle ear functioning also influences the cochlear response that is transferred back through the middle ear system (Hall III, Baer, Chase & Schwaber, 1993). It is therefore very important to determine the status of the middle ear before any interpretation of DPOAE findings can be attempted (Kemp et al., 1990).

Moulin et al. (1994) attempted to explain some of the reasons why DPOAEs can be measured in hearing impaired ears while all the other emission types are absent. The first explanation discusses the nature of the stimulus needed to elicit a response. The energy carried by a short transient stimulus (as in the case of TEOAEs) cannot be compared to the continuous stimulus of two pure tones, used to elicit a DPOAE. The continuous stimulus used to generate a DPOAE carries more energy at specific places in the cochlea, whereas the transient stimulus used to elicit a TEOAE is a short duration click and the energy is spread out across the whole cochlea. According to Moulin et al. (1994), this difference in stimulus type may account for the differences of OAE occurrence in ears with a hearing loss.

Another hypothesis described by Moulin et al. (1994) implies that in some ears with hearing loss, there might be residual functioning outer hair cells that are able to generate a distortion product at a specific cochlear region. The amount of residual outer hair cells is however insufficient to elicit TEOAEs on broad regions of the basilar membrane.

Lastly, the third hypothesis speculates that DPOAEs elicited with high level stimuli might depend on a different generation mechanism than low level stimuli. It seems possible that DPOAEs recorded with low levels are more dependent on the outer hair cells than DPOAEs recorded with high level stimuli. The recording of TEOAEs is entirely dependent on the state of the outer hair cells (Martin et al., 1990a; Moulin et al., 1994).

Prevalence of DPOAEs might also be affected by other factors than hearing loss. The effect of age and gender on the prevalence of DPOAEs will be discussed next.

2.7 The Effect of Age and Gender on DPOAEs

Subject age and gender influence many aspects of auditory function (Hall III et al., 1993). Within the first decade after the discovery of auditory brainstem response (ABR), many studies were conducted to investigate the influence of age and gender. Significant differences were found between different age and gender groups. Ever since then, these two factors have been routinely taken into consideration in the interpretation of ABR results (Weber, 1994).

There is some debate about the effect of age on distortion product otoacoustic emissions. Some authors found statistically significant decreases in amplitudes of other emission types such as TEOAEs with increasing age (Norton & Widen, 1990). In the case of DPOAEs, it seems possible that age related differences could be attributed to sensitivity changes related with aging, rather than aging itself (He & Schmiedt, 1996).

Lonsbury-Martin et al. (1990) indicated that in the presence of normal hearing (pure tone thresholds lower than 10 dB HL), DPOAE amplitudes and thresholds, especially those associated with high frequency primary tones, were significantly correlated with the subject's age. The subjects ranged from 21-30 years of age. It should be noted however, that the authors described the audiograms of the 30 year old subjects as "exhibiting a high frequency hearing loss pattern" (Lonsbury-Martin et al. 1990:10)

with hearing thresholds around 10dB HL. The younger subjects had pure tone thresholds of 0-5 dB HL. The lower DPOAE amplitudes and thresholds found in the results of the 30-year-old subjects can therefore be partly explained by higher pure tone thresholds and not solely by the subject's age.

A more recent study by Karzon, Garcia, Peterein and Gates (1994) investigated DPOAEs in the elderly to determine the age effect on DPOAEs. DPOAE results of 71 elderly volunteers, ranging from 56-93 years were compared to DPOAE results of normal hearing young adults, age 19-26 years. The authors found that the amplitudes of DPOAEs did not increase significantly with age, when adjusted for pure tone levels. "Although DPOAEs are reduced with age, this effect is largely mediated by age-related loss of hearing sensitivity." (Karzon et al., 1994:604). Avan and Bonfils (1993) confirmed this viewpoint and stated that many of the age related effects were due to high frequency hearing losses even when subjects were "normal" within their age category. He and Schmiedt (1996) also stated that when pure tone thresholds are controlled, there is not a significant aging effect on DPOAE amplitudes.

It would therefore seem that many authors agree that the negative correlation between DPOAE levels and age is due to changes in hearing threshold associated with aging rather than age itself (Avan & Bonfils, 1993; He & Schmiedt, 1996; Karzon et al., 1994; Kimberley et al., 1994; Nieschalk, Hustert & Stoll, 1998).

Another potentially relevant factor may be the influence of gender on the prevalence of distortion product otoacoustic emissions.

