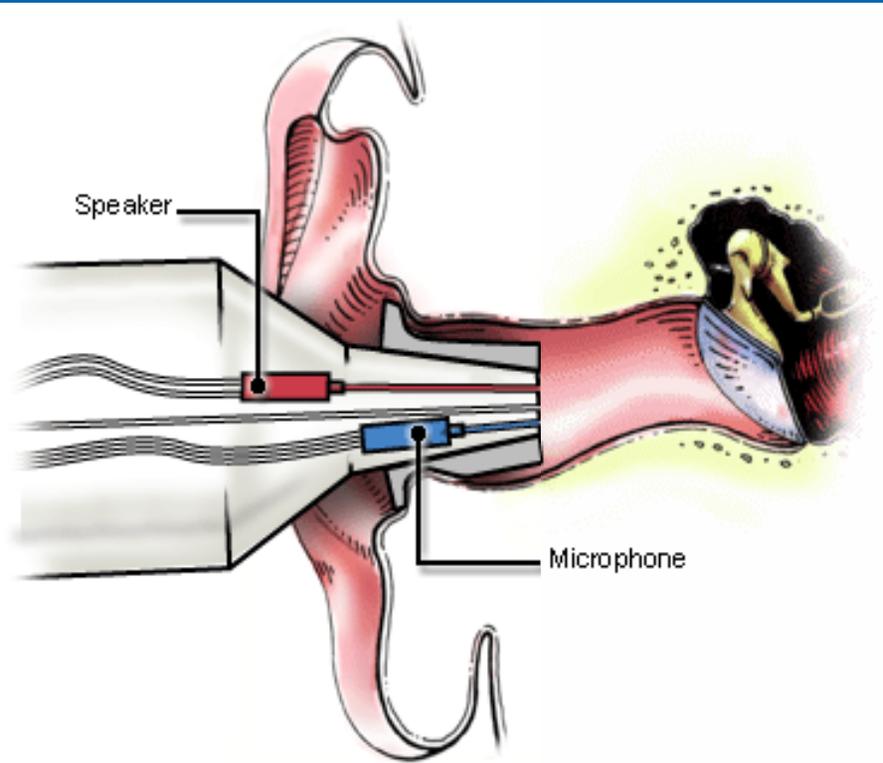


Use of stimulus-frequency otoacoustic emissions to evaluate cochlear function



Dawn Konrad-Martin, PhD

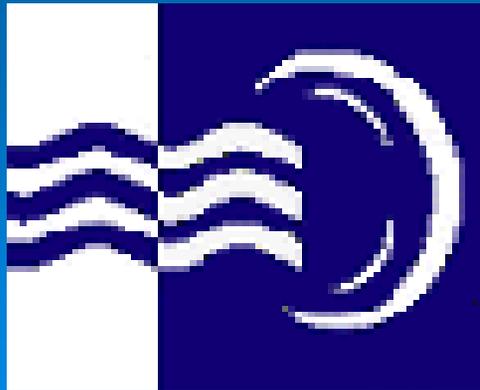
&

Kim Schairer, PhD

*Drawing by S. Blatrix from "promenade around the cochlea"
EDU website www.cochlea.org by Rémy Pujol et al., INSERM
and University Montpellier 1*

**National Center for
Rehabilitative Auditory Research**
Portland VA Medical Center
Portland, Oregon

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Omaha, NE

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Outline

- I. Learner Outcomes
 - II. Anatomy & Physiology
 - III. OAE Classification
 - IV. SFOAE Measures of Cochlear Function
 - Frequency Tuning
 - Response Growth
 - V. Summary
- 

I.

Learner Outcomes

- Underlying mechanisms of OHC electromotility
- Clinical importance of OHC electromotility
- How OAEs reflect OHC electromotility
- Different types of OAEs
- How SFOAEs can be used to estimate BM tuning
- How SFOAEs can be used to estimate BM response growth

II.

Anatomy & Physiology

A Brief Overview

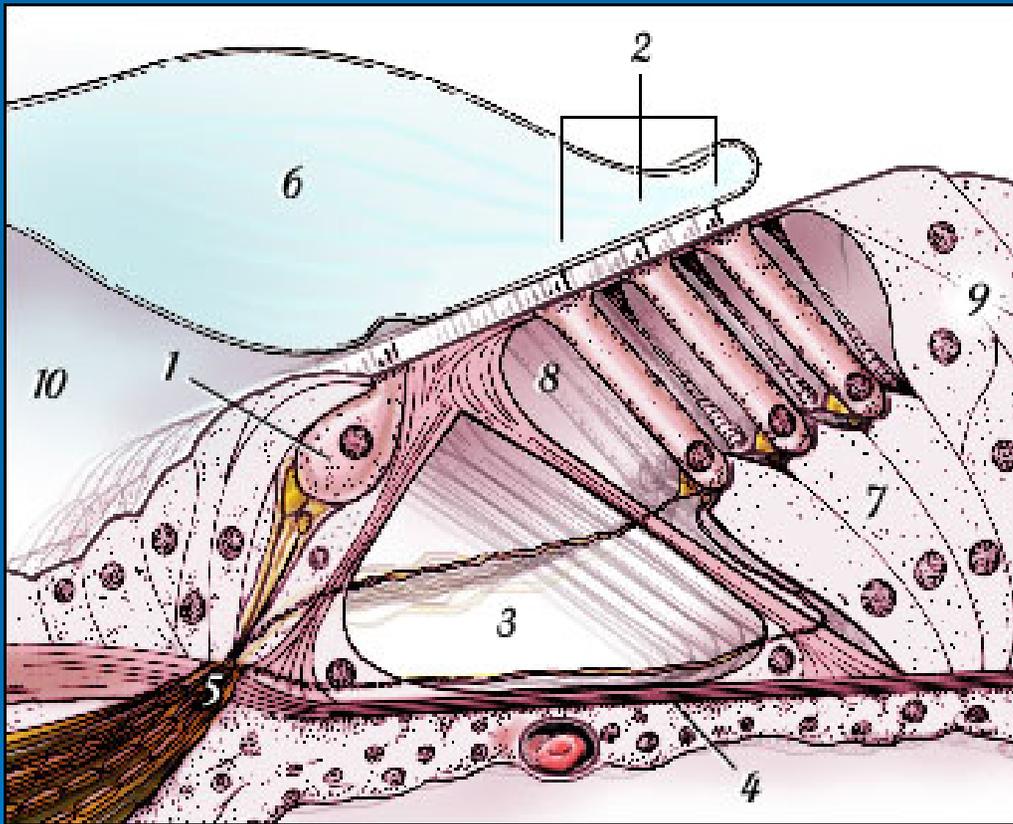


Mammalian Hearing

- Can distinguish between tones that are very close in frequency (frequency selectivity)
- Can distinguish large range of intensities (dynamic range)

These abilities are due in large part, to a better sensitivity toward soft sounds imparted by the cochlear amplifier

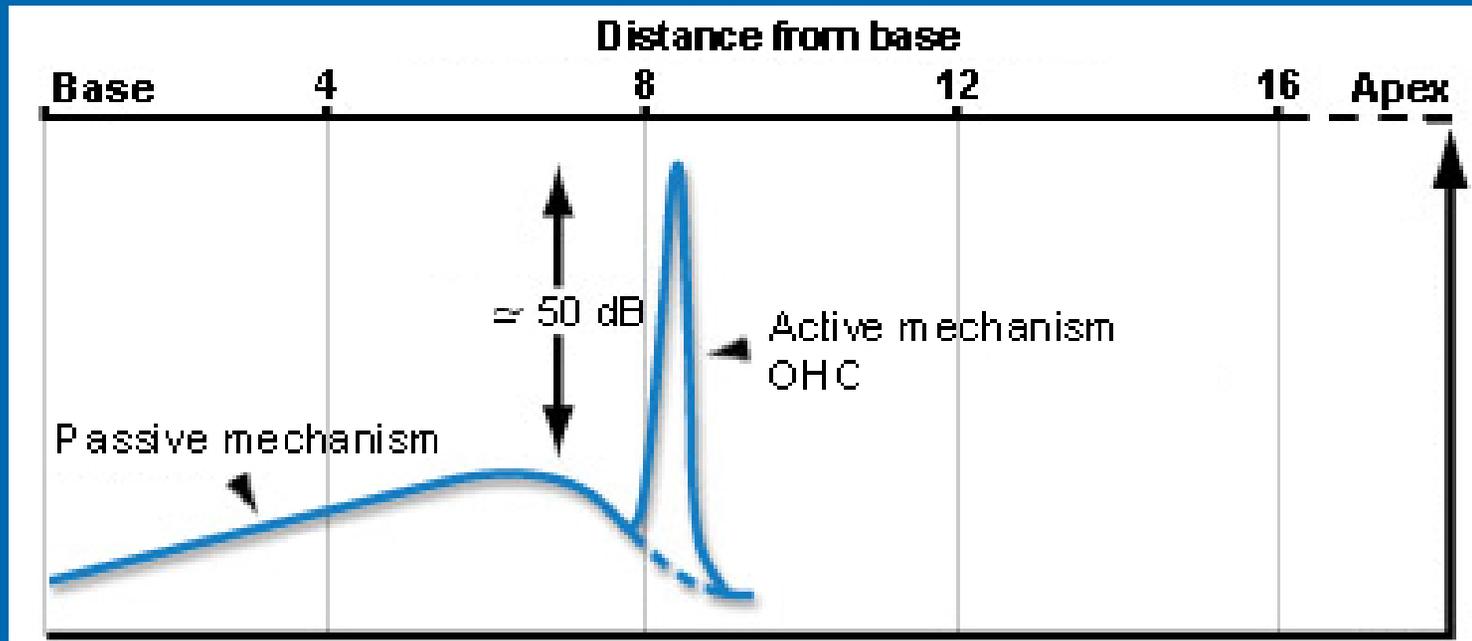
The Organ of Corti



OC sits on the Basilar Membrane
Pressure waves enter the ear
Vibrate the organ of Corti
Causes “shearing forces”
Deflects stereocilla of hair cells near CF

Cross section at a particular CF

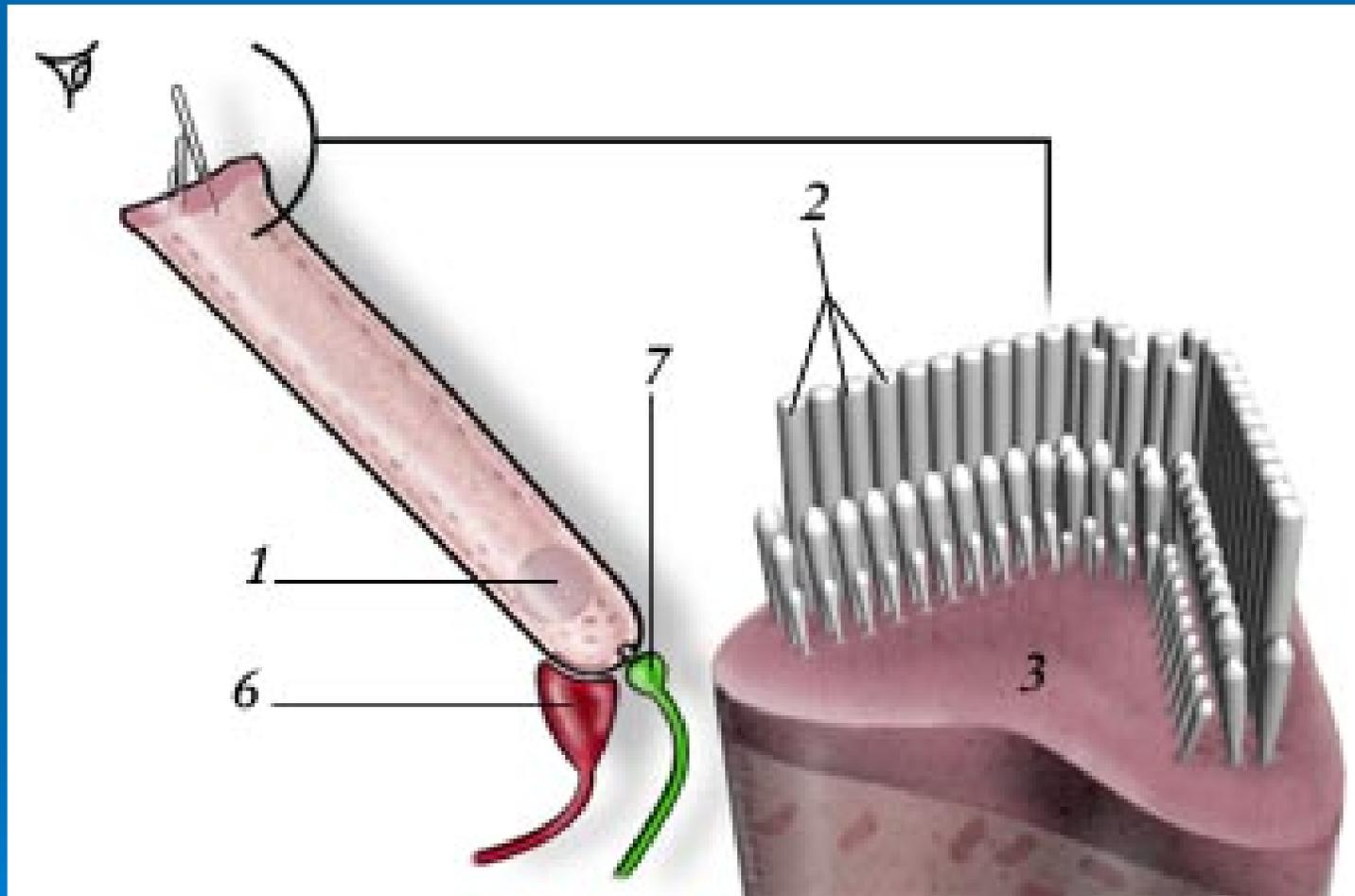
Mammalian Hearing



The cochlear amplifier aids sensitivity in a frequency specific way

Images by M. Lenoir from "promenade around the cochlea" EDU website www.cochlea.org by Rémy Pujol et al., INSERM and University Montpellier 1

Stereocillia Deflection



Drawing by S. Blatrix from "promenade around the cochlea" EDU website www.cochlea.org by Rémy Pujol et al., INSERM and University Montpellier 1

Cochlear Amplifier

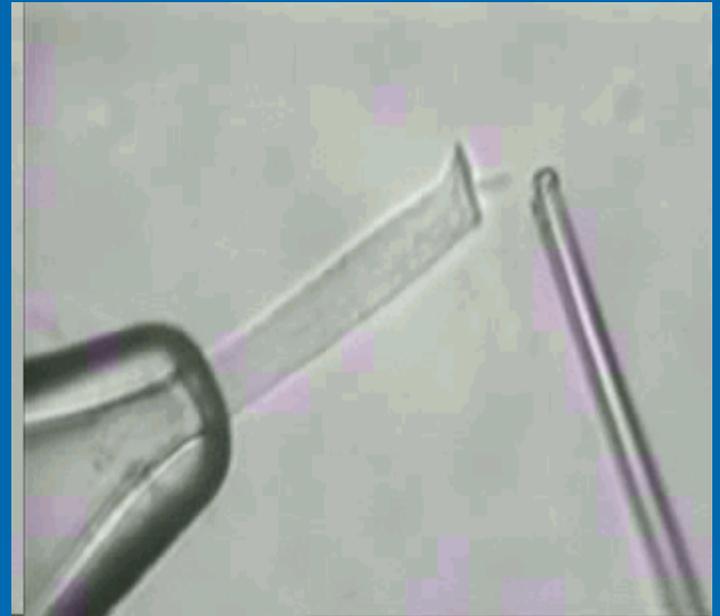
- Involves Outer hair cell motility.
- OHC movements feed energy into basilar membrane vibrations to certain sounds.
 - Low intensity sounds
 - Frequencies near CF
- Amplified vibration generates inner hair cells synaptic transmissions.
- Triggers action potentials in auditory nerve fibers.



Drawing found at <http://www.bcm.edu/oto/research/cochlea/> by Brownell, William et al., Bobby R. Alford Department of Otorhinolaryngology and Communicative Sciences

Cochlear Amplifier

- Early evidence of OHC motility came from Bill Brownell (Brownell et al., 1985)
- Using experiments like this one by David He.
- Electrical voltage is applied to the base of an OHC.
- A glass rod records changes associated with hair cell movement.



OHC Electromotility

The process where the length of a OHC changes with intracellular voltage

- Electromotility happens by virtue of a unique OHC lateral wall structure (plasma membrane, cytoskeleton, and subsurface cisternae).
- Lateral wall of the OHC plasma membrane is studded with motor proteins.
- Individual motors coupled through the cytoskeleton create net changes in hair cell length.
- Motors thought to be the Prestin protein (Zheng, Shen, He et al., 2000)

Source of voltage Drive?

Reviewed in Withnell, Shafer, Lilly, 2002.

1. Receptor Potential

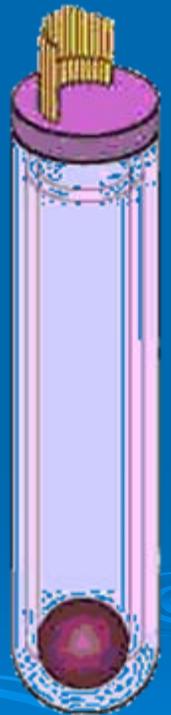
- might not work at high frequencies

2. Extracellular voltage drive

- Electrical fields generated within the cochlea by differences in the charges of (many) OHCs and the endolymph.
- Contributions by many OHCs (Dallos & Evans, 1995)

3. Electrical Energy as drive

- Membrane filtering may not matter
- Length decreases increase motor density



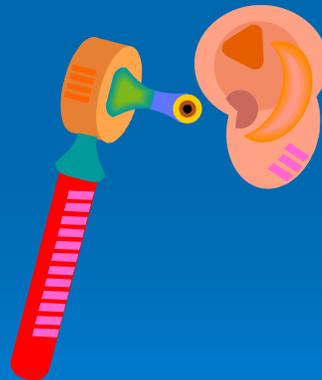
Other “active” mechanisms?