Gender differences have been reported in other emission types. Cacace, McClelland, Weiner and McFarland (1996) reported spontaneous otoacoustic emissions to be more prevalent in females than males and higher incidence of SOAEs in right ears than left ears. Hall III et al. (1993) indicated that TEOAE amplitudes are significantly larger for females than males.

Lonsbury-Martin et al. (1990) conducted a study to investigate basic properties of the distortion product including the effect of gender on the prevalence of DPOAEs. A comparison of DPOAE amplitudes and thresholds failed to reveal any significant differences except at 4 kHz. Women revealed significantly lower DPOAE thresholds at 4 kHz (about 10 dB lower). The pure tone audiometry thresholds for men and women at 4 kHz were the same. Gaskill and Brown (1990) and Cacace et al. (1996) reported that DPOAEs were significantly larger in female than male subjects tested in the frequency range of 1000- 5000Hz. Both studies however, indicated that the female subjects in their studies had more sensitive auditory thresholds than the males (an average of 2.4 dB better). The differences found between the two groups could therefore not be explained by gender only.

Cacace et al. (1996) attempted to explain some of the reasons why the females had higher amplitudes than the males in the higher frequencies. One reason is the existence of a spontaneous otoacoustic emission (SOAE) in conjunction with DPOAE measurement. Several authors described the effect that a SOAE could have on a DPOAE (Kulawiec & Orlando, 1995; Moulin et al., 1994; Probst & Hauser 1990). If a spontaneous emission exists within 50 Hz of the primary frequencies used to elicit a DPOAE, the spontaneous emission could enhance the DPOAEs amplitude

significantly under certain experimental conditions (Kulawiec & Orlando, 1995; Probst & Hauser, 1990). Spontaneous emissions are more prevalent in females than in males and could therefore possibly explain the higher DPOAE amplitudes in females.

This amplitude amplification effect that SOAEs have on DPOAEs can not always clearly be seen. Cacace et al. (1996) reported that no systematic peaks or notches could be observed in DPOAE responses in the presence of a spontaneous otoacoustic emission in any of the subjects they tested. The mere presence of a SOAE in a frequency region close to the primaries can not be taken as evidence of amplitude amplification. It is however so, that this gender effect is greatly reduced when only subjects with no SOAEs are considered.

Gender effects on DPOAEs are apparently limited to minor differences in DPOAE amplitudes and thresholds.

The fact that the distortion product is present in normal and hearing impaired ears and has only minimal age and gender effects makes it the emission type that has great potential as a new test of auditory function. In any test of auditory function, one very important factor to consider is the frequency specificity with which measurements can be made. The distortion product's frequency specificity warrants some discussion.

2.8 Frequency Specificity of DPOAE Measurements

Many authors reported DPOAE measurement to be the most frequency-specific type of otoacoustic emission currently available (Durrant, 1992; Lee et al., 1993; Nielsen,

et al., 1993; Probst & Hauser, 1990; Rasmussen, Popelka, Osterhammel & Nielsen, 1993; Spektor, et al., 1991).

The explanation for this frequency specificity lies with the stimuli used to elicit different types of otoacoustic emissions. The stimulus used to elicit a TEOAE, such as a click or tone burst, has broad spectral qualities and stimulates broad regions of the basilar membrane simultaneously (Lee et al., 1993). The stimuli used to elicit DPOAEs are two pure tones that stimulate the basilar membrane at two discrete locations. DPOAEs can therefore be elicited at almost any selected frequency since it depends on the frequencies of the primaries (Lonsbury-Martin et al., 1990; Probst & Hauser, 1990). The measurement of otoacoustic emissions at the lower frequencies are always more difficult due to interference of low frequency noise such as breathing and swallowing. According to Stover et al. (1996a), the distortion product can differentiate normal from impaired ears for frequencies as low as 707 Hz (or 725 Hz according to Bonfils, Avan, Londero, Trotoux & Narcy, 1991).