- In non-mammalian vertebrates, active bundle movements appear responsible for OAEs.
- Two types, both have speed limitations
 1. Actin-myosin interactions change tip link tension
 2. Calcium-mediated tip link closure changes tension
- In mammals these may shape the hair cell receptor potential.

Rationale for OAE Use

- OAEs may reflect changes in cochlear amplifier gain and related deficits in sensitivity, tuning and response growth because...
 - OAEs are by-products of amplified basilar membrane motion
 - Sources of cochlear amplifier include OHC system
 - OHCs are physiologically vulnerable
- 
- The background of the slide features several sets of concentric circles in a lighter shade of blue, resembling ripples in water. These circles are scattered across the lower half of the slide, with a larger set on the right and several smaller ones on the left and bottom.

III. OAE Classification

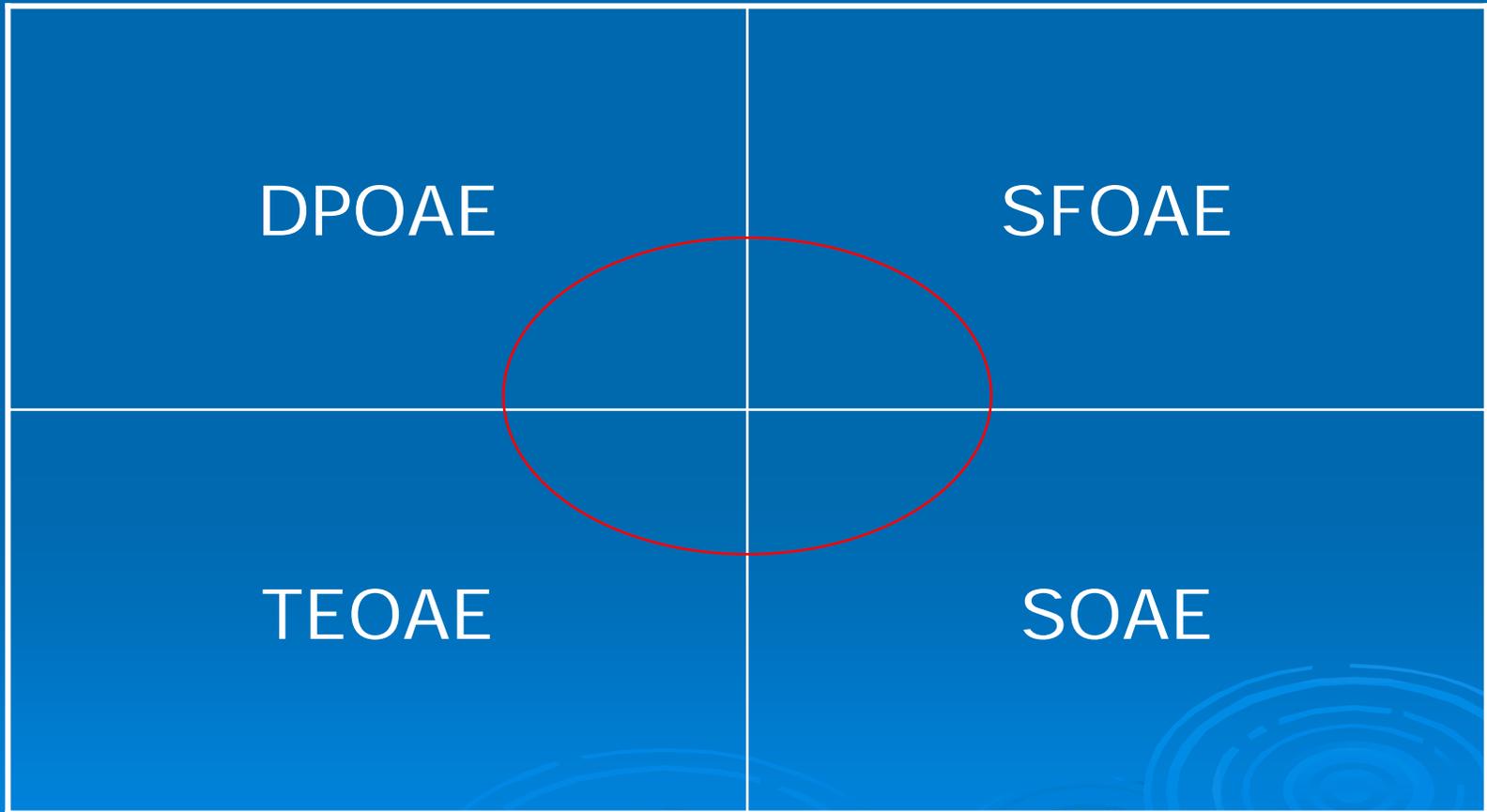


Measurement-based Classification

- **Spontaneous (SOAE):** Narrowband Signals measured in the absence of deliberate acoustic stimulation
- **Transiently evoked (TEOAE):** Responses evoked by transient (click or tone-burst) stimulation
- **Stimulus-frequency (SFOAE):** Additional acoustic energy from the cochlea at the frequency of stimulation by low-level tones
- **Distortion product (DPOAE):** Acoustic distortions created by the cochlea at frequencies different from those of the two stimulating tones

Probst, R. (1990). "Otoacoustic emissions: An overview," *Advances in Oto-Rhino-Laryngology*, 44, 1-91.

Which One Doesn't Belong?



Mechanism-based Classification

➤ **Reflection Emissions**

OAEs that arise by Linear Reflection due to coherent reflection of traveling wave from random impedance perturbations (e.g., SOAEs)

➤ **Distortion Emissions**

OAEs that arise by Non-linear Distortion due to nonlinearities acting as sources of cochlear traveling waves

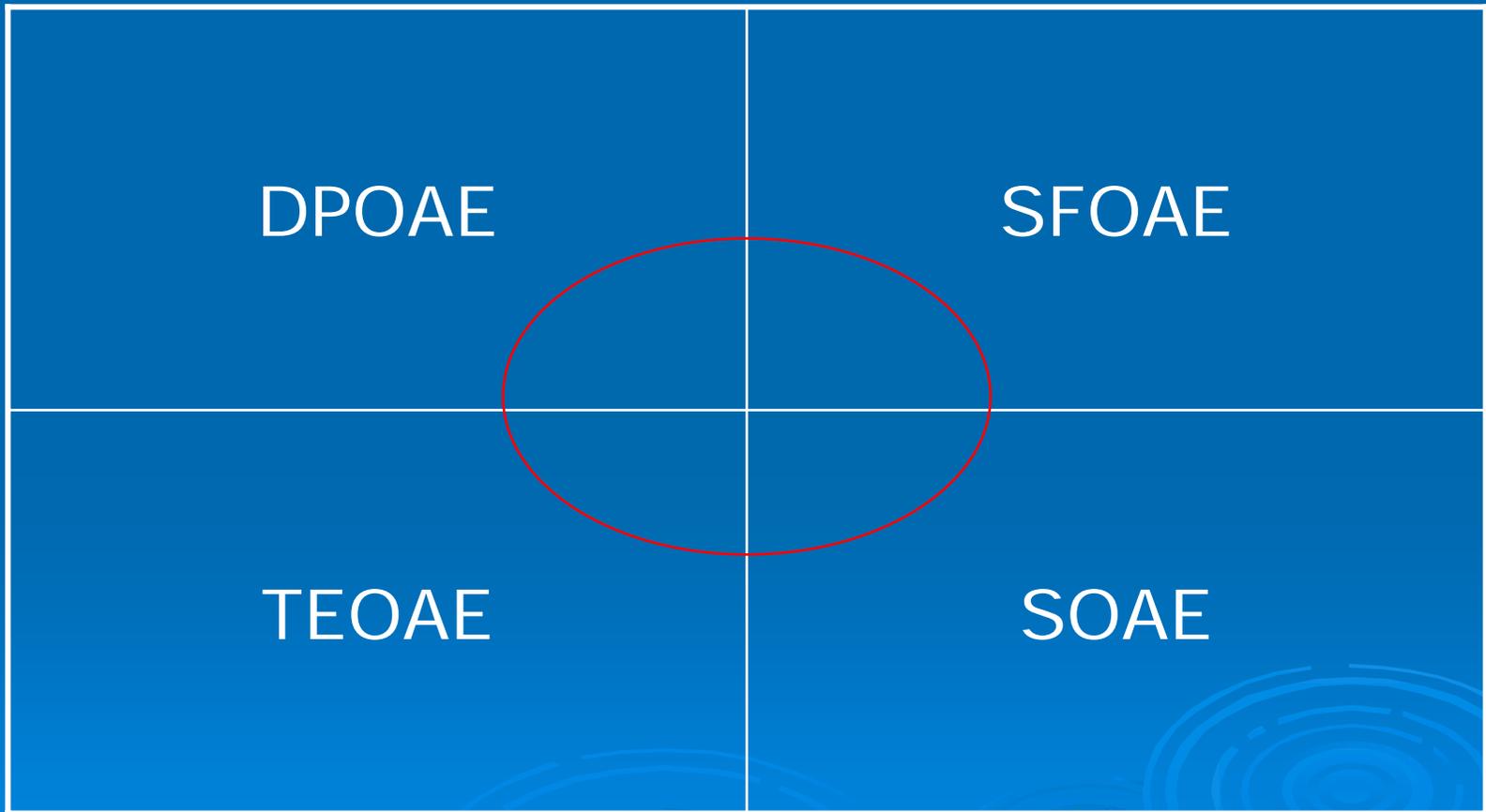
All Evoked Emissions are a Combination of Linear Reflection and Non-linear Distortion Mechanisms

Mechanism-based Classification

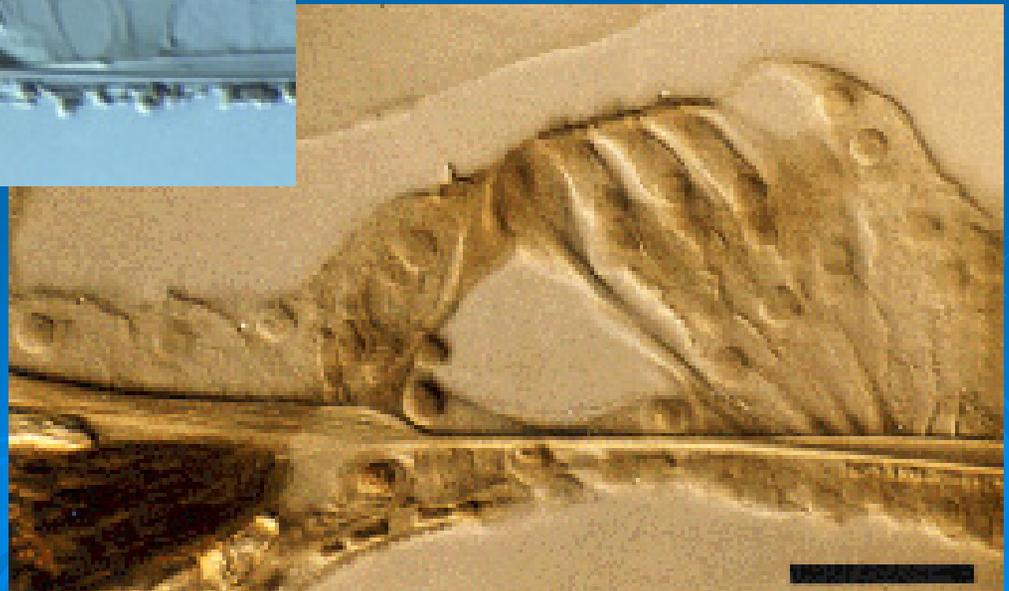
- **Stimulus-frequency (SFOAE)**: Reflection emission at low levels; distortion emission at high levels
- **Transiently evoked (TEOAE)**: Mainly reflection emission at low levels; distortion emission at high levels (Kalluri et al., 2004 ARO poster)
- **Distortion product (DPOAE)**: Always initiated by non-linear distortion; may have additional reflection component

Shera, C.A., & Guinan, J.J. (1999). "Evoked otoacoustic emissions arise by two fundamentally different mechanisms: A taxonomy for mammalian OAEs," *Journal of the Acoustical Society of America*, 105, 782-98.

Which One Doesn't Belong?

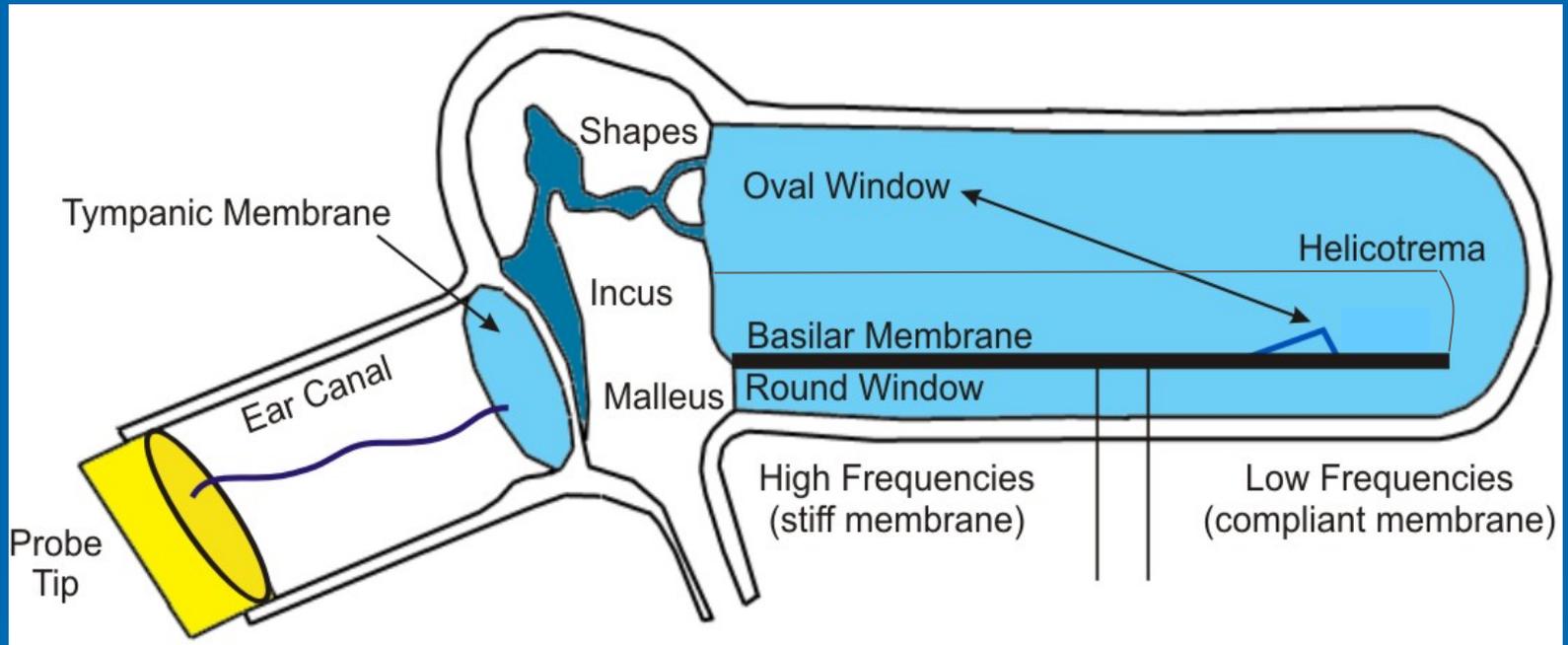


IV. SFOAE Measures of Cochlear Function



Images by M. Lenoir (top) and R. Pujol (right) from "promenade around the cochlea" EDU website www.cochlea.org by Rémy Pujol et al., INSERM and University Montpellier 1

SFOAE



- Due to reflection of forward-traveling basilar membrane response near the characteristic place
- Reflection might be caused by slight anatomical abnormalities present in normal ears

Frequency Tuning

- Established at the basilar membrane
- Basilar membrane tuning decreases with hearing loss
- In normal-hearing ears, tuning is sharpest at higher stimulus *frequencies* and at lower stimulus *levels*

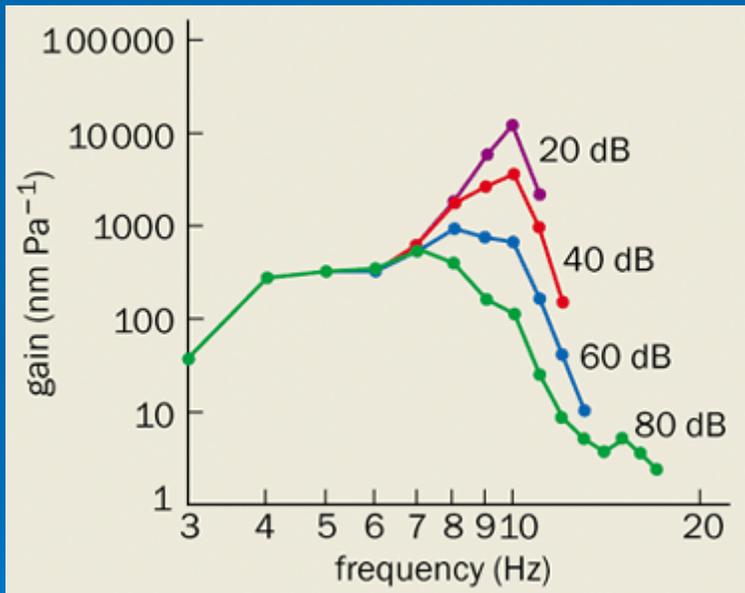


Image provided by Luis Robles and Mario A. Ruggero, Northwestern University. As published in *Mechanics of the Mammalian Cochlea*, *Physiol. Rev.* 81: 1305-1352, 2001.

Background

- Basilar membrane forward traveling wave slows down near the tonotopic place,
 - Slower oscillation associated with sharper tuning of the resonant peak
 - SFOAE group delays at low levels predict behavioral tuning curve data in normal ears (Shera et al., 2002)

Hypothesis

- SFOAE latency is determined by bm traveling wave delay (Neely et al., 1988)
 - At low levels (Zweig, 1991; Zweig & Shera, 1995)
 - For a bm modeled as a set of minimum phase filters (Zweig, 1976; de Boer, 1997)

Purpose

For SFOAE latencies, measured directly in the time domain:

- 1) Do they vary with level and hearing status?
- 2) Do they allow separation of multiple components (e.g., reflection and distortion components, multiple internal reflections)?
- 3) Are they consistent with model results?

Subjects

- 17 normal-hearing subjects
 - pure-tone thresholds 15 dB HL or better at half-octave frequencies from 0.25 to 8.0 kHz
 - no worse than 10 dB HL at test frequencies
- 11 subjects with impaired hearing.
 - 11 had thresholds > 20 dB HL at 4 kHz
 - 10 had thresholds > 20 dB HL at 3 kHz
- All subjects had normal 226-Hz tympanometry at time of testing

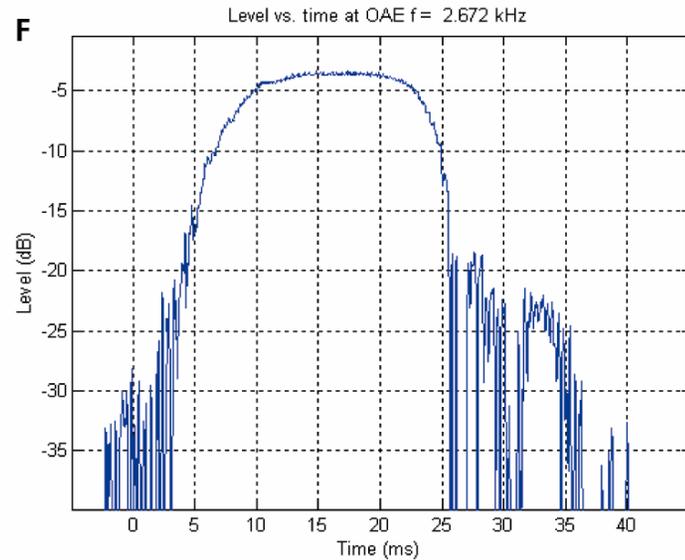
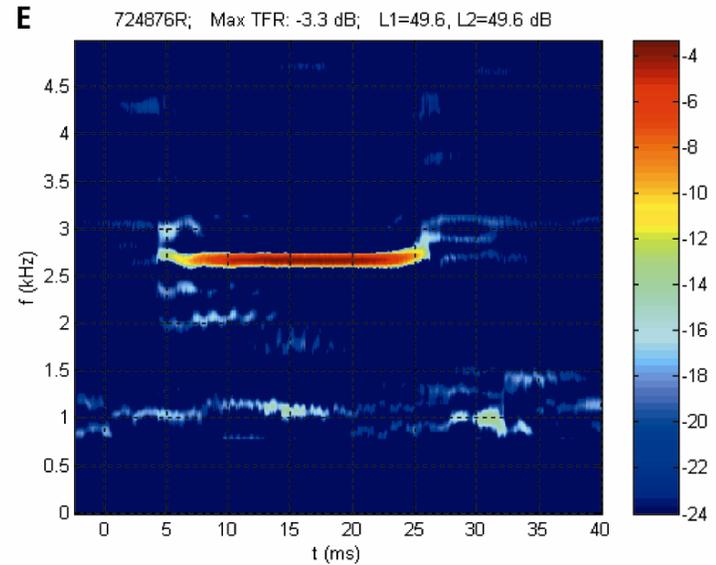
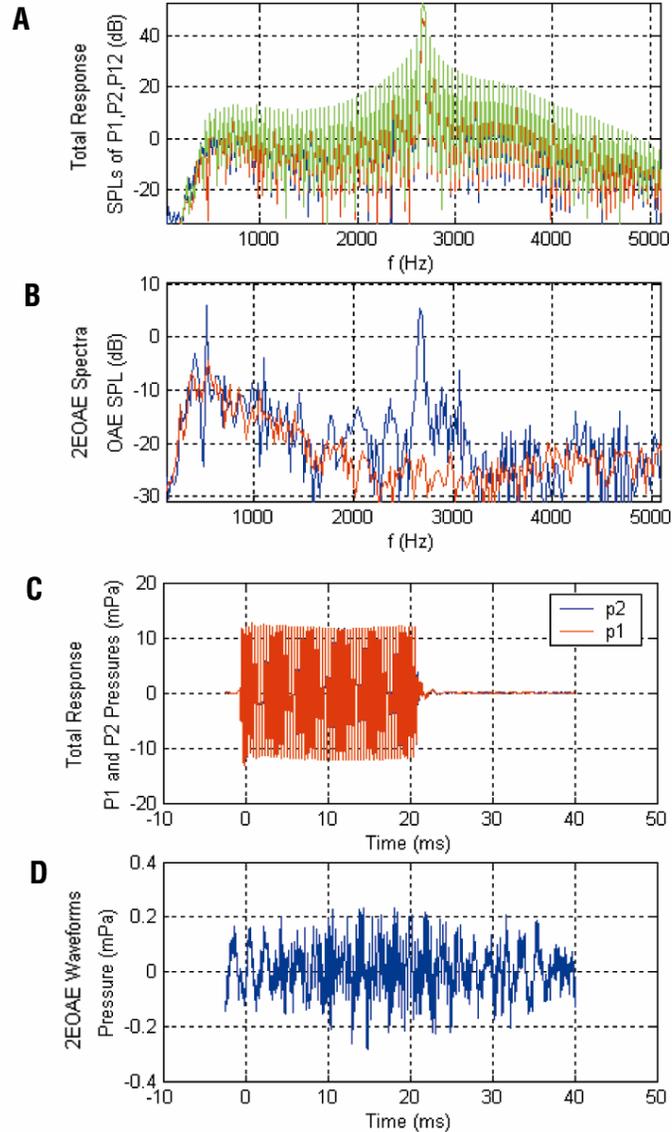
Stimuli

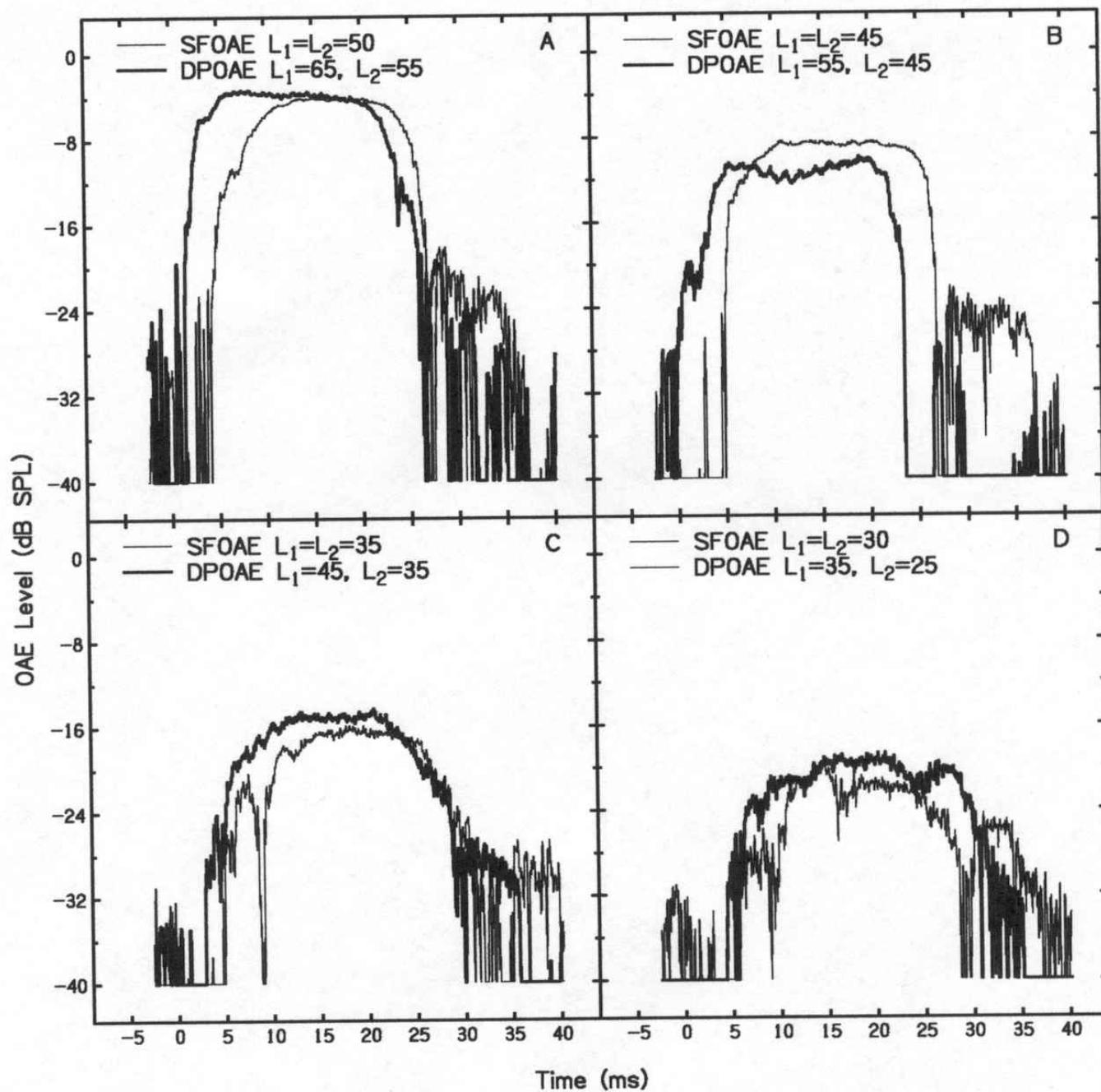
- To elicit SFOAE we used
 - **tone pips** (band-limited impulses)
 - **gated tones** (tonal stimuli with well-defined onset, steady state and decay)
- Center frequency was 2.7 or 4.0 kHz
- Stimulus Level was varied

OAE Recording and Analysis

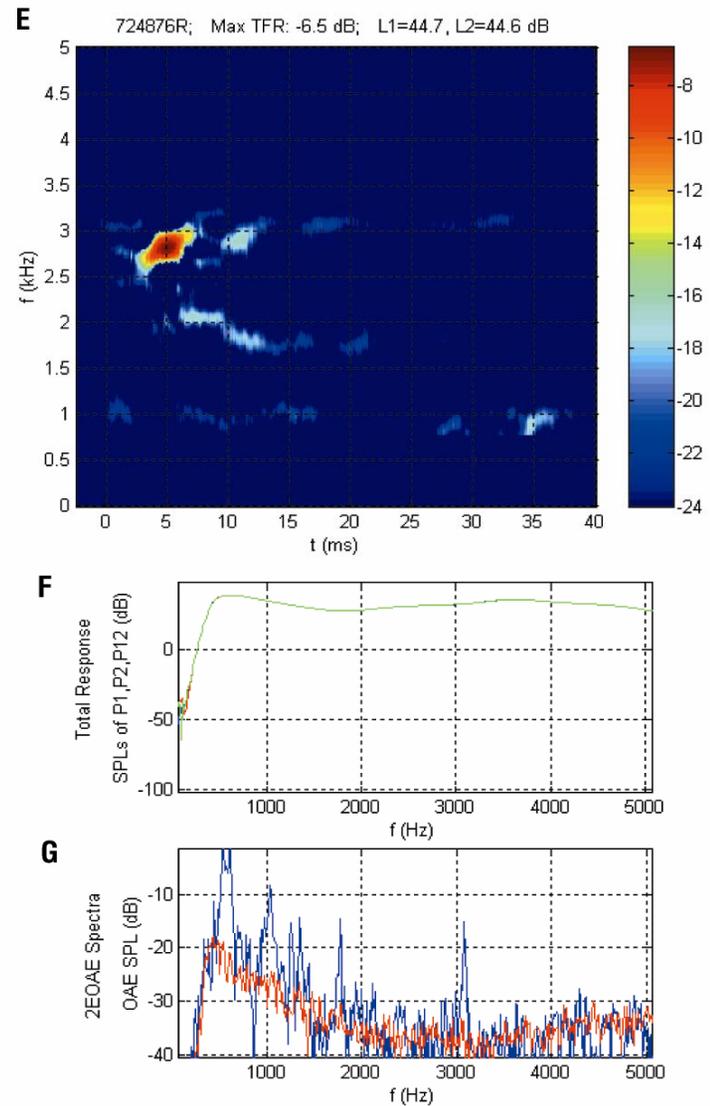
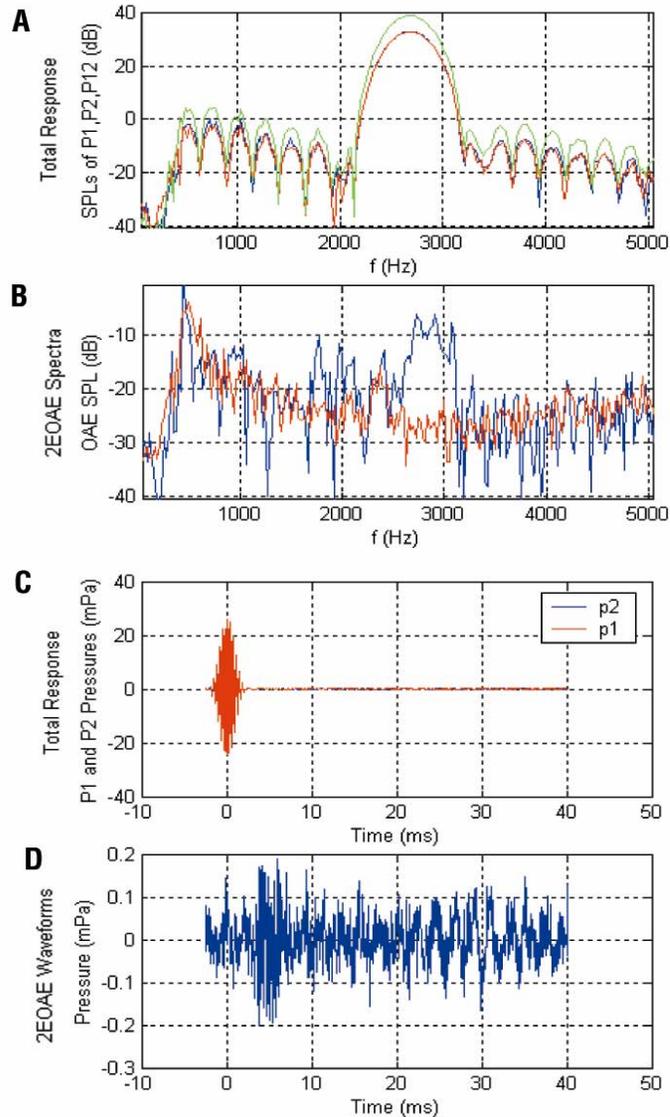
- Recorded in the time domain
- Extracted using nonlinear residual technique (Keefe and Ling, 1998)
 - Time-frequency Response calculated (discrete cone kernel)
 - Narrow-band filtered (Kaiser), and envelopes extracted (Hilbert transform)
 - Equivalent auditory filter bandwidth calculated (eQ_{ERB})
- Synchronous SOAEs measured to assess their contribution to SFOAE

SFOAE

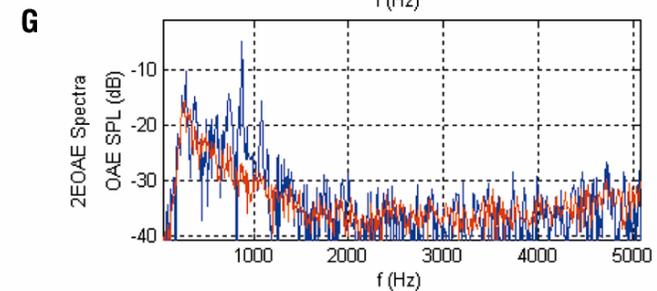
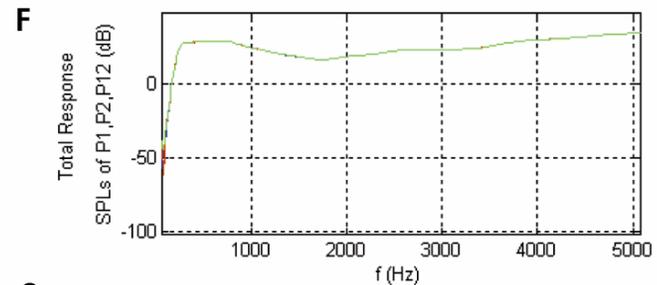
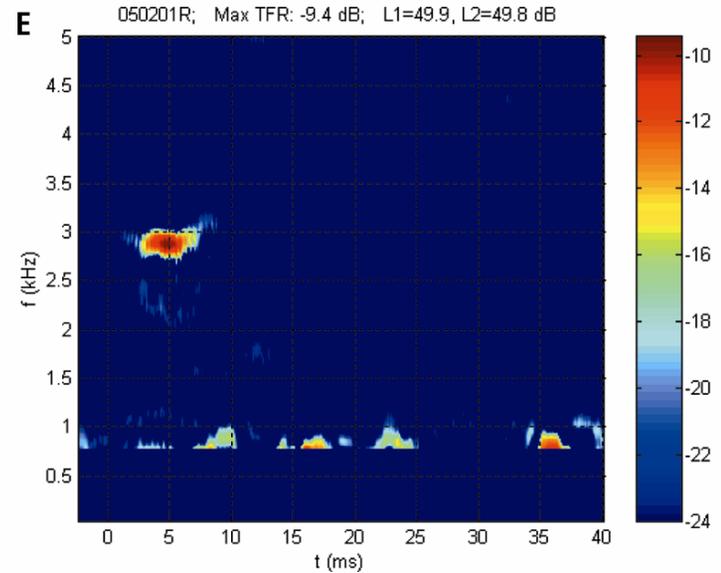
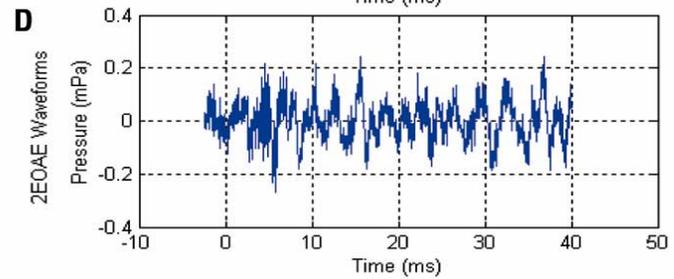
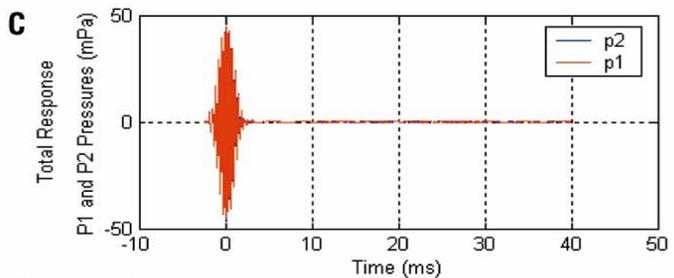
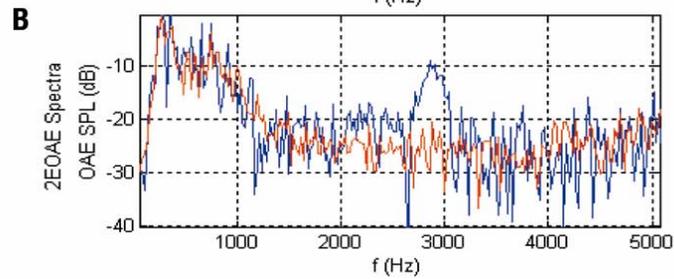
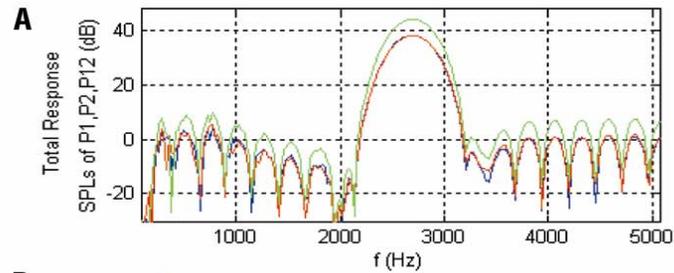