One very interesting study by de Boer (1983) (cited in Avan & Bonfils, 1993), investigated frequency specificity of DPOAEs by measuring the number of outer hair cells (OHC) contributing to a DPOAE on the basilar membrane of a guinea-pig cochlea. The author concluded that about 1mm on the basilar membrane (which represents about a third octave in the guinea-pig cochlea) contributed to a single DPOAE. The number of outer hair cells (OHC) involved is of course depending on the level of stimuli used to elicit the DPOAE. For loudness levels over 60 dB SPL, broader regions of outer hair cells are involved in the distortion product emission. Mills, (1997) refers to this phenomenon as "active" and "passive" emissions. In the

case of high stimulus levels, broader areas of the basilar membrane are stimulated. With high intensity stimuli, phase relationships between travelling waves that generated emissions evoke a different type of emissions, namely a "passive" emission. A passive emission is less frequency-specific and has less correspondence to auditory sensitivity. When low intensity primaries are used, it seems that only a very small number of OHC contribute to the distortion product emission. The fact that such a small number of OHC contributes to the generation of a DPOAE evoked at low intensities is in itself an indication of the frequency specificity with which measurements can be made.

There is, however, not clear consensus on which frequency variable of the DPOAE correlates best with the region on the basilar membrane that is responsible for the measured distortion product. In other words, does a DPOAE indicate the state of the OHC on the basilar membrane in the region of the f1 frequency, the f2 frequency, the geometric mean of the two primary frequencies (GM) or at the 2f1-f2 frequency? Many authors also disagree on which frequency variable of the DPOAE should be compared to the pure tone threshold (PTT).

According to research conducted by Kimberley et al., (1994) and Harris et al., 1989, the features that best correlate with pure tone thresholds (PTTs) are those associated with f2 values close to the pure tone threshold frequency. The distortion product, according to these authors, is generated very close to the f2 cochlear place.

Other studies support the notion that the generation of the distortion product correlates best with the cochlear place near the geometric mean (GM) of the primaries (Bonfils

et al., 1991; Lonsbury-Martin & Martin, 1990; Martin et al., 1990b). These authors concluded that the acoustic distortion product at 2f1-f2 should be correlated with PTTs near the GM of the primaries.

According to Moulin et al. (1994) no attempt has been made to compare the correlations between DPOAEs and PTTs measured at the GM frequency with the correlations between DPOAEs and PTTs measured at the f2 frequency, because the GM and f2 frequencies are too close.

Avan and Bonfils (1993) discussed factors that contribute to the difficulty of determining which frequency region of the basilar membrane corresponds with the distortion product. First, the presence of a simple correlation between a DPOAE parameter and a PTT at some frequency does not mean that the DPOAE is a valid predictor of hearing loss at that frequency. It would only be valid if auditory thresholds were independent variables, which is not true in typical sensorineural hearing losses (Avan & Bonfils, 1993; Moulin et al., 1994). Second, DPOAEs may be generated at any place where nonlinear interactions between travelling waves f1 and f2 are possible and that basal spreading of such places is not precisely known, especially for high intensity stimuli (Avan & Bonfils, 1993). It seems that high level stimuli causes a spread of energy along the basilar membrane and causes a lack of frequency specificity (Bonfils et al., 1991; Harris & Probst, 1991; Moulin et al., 1994).

It is therefore not clear, whether it is in fact f1, f2, the GM frequency or 2f1-f2 frequency that is actually being stimulated on the basilar membrane. Most authors

agree that DPOAEs appear to be generated in the region stimulated between the primary frequencies, rather than the frequency at the distortion product (Harris et al., 1989; Kimberley et al., 1994; Martin et al., 1990b; Moulin et al., 1994; Smurzynski et al., 1990). To illustrate this concept: if f1 = 1000 Hz and f2 = 1187 Hz (the frequency ratio 1.2), then the GM = 1093 Hz and the 2f1-f2 distortion product 812 Hz. According to all the above authors, the basilar membrane region that is being stimulated in this case, is between f1 = 1000 Hz and f2 = 1187 Hz. Although the question of precise frequency stimulation on the basilar membrane is still not solved, it is clear that the narrow region that is being stimulated on the basilar membrane is quite frequency specific.

"Compared to other classes of otoacoustic emissions, distortion product emissions are highly frequency-specific in a manner easily controllable by stimulus conditions. Therefore, they are of clinical interest as a means by which cochlear activity at specific sites along the basilar membrane may be monitored in a simple non-invasive manner." (Rasmussen et al., 1993:22).

Another very important aspect of DPOAEs that received much attention in the literature is the relationship of the distortion product to auditory sensitivity. This is probably the single most important factor in the development of DPOAEs as an objective test of auditory function and warrants a detailed discussion.