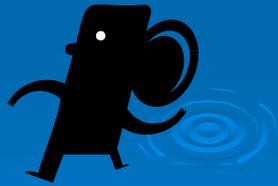
SFOAE

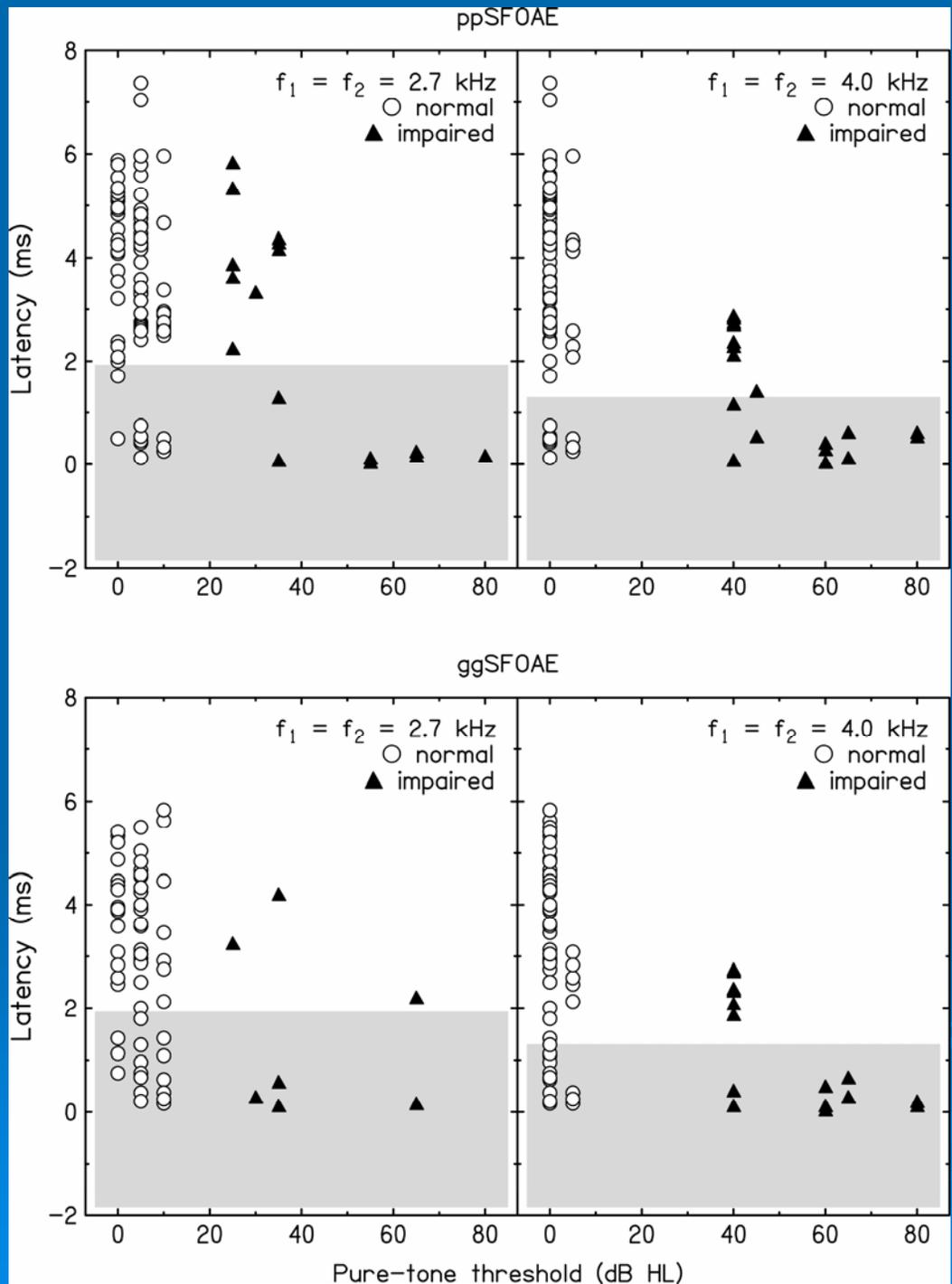


SFOAE



Effect of Hearing Status on SFOAE





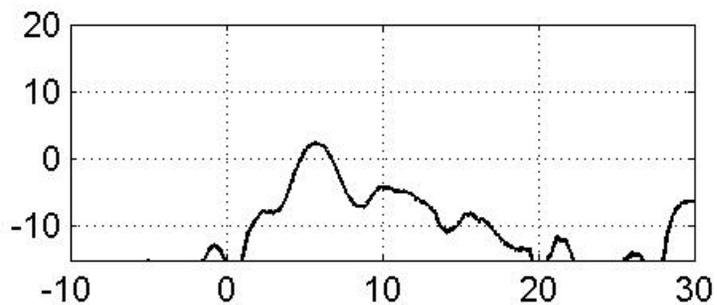
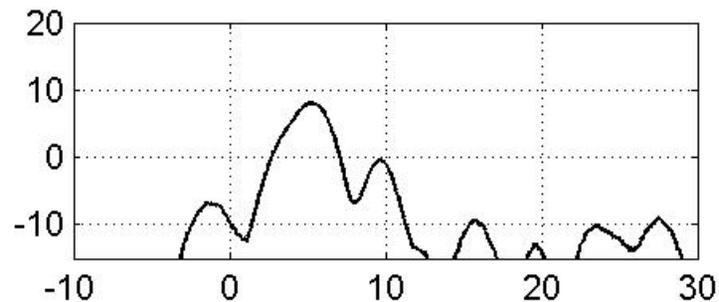
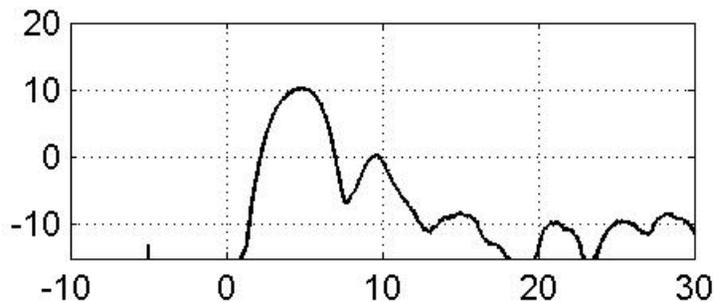
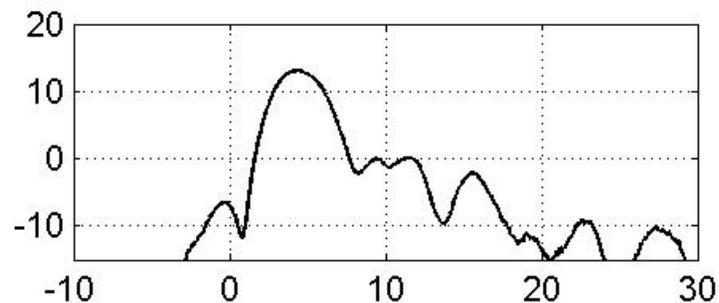
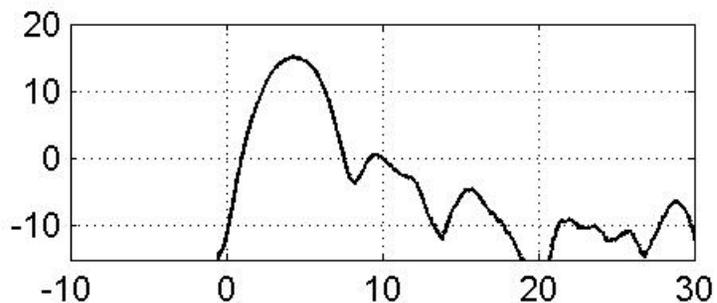
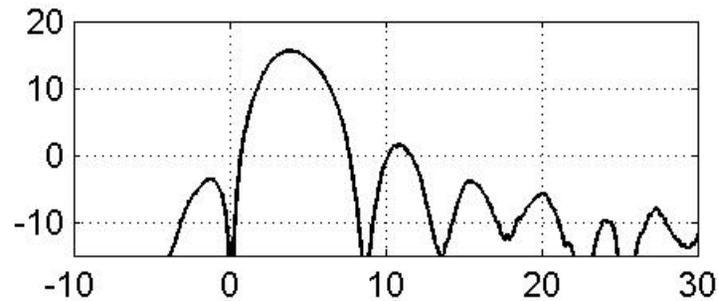
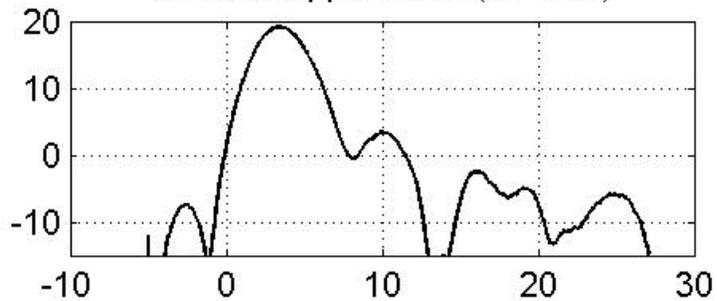
Results

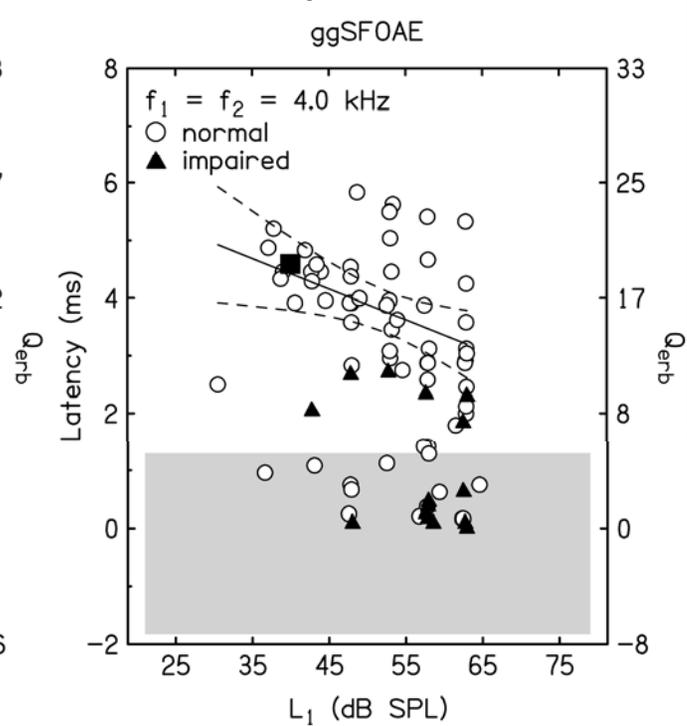
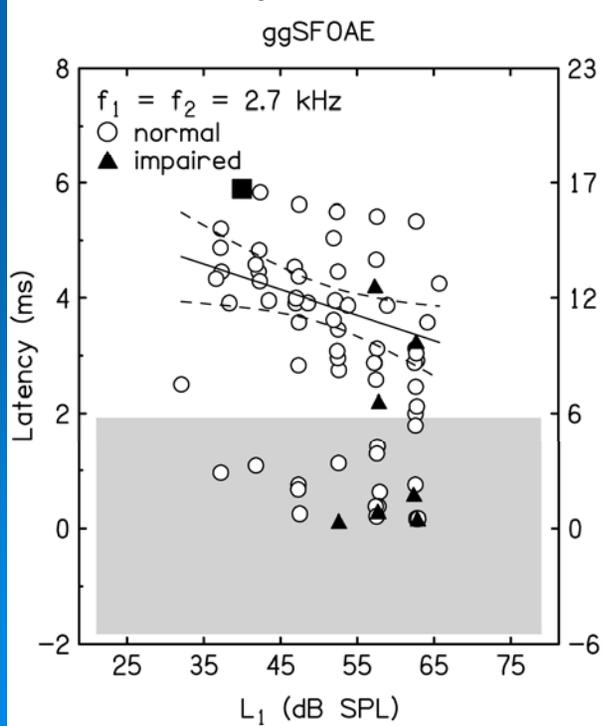
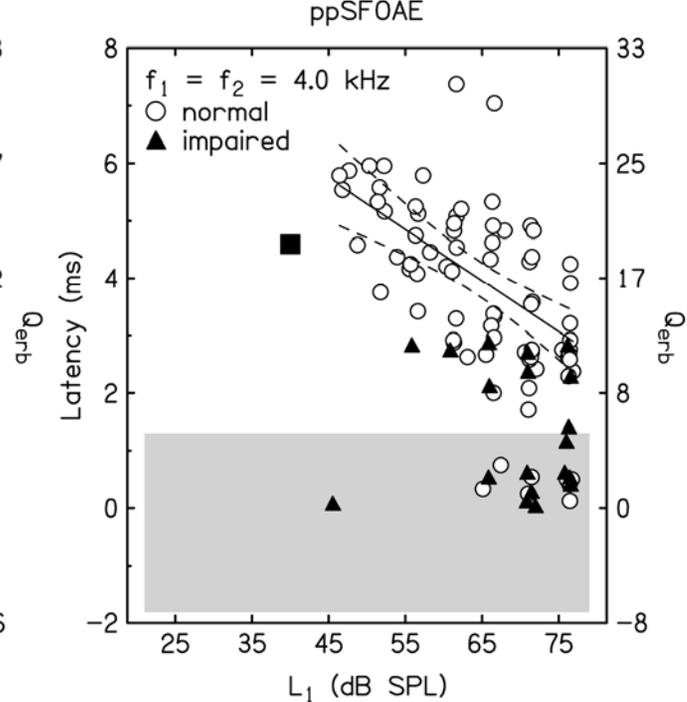
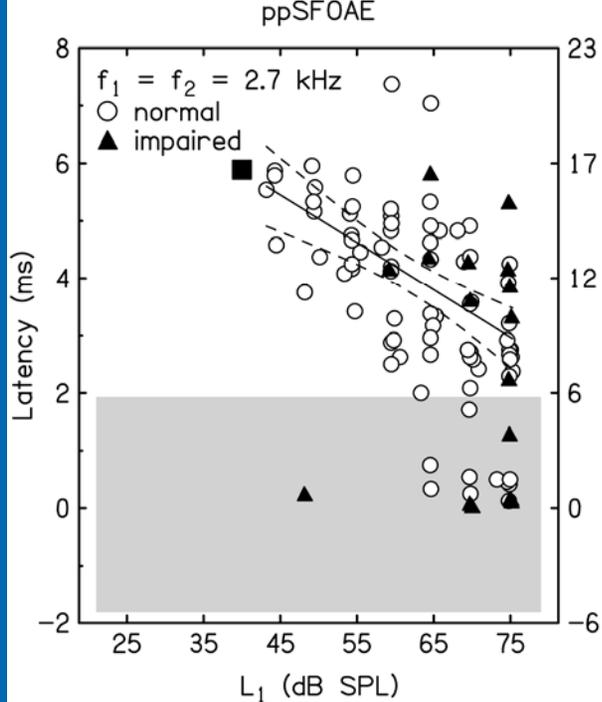
- Responses with 6 dB signal to noise ratio (SNR) obtained for a wide range of audiometric threshold levels.
- However, valid latencies ($> T_{\min}$) were obtained only in subjects with pure-tone thresholds below about 45 dB HL.
- For further analyses, excluded latencies shorter than T_{\min} , since they may be related to artifact.

Effect of Stimulus Level on SFOAE



724876R: ppSFOAE (2.7 kHz)





Results

- Increasing the stimulus level decreases ggSFOAE & ppSFOAE latencies.
- Valid impaired-ear latencies were similar or shorter compared to normal-ear latencies at equal SPL.
- Low-level SFOAE latencies consistent with model predictions for reflection mechanism; high-level latencies consistent with distortion mechanism

Results

- Good correspondence between temporal envelopes using narrow-band filtering and TFR analysis



Conclusions

➤ SFOAE latency variation with level and hearing status are consistent with expected changes in tuning under the same conditions.

Thus, transient-evoked SFOAE may provide a rapid, non-invasive measure of cochlear tuning.

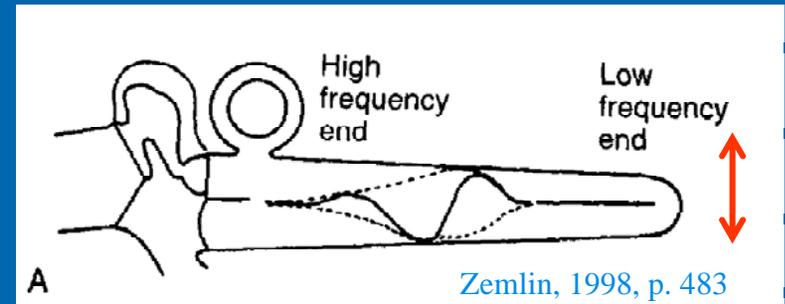
➤ TFR technique valid for exploring OAE elicited by complex stimuli

Full Citations

Konrad-Martin, D, & Keefe, D.H. (2003). Time-frequency analyses of transient-evoked stimulus-frequency and distortion-product otoacoustic emissions: Testing cochlear model predictions. *J. Acoust. Soc. Am.* 114, 2021-2043.

Konrad-Martin, D, & Keefe, D.H. (2005). Transient-evoked stimulus-frequency and distortion-product otoacoustic emissions in normal and impaired ears. *J. Acoust. Soc Am.* 117, 3799-3815.

Intensity Encoding

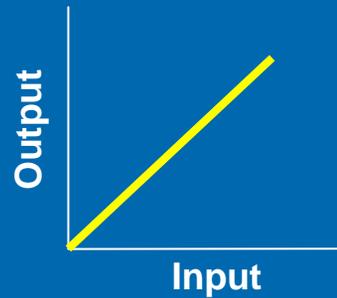
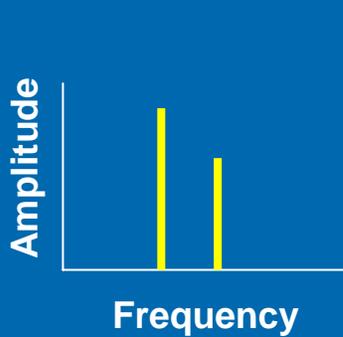


- Intensity of an incoming sound is encoded by the amplitude of displacement of the BM.
- Changes in response output (physiological or behavioral) as a function of changes in stimulus intensity or input = “**Response Growth**”
- Response growth can be represented by:
 - Input-output (I/O) functions (BM, 8th nerve, OAE)
 - Rate response curves (8th nerve)

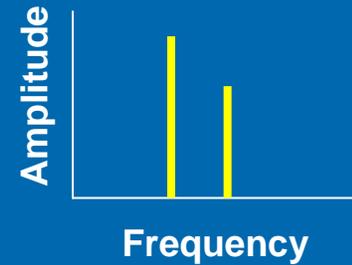
Input-Output (I/O) Function

**Linear
System**

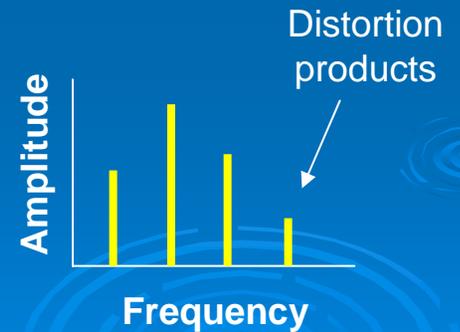
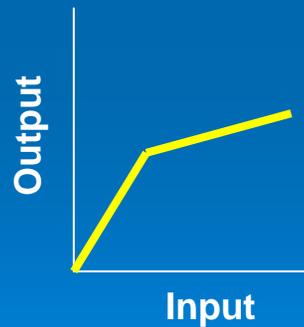
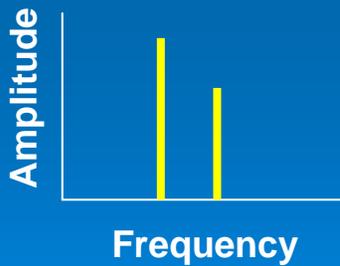
Input Spectrum



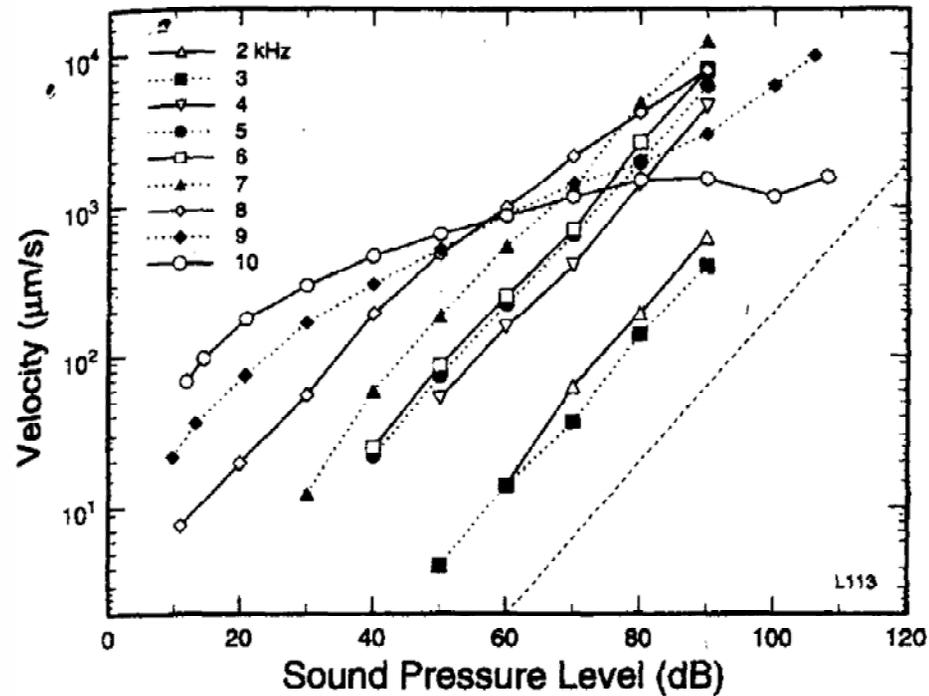
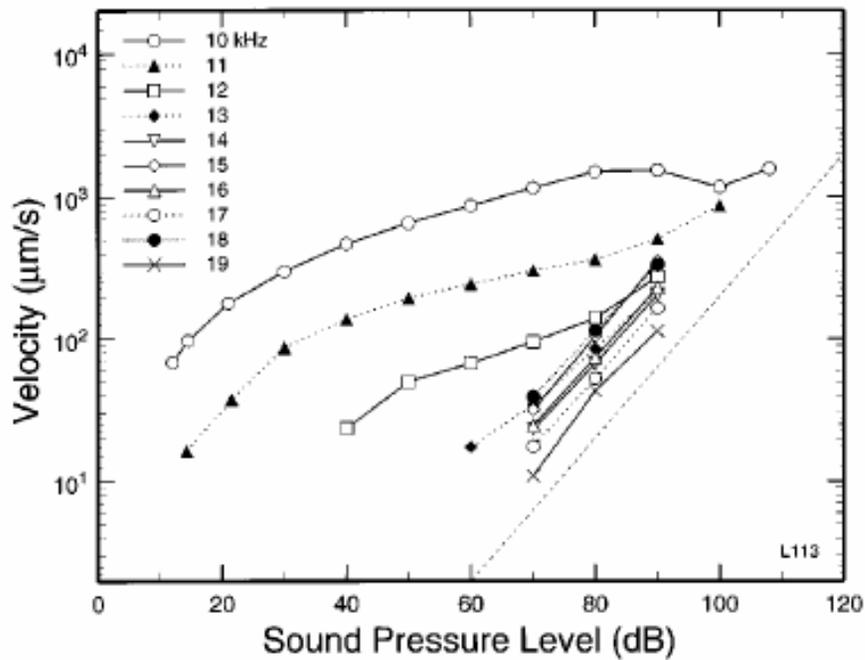
Output Spectrum



**Nonlinear
System**



BM I/O Functions



On-frequency and higher than CF (10 kHz)

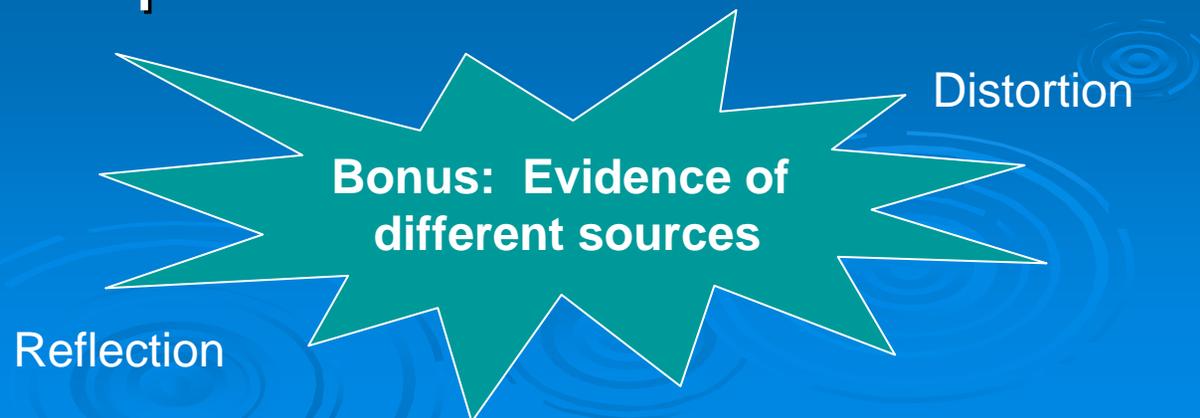
On-frequency and lower than CF (10 kHz)

Why do we care about BM response growth?

- Nonlinear in normal-hearing ears
- Becomes more linear with hearing loss (lose dynamic range)
- May be related to loudness growth, recruitment

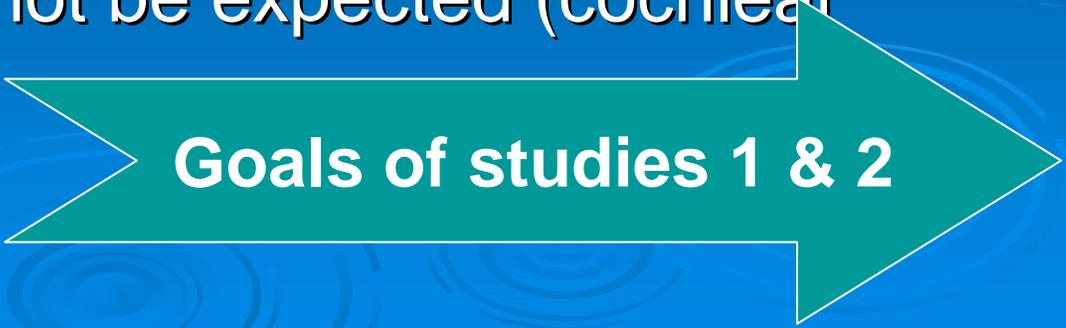
Why do we care about SFOAE response growth?

- Can we use it to estimate BM response growth?
- Can we use it to predict loudness growth (e.g., in people who cannot respond behaviorally)?
- Can we use it to predict audiometric threshold?



What questions do we need to ask first?

- How much variability is there across ears with normal hearing?
- How much variability is there within ears with normal hearing?
- Is signal-to-noise (SNR) sufficient to measure responses across a range of stimulus levels?
- Are the responses absent in ears in which a response would not be expected (cochlear implants)?



Goals of studies 1 & 2

Common

- Normal tympanometry, no ABG > 10 dB
- ER10-C modified to increase output of receivers by 20 dB
- Double-evoked OAE software (Keefe, 1998)
 - Extracts nonlinear residual (OAE)

1. Equal-frequency primaries

➤ Schairer et al. (2003)

➤ Subjects

- N = 30 adult ears with normal hearing (15 left, 15 right)
- N = 3 adult ears (2 subjects) with cochlear implants

SFOAE Stimuli

- $f_1=f_2$ (Equal-frequency)
- f_2 = half-octaves from 500 to 8000 Hz
(eventually dropped 500 and 8000 Hz)
- $L_1 = L_2$ (Equal-level)
- L_2 0 to 85 dB SPL in 5-dB steps

For comparison: DPOAE stimuli

- $f_2 / f_1 = 1.21$
- $f_2 = 2000$ and 4000 Hz
- L_1 and L_2 based on Kummer et al. (1998)
 - $L_1 = L_2$ at ≥ 65 dB SPL
 - $L_1 = 0.4L_2 + 39$ dB < 65 dB SPL

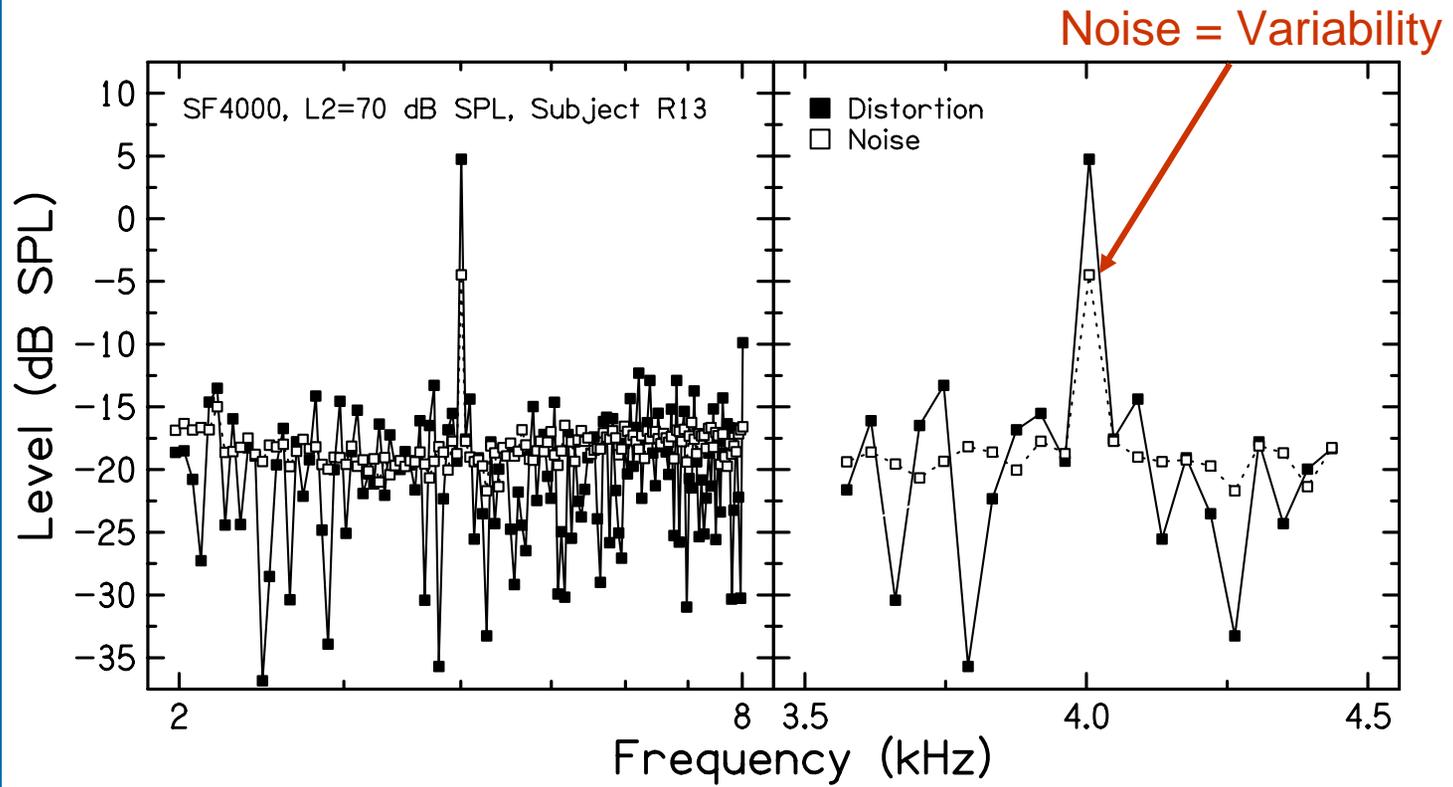
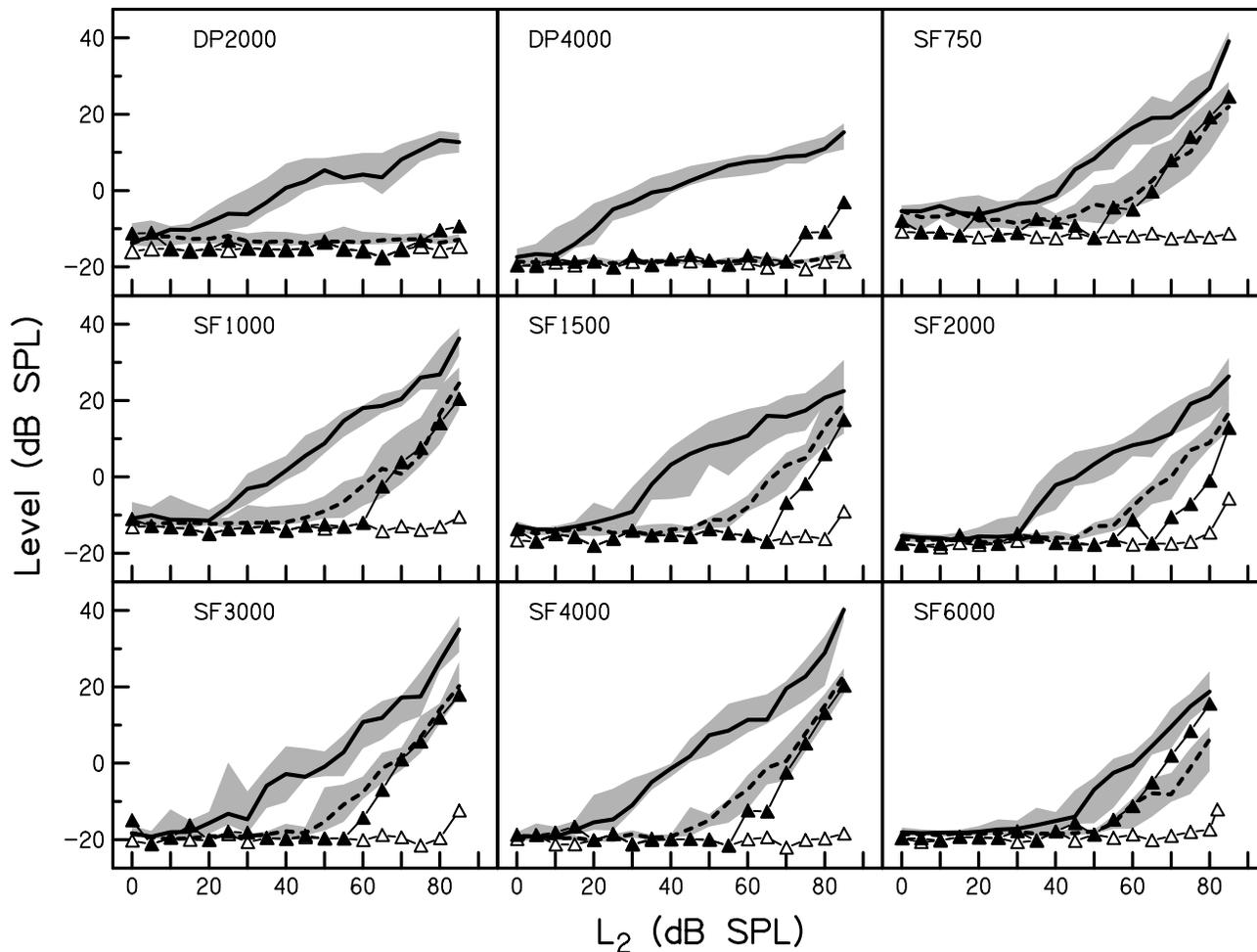