2.9 Relation of the Distortion Product to Auditory Sensitivity

Otoacoustic emissions reflect the status of the outer hair cells on the basilar membrane. Pure tone behavioral thresholds not only reflect the physiology of the auditory system at numerous parts, but also involve auditory perception (Lee et al., 1993). Despite these fundamental differences, many studies that attempted to describe the relationship of the distortion product to auditory sensitivity came to the same conclusion. It seems that there is a positive relationship between DPOAEs and hearing thresholds. DPOAEs are elevated in subjects with mild hearing losses and are absent when hearing sensitivity is moderately or significantly impaired (Avan & Bonfils, 1993; Durrant, 1992; Gorga, et al., 1993). It is very important to understand the exact relationship between DPOAEs and pure tone thresholds. "An understanding of that relationship is essential if DPOAE measurements is to gain acceptance as an objective diagnostic test in audiologic and otologic settings" (Lee et al., 1993:18).

Early studies of the relationship between otoacoustic emissions and hearing thresholds investigated the relationship of TEOAEs to pure tone thresholds. These studies found only a categorical relationship, that is, ears with pure tone thresholds < 30 – 40 dB HL generated emissions and ears with greater hearing losses did not (Bonfils, Uziel & Pujol, 1988; Collet, Gartner, Moulin, Kauffmann, Disant, Morgon, 1989; Kemp, 1978).

An early study by Kimberley and Nelson (1989) investigated the correlation between distortion product otoacoustic emissions and hearing threshold. Subjects were selected without regard to age, sex, and etiology of hearing loss or pattern of hearing loss. The

frequency ratio of the primaries (f2/f1) was 1.2. Distortion product otoacoustic emissions were measured over a stimulus range from 30 dB SPL to 80 dB SPL in 6 dB steps. DPOAE I/O functions were measured covering the frequency range from 700 Hz to 6000 Hz. Kimberley and Nelson (1989) then plotted emission thresholds and auditory thresholds of 21 ears on a scattergram. (Emission thresholds represent the stimulus level required to just raise the emission above the noise floor.) Kimberley and Nelson's (1989) scattergram can be viewed in Figure 2.6. The linear fit shown with the data points has a slope of 1.0 and a correlation coefficient of .86.

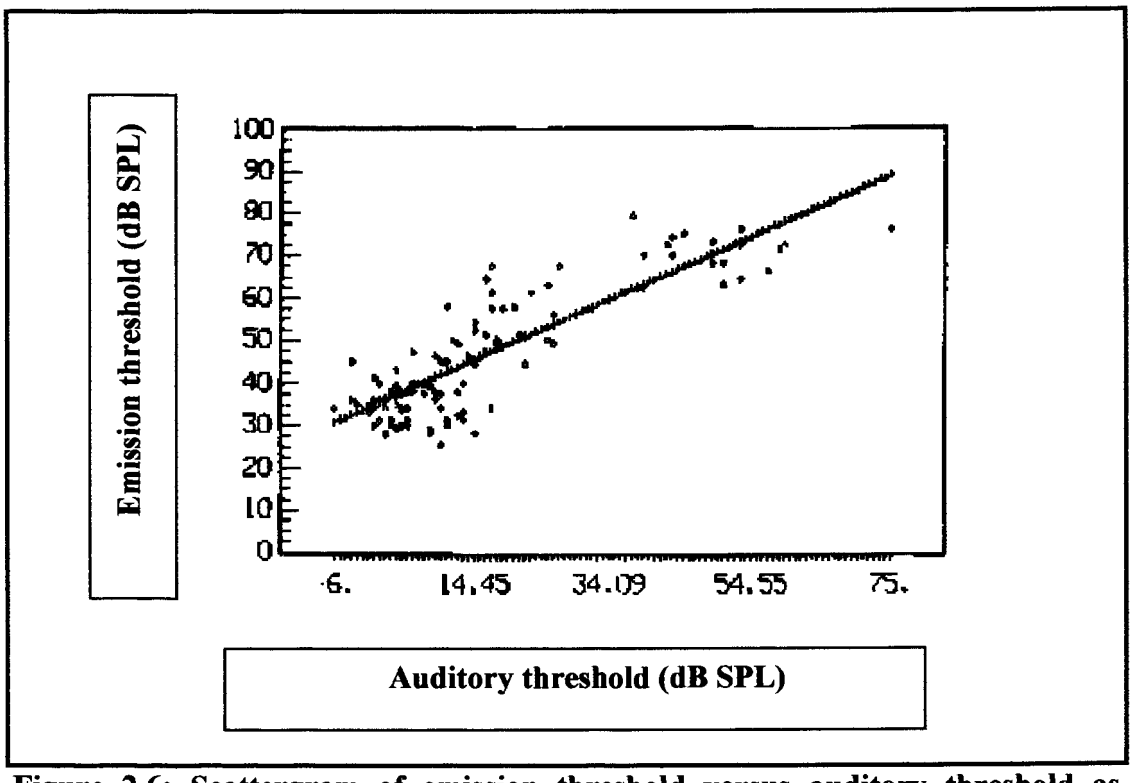

Figure 2.6: Scattergram of emission threshold versus auditory threshold as measured by Kimberley and Nelson, (1989:368).

The results displayed in this scattergram in Figure 2.6 suggest that DPOAE measurements can predict auditory thresholds within 10 dB over a range from 0 dB

SPL to 60 dB SPL. The authors claim that this was the first report of such a precise correlation.

Studies that are more recent continued to investigate the correlation between DPOAE responses and pure tone thresholds. The primary goal of these investigations was to develop another objective tool for the evaluation of "difficult-to-test" populations or mass hearing screening (Gorga, et al., 1993; Kimberley et al., 1994; Moulin et al., 1994; Stach, Wolf & Bland, 1993). A few of these studies would be reviewed.

Gaskill and Brown (1990) investigated the behavior of the acoustic product in humans and its relation to auditory sensitivity. They concluded that with certain optimal stimulus parameters (stimulus levels below 60 dB SPL; L1>L2 by 15 dB; f1/f2 = 1.225), half of the subjects showed a statistically significant correlation between DPOAE results and auditory sensitivity at the corresponding f1 stimulus. According to Gaskill and Brown (1990), there are probably differences in the mechanisms responsible for producing DPOAEs using high versus low-level stimuli. High level DPOAEs may not correspond well to hearing sensitivity. DPOAEs generated with low intensity stimuli approximate hearing thresholds more closely (Bonfils et al., 1991; Gaskill & Brown, 1991; Harris & Probst, 1991).

Avan and Bonfils (1993) confirmed these findings. The authors conducted a study on DPOAEs in 25 normal hearing and 50 hearing impaired ears. Their results indicated that the DPOAEs evoked by low intensity primary tones (below 62 dB SPL) were strongly correlated with the auditory threshold at the mean frequency of f1 and f2 and that DPOAEs disappear for hearing losses larger than about 30dB. This research also

suggests that when low intensity primaries are used, DPOAEs provide frequency-specific information on the local cochlear state of the primaries.

Gorga, et al. (1993) measured DPOAEs in normal hearing and hearing-impaired human subjects. They investigated the extent to which DPOAEs can be used to correctly distinguish between normal and impaired hearing. DPOAE amplitude was able to distinguish between normal and impaired subjects at 4000 Hz, 8000 Hz and to a lesser extent at 2000 Hz. At 500 Hz, performance was no better than chance, due to high biological noise levels such as breathing and swallowing. They concluded that DPOAE measurement could successfully be implemented to identify high frequency hearing loss, but that it was not an accurate predictor of hearing loss in the lower frequencies.

A study by Bonfils et al. (1991) on low frequency audiometry by distortion product otoacoustic emissions revealed interesting findings. Two different experiments were conducted. In the first experiment, the frequency ratios varied from 1.06 to 1.38 by steps of 0.02 to determine the most suitable frequency ratio for low frequency testing. Equilevel stimuli ranging from 84 dB SPL to 30 dB SPL were delivered in 6 dB steps to determine the most suitable loudness level for low frequency testing. In the second experiment, the frequency ratio was fixed at 1.22 and equilevel primaries ranging from 84 dB SPL to 30 dB SPL were delivered over a geometric mean frequency range of 485 Hz to 1000 Hz. Two important points were derived from this study. First, I/O functions tested with low level primaries (intensities below 60 dB SPL) and frequency ratios around 1.2 showed saturated growth. When primary intensities exceeded 66 dB SPL or when frequency ratios were greater than 1.3 or lower than 1.14, the input