Fig. 5 from Schairer et al. 2003

Variability across normal-hearing ears



Median across
15 right ears

Solid line =
distortion in ears

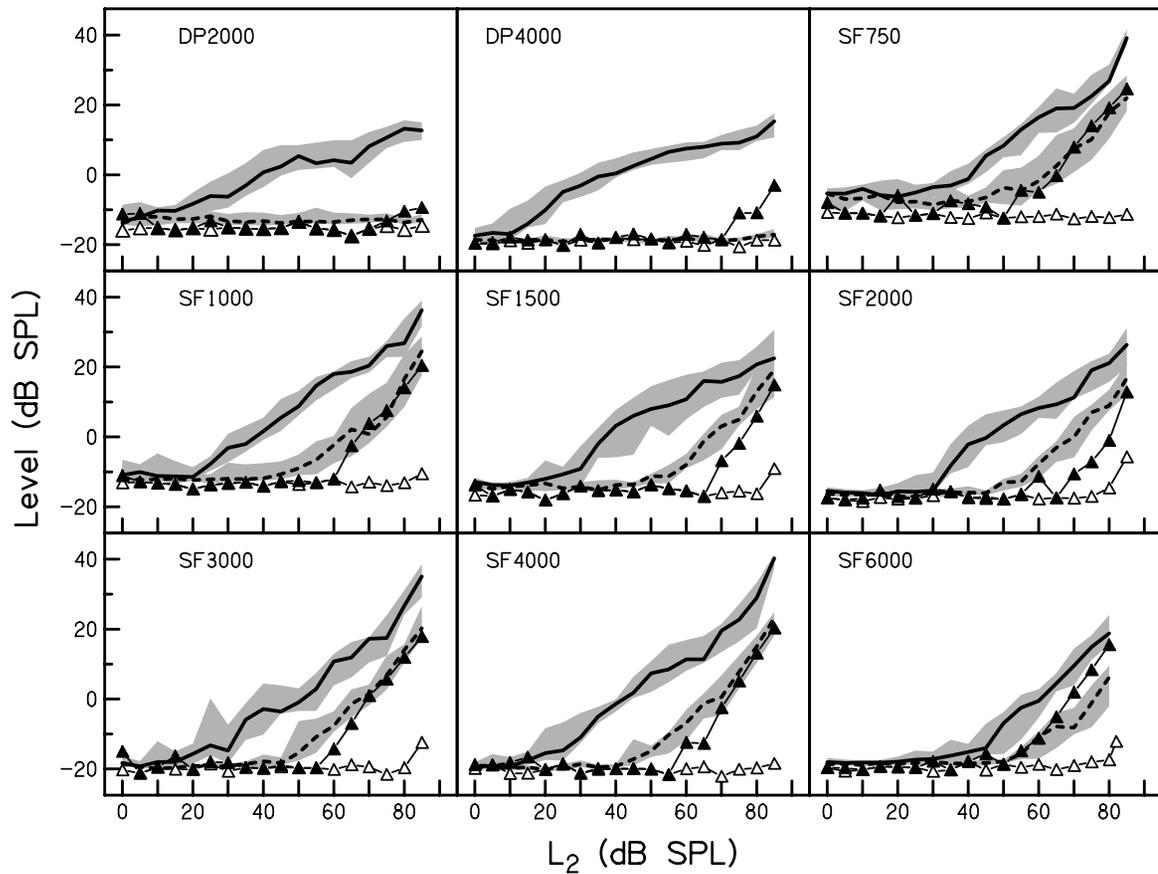
Dashed line = noise
in ears

Filled triangles =
distortion in coupler

Open triangles =
noise in coupler

Shaded area = 25th
to 75th percentile

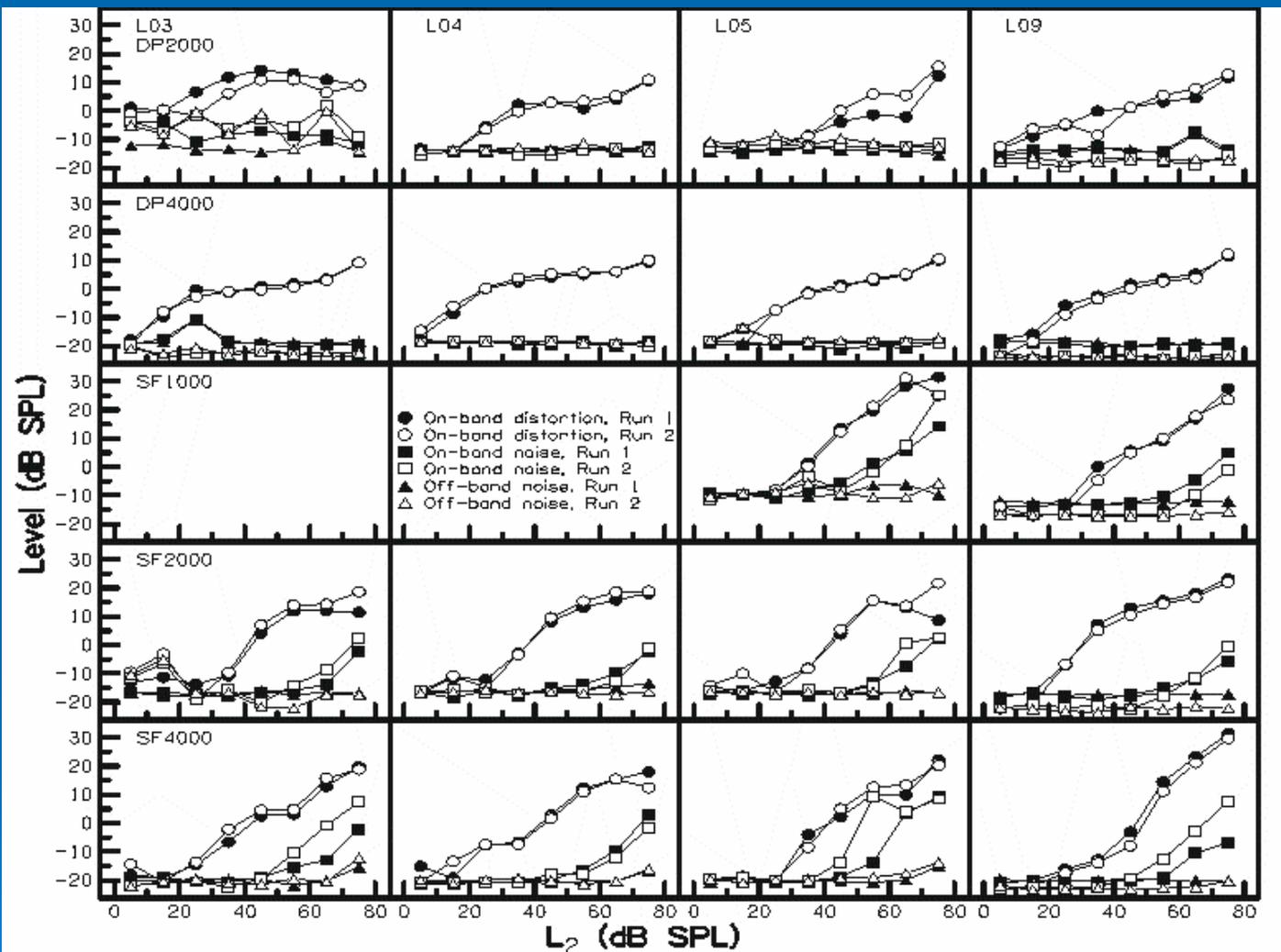
Fig. 1 from Schairer et al. 2003



SFOAE (compared to DPOAE)

- Higher threshold
- Steeper growth
- Higher coupler distortion at high stimulus levels
- Level-dependent noise

Variability within normal-hearing ears



Visit 1 = Filled symbols

Visit 2 = Open symbols

At least 1 month between visits

Fig. 6 from Schairer et al. 2003

SNR

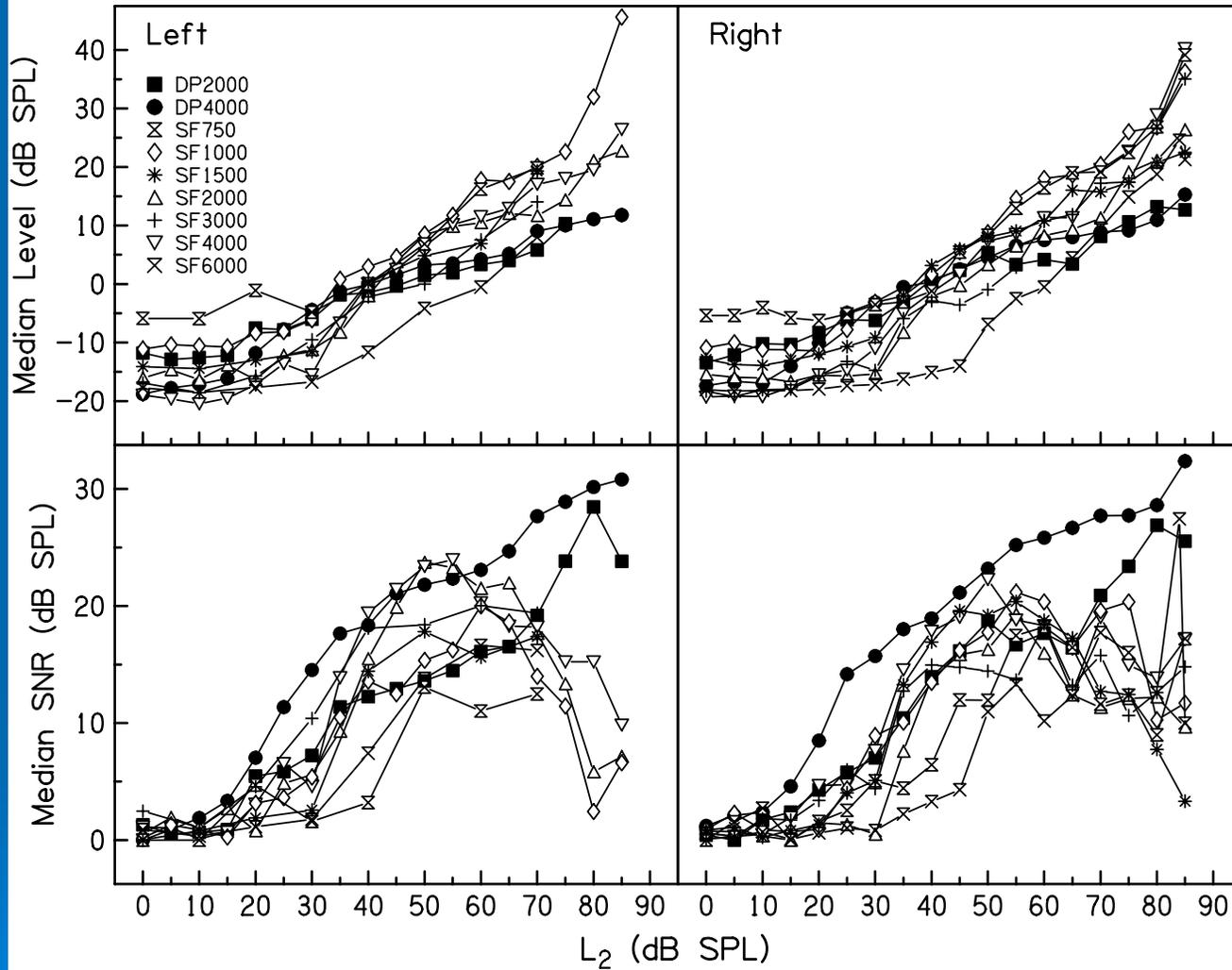
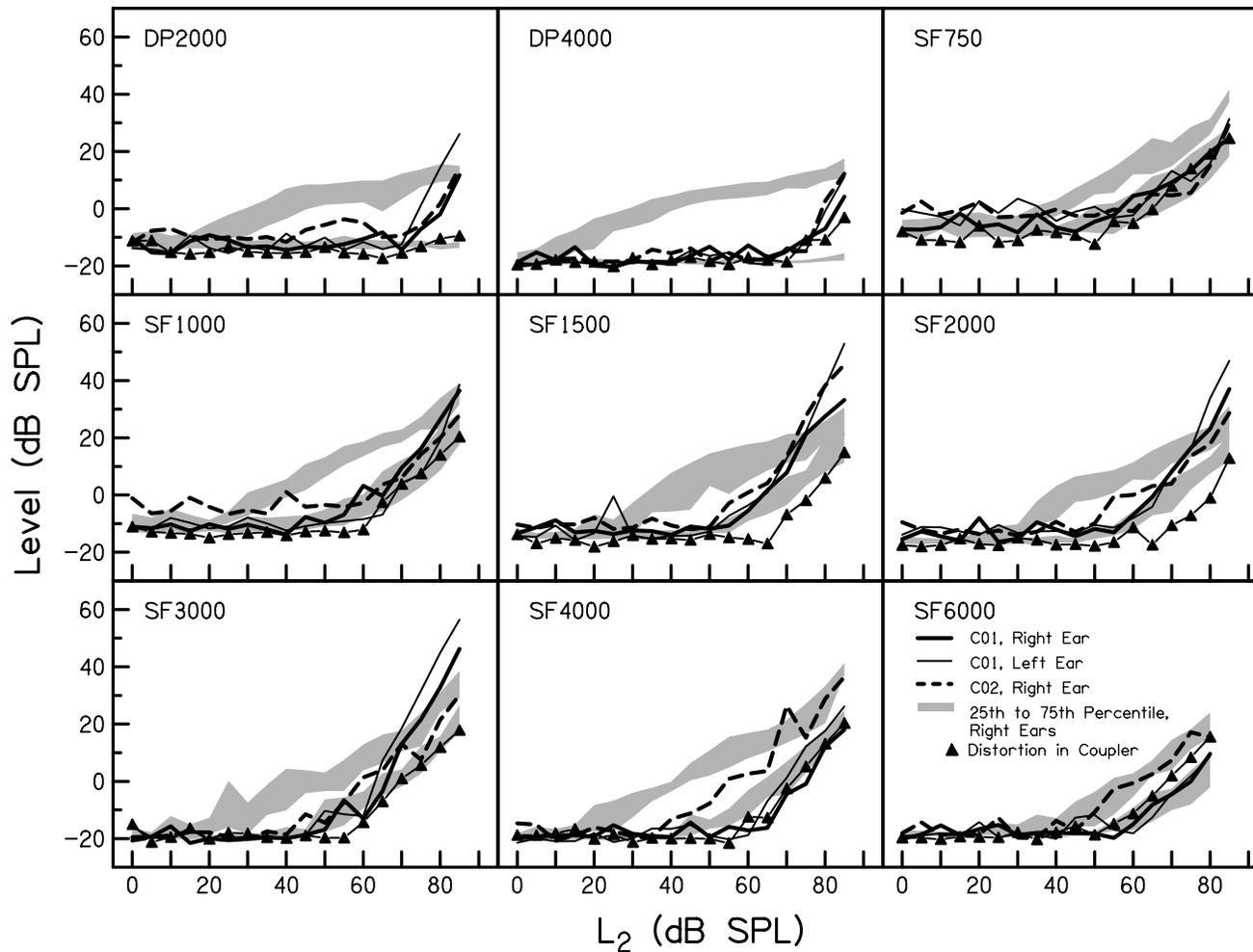


Fig. 8 from Schairer et al. 2003

Cochlear Implants



Speech
processors
turned off and
removed.

Contralateral
ear unaided.