output functions became linear without any clear saturating plateau. The authors concluded that DPOAEs generated by primary intensities below 60 dB SPL probably have their origin in the outer hair cells. With high level stimuli however, it is probable that only passive properties of the cochlea contribute to the emission. The high level versus low level testing is therefore just as important in low frequency testing. The second important factor derived from this study is variations of DPOAE properties as a function of DPOAE frequency. It seems that for primary intensities below 60 dB SPL, DPOAEs at frequencies lower than 725 Hz (DPOAE frequency of 512.5 Hz) were absent or had no saturating portion. "As the saturating behavior of DPOAE input-output functions probably has its origin in the properties of the outer hair cells, these results suggest that active mechanisms are absent below 725 Hz in the human cochlea." Bonfils et al., (1991:1171). It seems that DPOAEs at frequencies lower than 725 Hz are generated by passive components in the cochlea. This could explain the absence of SOAEs and other evoked otoacoustic emissions below 725 Hz.

A study conducted by Stover et al., (1996a) examined the effect of the primary stimulus levels on the ability of DPOAE measurements to separate normal hearing from hearing impaired ears. Clinical decision theory was used to assess both DPOAE threshold and DPOAE amplitude as diagnostic indicators of hearing status. This research suggests that DPOAE threshold and DPOAE amplitude perform equally well in distinguishing normal from impaired hearing but DPOAE amplitude is more suited as a screening method due to shorter testing times.

Probst and Hauser (1990) performed similar research in 1990 and concluded that the measurement of DPOAE amplitude alone might fail to detect a mild hearing loss. To

determine hearing ability more accurately, more detailed measurements such as I/O functions with DPOAE thresholds should be performed.

Kimberley et al. (1994), tried to predict hearing status in normal and hearing impaired ears with distortion product otoacoustic emissions at 6 frequencies ranging from 1025 Hz-5712 Hz. They used a statistical technique known as discriminant analysis which attempts to determine which attributes (variables) such as DPOAE levels, age and gender are most significant in defining normal versus abnormal pure tone thresholds. After these discriminant functions were determined, they were applied to a new set of unfamiliar data to determine their predictive accuracy at each frequency. They found that the more attributes they included as being significant in the prediction of the data, the more the prediction of the data worsened. By including only 5-10 of the "best" variables, the prediction was at its best. Classification accuracy varied from 71% correct classification of normal hearing at 1025 Hz to 92% correct classification of normal hearing at 2050Hz. The lowest frequency evaluated was 1025 Hz where the worst performance was observed. Kimberley et al., (1994) concluded that DPOAE measures can reliably categorize pure tone thresholds as being normal or impaired in a population with varied cochlear hearing status.

A few other studies indicated positive relationships between DPOAEs and pure tone thresholds. Spektor, Leonard, Kim, Jung and Smurzynski (1991) reported a positive qualitative relationship between pure tone thresholds and DPOAE thresholds in 19 children (although these authors did not quantitatively correlate DPOAE thresholds with pure tone thresholds). It seemed that the configuration of the hearing loss correlated well with the frequency pattern of the DPOAEs. Lonsbury-Martin and

Martin, (1990) assessed DPOAEs in subjects with noise induced hearing loss. They found that DPOAE thresholds provide reasonably good estimates of hearing loss in cases where primary damage to the outer hair cells can be assumed (such as noise induced hearing losses). The authors found a relatively strong correlation between DPOAE thresholds and magnitude of hearing loss. In the subjects they examined, for every 1dB increase in DPOAE threshold, hearing level increased by 1dB. When DPOAE threshold was > 63 dB SPL, the accompanying hearing level was > 20 dB HL. Such a strong correlation between DPOAEs and pure tones in subjects with OHC pathology proves it as an efficient measurement of cochlear functioning. DPOAEs could potentially be successfully applied to other cochlear pathologies such as Meniere's disease and ototoxicity.

Conclusion: It seems that a certain set of stimulus parameters and conditions are needed to elicit DPOAEs that are comparable to pure tone thresholds. First, the frequency ratio should be close to 1.2 (Bonfils et al., 1991; Gaskill & Brown, 1991; Harris et al., 1989). Second, the loudness levels should preferably be 10-15 dB apart, with L1>L2 (Gaskill & Brown, 1991; Mills, 1997). Third, the loudness levels of the primaries seem to be a very important factor in DPOAE measurement and should not exceed 65 dB SPL (Bonfils et al., 1991; Gaskill & Brown, 1991; Mills, 1997). When primary intensities exceed 65 dB SPL, measurements are less frequency-specific and might not indicate true outer hair cell functioning but rather some passive reaction of the basilar membrane to the stimuli. Another aspect to keep in mind is the limited range in which low frequency DPOAEs can be elicited. According to Stover et al., (1996a) the lowest frequency to be tested with DPOAEs is 707 Hz or 725 Hz (Bonfils et al., 1991). Lastly, it seems that DPOAE amplitude is more suitable for screening

purposes (Gorga, et al., 1993; Stover, Neely & Gorga, 1996b) whereas information obtained from DPOAE I/O functions compare better with pure tone thresholds (Gorga et al., 1996; Kimberley & Nelson, 1989; Probst & Hauser, 1990).

There is therefore consistent qualitative and quantitative evidence that there is a relationship between behavioral pure tone thresholds and DPOAE thresholds (Lee, et al., 1993). "Although DPOAE output is not a direct measure of hearing sensitivity and may not follow the audiogram perfectly, it does demonstrate impressively good quantitative correlation with degree of hearing loss and good qualitative correspondence with configuration of hearing loss, at least for mild to moderate losses" (Durrant, 1992:43).

If DPOAEs were proven to be highly frequency specific, strongly correlated with pure tone thresholds and only slightly influenced by aspects such as age and gender, then why is there still so much controversy on its effectiveness to predict hearing ability accurately? These issues are discussed in the next section.

2.10 Limitations of Previous Studies Investigating Possible Correlation between DPOAEs and Pure Tone Audiometry

"While several investigators have studied the relationship between DPOAEs and pure tone thresholds, there have been no reports of a general rule that accurately predicts pure tone threshold on the basis of DPOAEs or any other features in large populations of ears with varying cochlear hearing losses. Defining such a predictive relationship, if one exists, could be of great clinical significance. A strong correlation between

DPOAEs and pure tone thresholds could provide important insights into how frequency-specific cochlear function relates to behavioral measures of auditory function (pure tone threshold)." (Kimberley et al., 1994:199).

Statistical methods used to date, such as multivariate (discriminant) analysis in the case of the study of Kimberley et al., (1994), but also in all the other studies previously discussed, indicated a correlation between DPOAE measurements and behavioral pure tones. These studies however, could not predict the actual pure tone thresholds given only the distortion product responses. "However, at the present time, there are no quantitative studies identifying a precise mathematical relationship such that behavioral thresholds may be accurately predicted. Additional research in this area is needed in order to predict behavioral thresholds from DPOAE threshold values." (Lee, et al., 1993:19).

To define such a relationship between two sets of data (DPOAE measurements and pure tone thresholds), a mathematical tool is needed that has excellent correlation finding capabilities, even in the case of a possible non-linear correlation. This mathematical technique should also be able to predict pure tone thresholds given only the distortion product responses. One such a mathematical tool, that has excellent correlation finding and prediction abilities, is a relatively new method of computational analysis called artificial neural networks. This new information processing technique is discussed in Chapter 3.

2.11 Summary

Distortion product otoacoustic emissions can be evoked by the simultaneous presentation of two pure tones. The emission is a third tone of frequency, produced internally and by the outer hair cells on the basilar membrane. The distortion product is affected by a large number of stimulus parameters including the frequencies and loudness levels of the primaries as well as frequency and loudness level ratios. DPOAEs can be recorded in virtually all normal hearing ears. The prevalence of DPOAEs are impaired in subjects demonstrating hearing loss and can be recorded in ears with a hearing loss of up to 65dB HL. The distortion product is relatively unaffected by age and gender effects. Many studies examining DPOAEs in hearing-impaired subjects concluded that DPOAEs correlate well with degree of hearing loss as well as configuration of hearing loss. The distortion product was also found to be highly frequency-specific and recordable in broad frequency areas as low as 707 Hz (Stover et al., 1996a). All those aspects indicated that DPOAEs might be the revolutionary new objective, non-invasive, rapid and accurate test of hearing that has been so long awaited. Many researchers studied the distortion product with the prime objective to develop a new diagnostic procedure for special populations such as neonates, infants and malingerers. Although most of the studies found a strong positive correlation between pure tones and DPOAEs, none of these studies could formulate the precise mathematical relationship between these two measurements with conventional statistical methods. It seems that in order to predict pure tone thresholds with DPOAEs a special mathematical model with excellent correlation finding and prediction capabilities is needed. One such mathematical model that might prove to be able to solve this complex problem is an artificial neural network.