Fig. 4 from Schairer et al. 2003

Bonus: Source interactions

R11

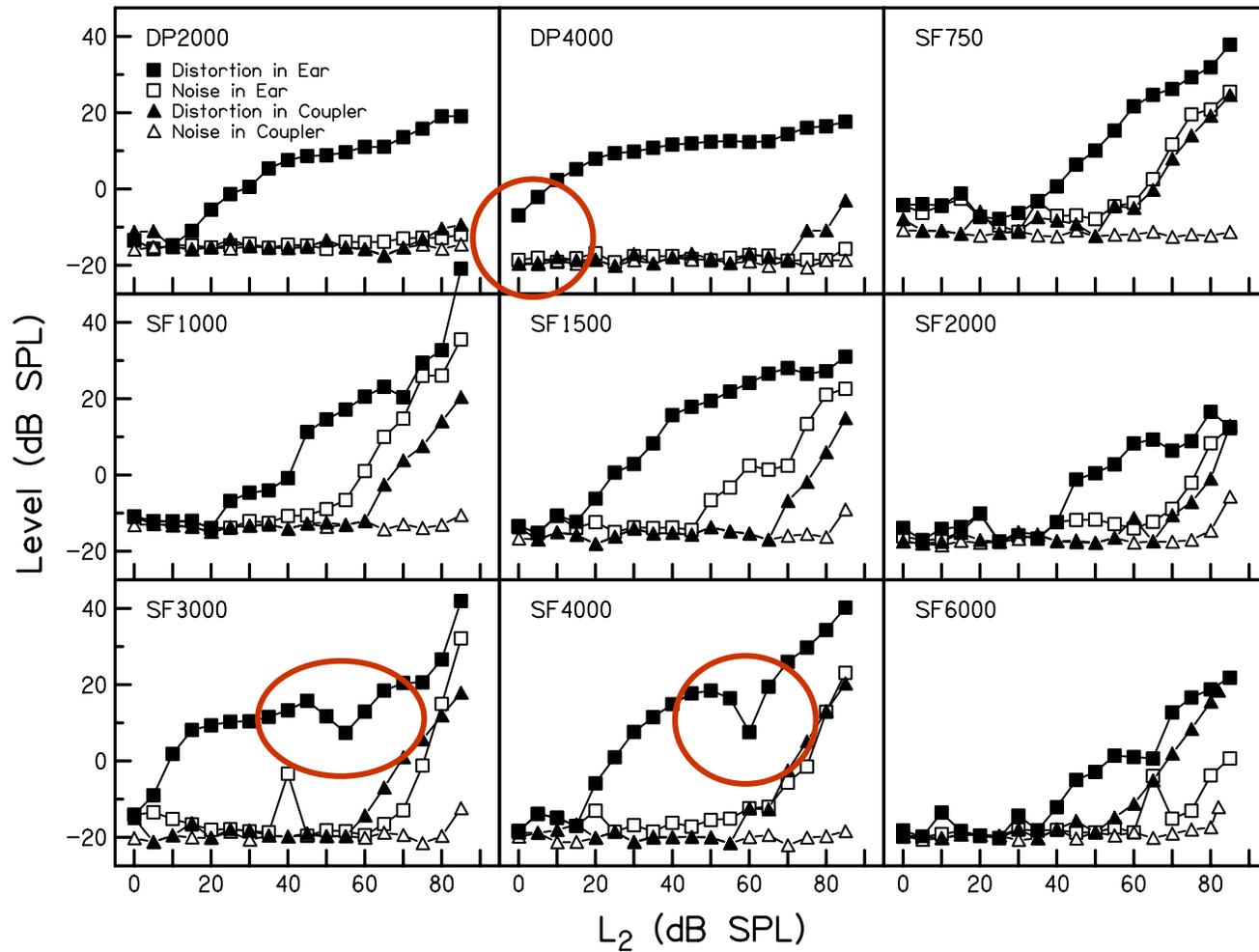


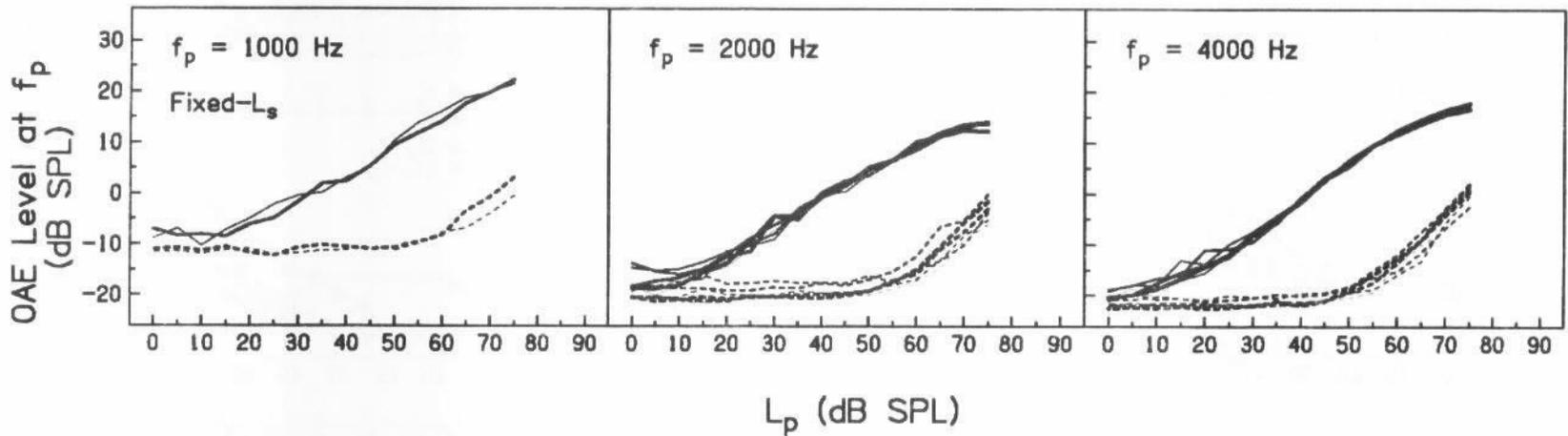
Fig. 2 from Schairer et al. 2003

2. Slightly off-frequency primaries

- Schairer and Keefe (2005)
- Subjects
 - N = 32 adult ears with normal hearing (16 right, 16 left)
 - N = 2 adult ears with cochlear implants

SFOAE Stimuli

- $f_p = 1000, 2000, \text{ and } 4000 \text{ Hz}$, with various f_s/f_p (≤ 1.07)
- Equal-level condition (for comparison with equal-frequency primary study)
 - $L_S = L_P$
 - L_P 0 to 85 dB SPL in 5-dB steps
- Fixed- L_S condition (for less complicated interpretation of response growth)
 - $L_S = 80 \text{ dB SPL}$
 - $L_P = 0$ to 75 dB SPL in 5-dB steps



$N = 32$ normal-hearing ears in $L_s = 80$ dB SPL condition

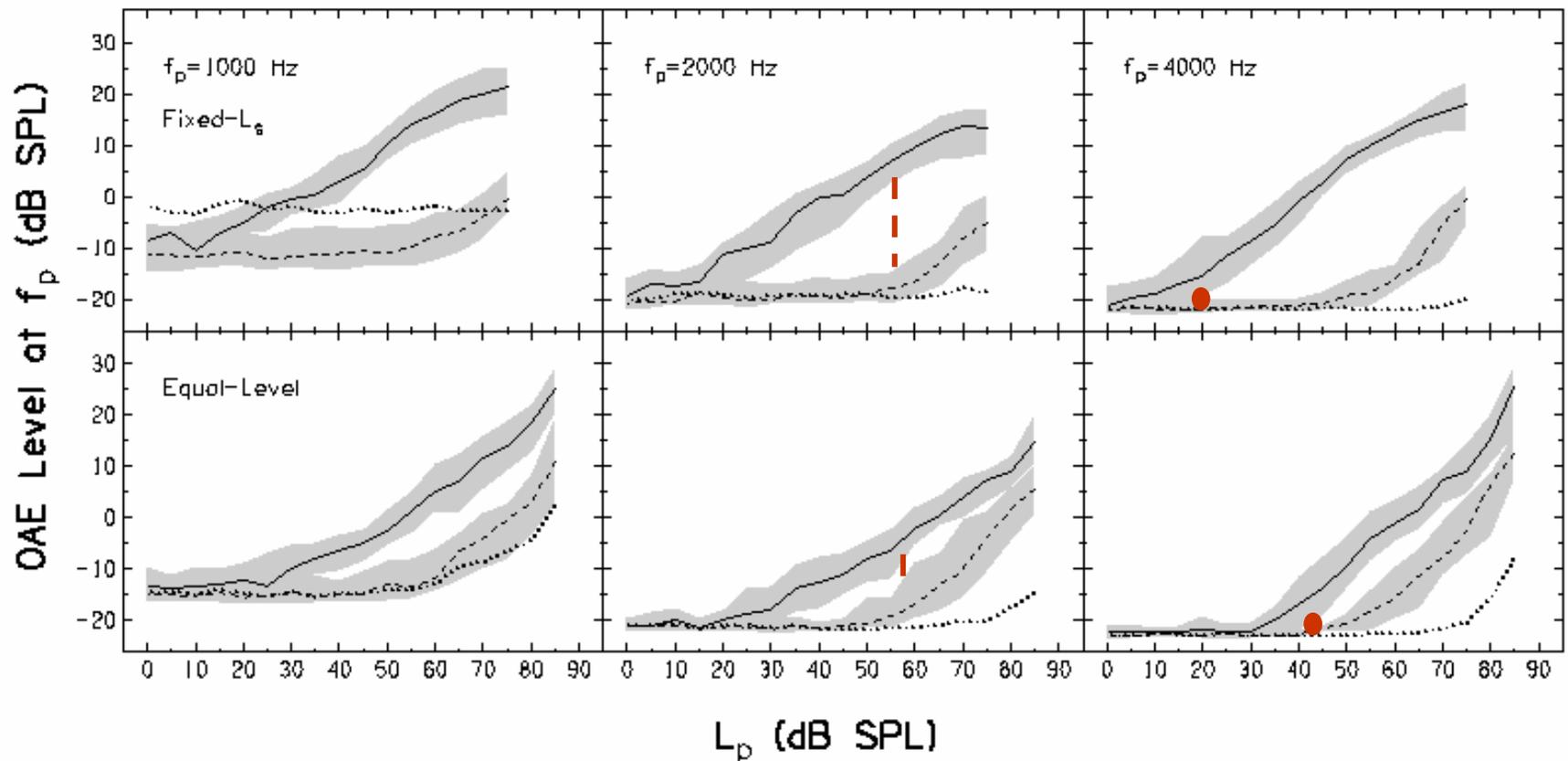
Solid lines = median distortion

Line thickness = f_s/f_p conditions

Dashed lines = median noise

Fig. 2 from Schairer and Keefe 2005

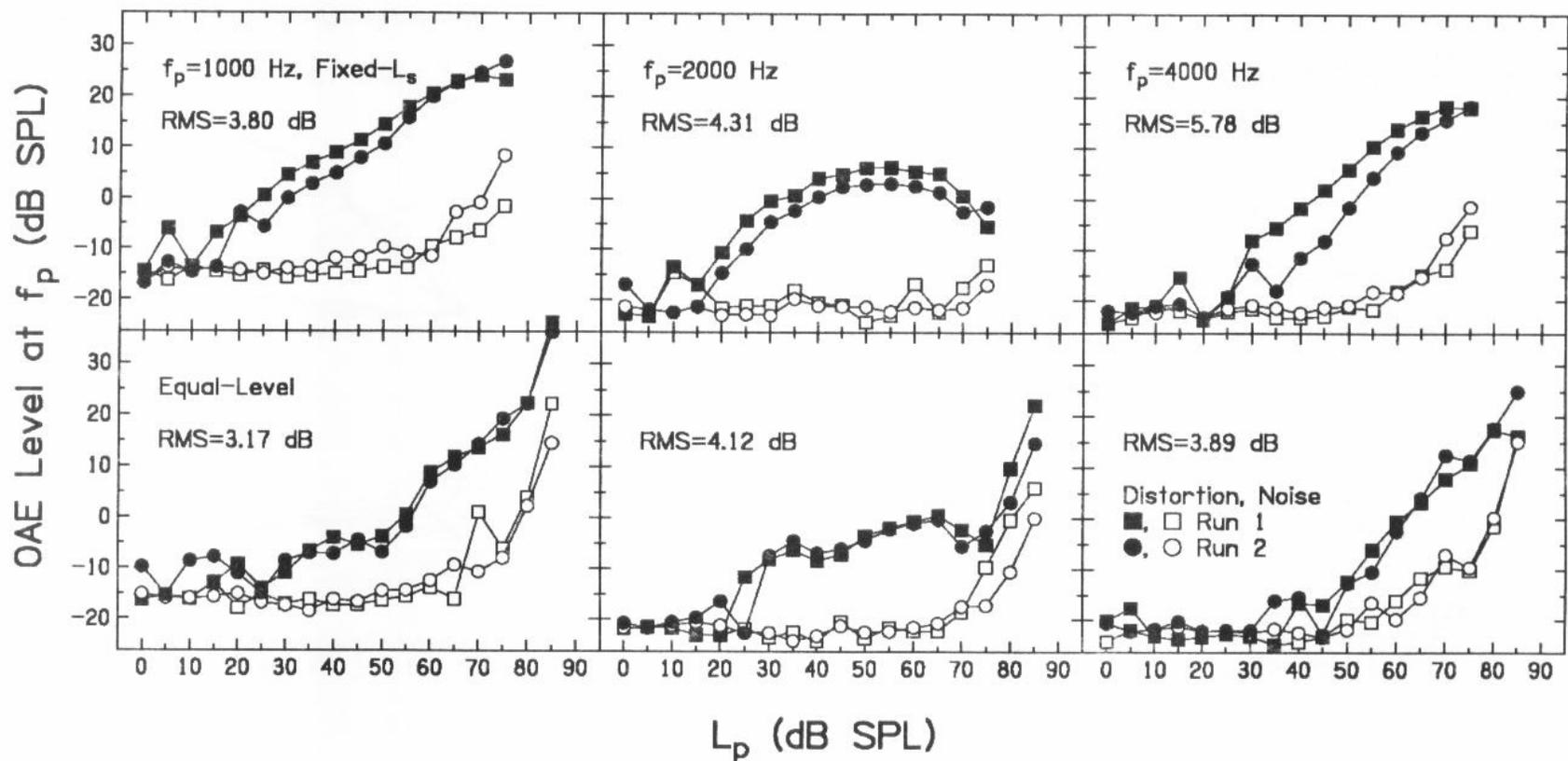
Variability across normal-hearing ears



$f_s/f_p = 0.96$ in Fixed- L_s condition
Dotted line = off-band noise

Fig. 3 from Schairer and Keefe 2005

Variability within normal-hearing ears

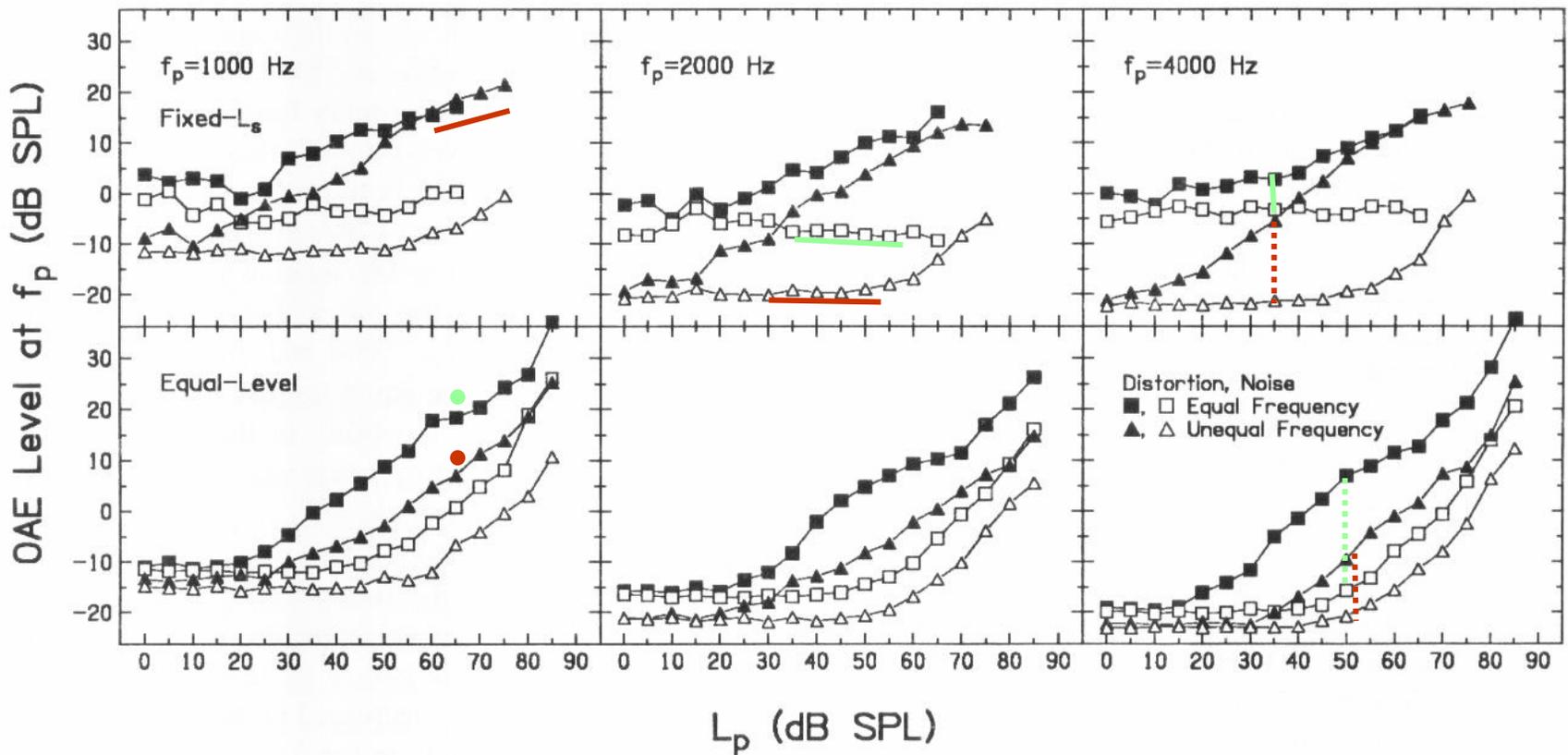


SFS04, Left Ear (one of four who returned)

1 year, 5 months between visits

Fig. 7 from Schairer and Keefe 2005

SNR



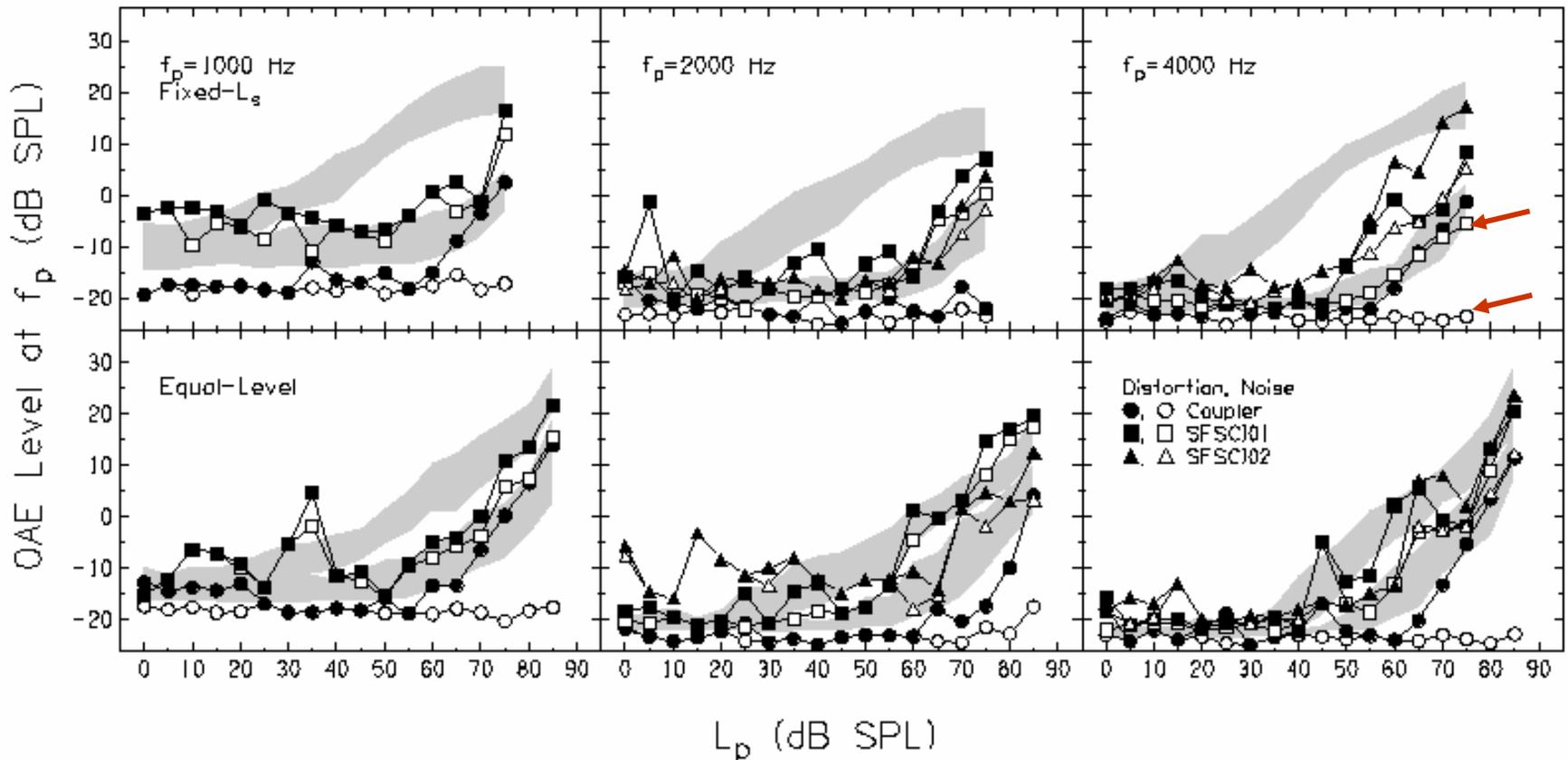
Median data

Equal-frequency, $L_s = 70$ dB SPL data from Schairer et al. 2003

$f_s/f_p = 0.96$ in the unequal-frequency primary conditions

Fig. 9 from Schairer and Keefe 2005

Cochlear Implants

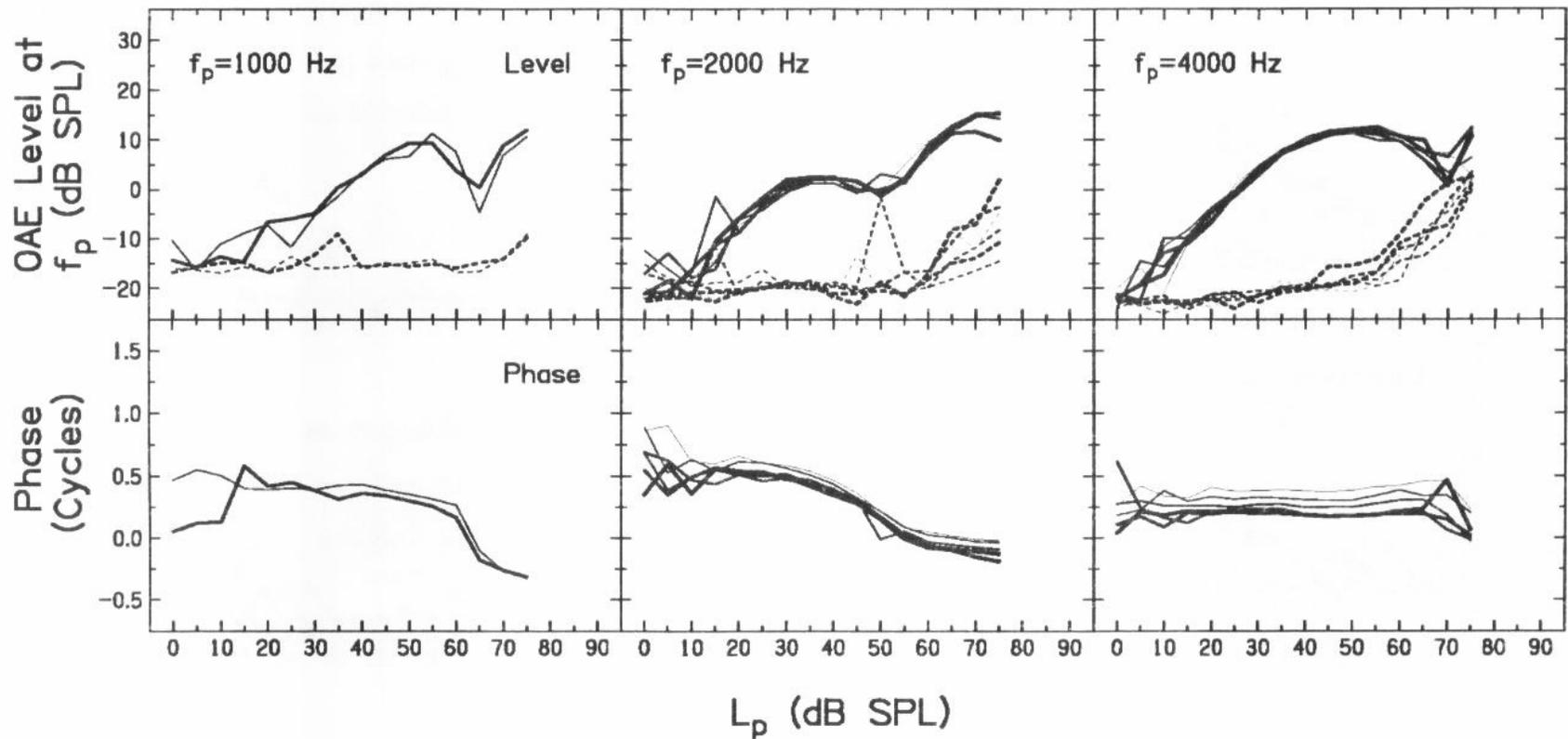


Speech processors turned off and removed
Contralateral ear unaided

Shaded area = 25th to 75th percentile for normal-hearing ears in the
 $f_s/f_p = 0.96$ conditions

Fig. 8 from Schairer and Keefe 2005

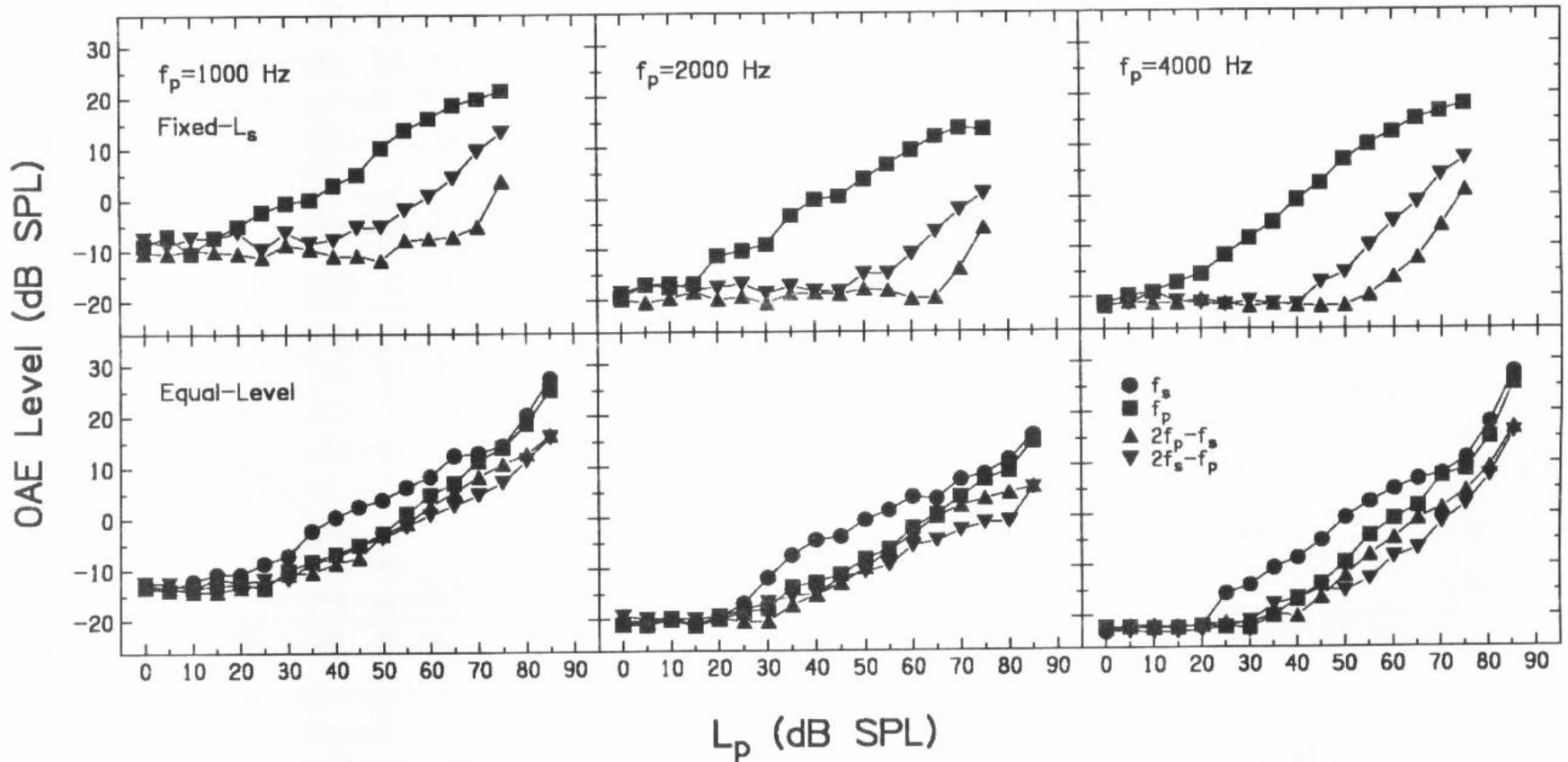
Bonus: Source interactions



Fixed- L_S condition
SFS19, right ear

Fig. 5 from Schairer and Keefe 2005

Bonus: Source interactions



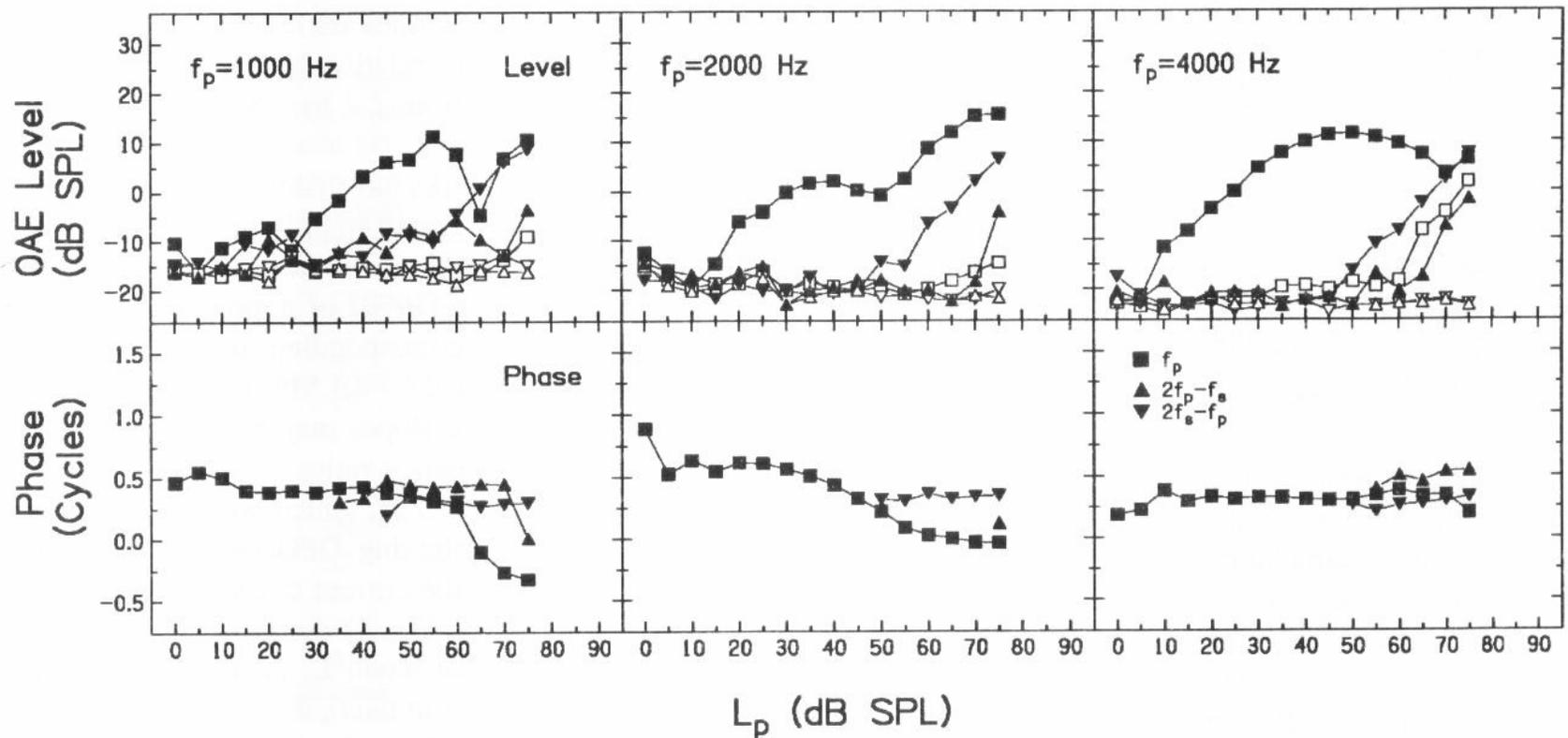
Median data in the $f_s/f_p = 0.96$ condition

$$2f_p - f_s = 2f_2 - f_1$$

$$2f_s - f_p = 2f_1 - f_2$$

Fig. 4 from Schairer and Keefe 2005

Bonus: Source interactions



$f_s/f_p = 0.96$
Fixed- L_s condition
SFS19, right ear

Fig. 10 from Schairer and Keefe 2005

Conclusions for studies 1 & 2

- How much variability is there across ears with normal hearing?
 - More than for DPOAEs, but not enough to obscure SFOAE SNR across a range of moderate stimulus levels
- How much variability is there within ears?
(across 4 subjects, all conditions)
 - Equal-frequency, equal-level: average $r^2 = 0.95$
 - Unequal-frequency, equal-level: RMS error 4.97 dB
 - Unequal-frequency, fixed- L_S : RMS error 5.04 dB

Conclusions for studies 1 & 2

- Is signal-to-noise (SNR) sufficient to measure responses across a range of stimulus levels?
 - Best condition is slightly off-frequency, fixed- L_S conditions

Conclusions for studies 1 & 2

- Are the responses absent in ears in which a response would not be expected (cochlear implants)?
 - Can overlap with normal range at high levels
 - Worst condition is slightly off-frequency, equal-level condition
 - Best condition is slightly off-frequency, fixed- L_S conditions

Conclusions for studies 1 & 2

➤ Noise

- On-band, level-dependent variability has a biological source, and is observed in normal and impaired ears, but not in a coupler
- Represents variability in sound transmission through the middle ear?

Conclusions for studies 1 & 2

➤ Sources

- Simultaneously elicited DPOAEs (in unequal-frequency primary conditions) may identify onset of nonlinear distortion source
- Notches in individual SFOAE I/O functions may occur due to varying degrees of cancellation of two sources

3. Total suppression with off-frequency primaries

➤ Ellison and Keefe, 2005

➤ Goals

- Determine how well SFOAEs identify hearing loss (thresholds > 15 dB HL)
- Determine how well SFOAEs classify hearing loss as mild (20 to 45 dB HL) or moderate-severe (50 to 95 dB HL)
- Correlate SFOAEs with pure-tone thresholds

Subjects

- Subjects (85 ears total)
 - 22 ears with normal hearing
 - AC thresholds ≤ 15 dB HL, 250 to 8000 Hz
 - 19 to 39 yrs (mean 28.7 yrs, SD = 6.5 yrs)

Subjects

- 63 with sensorineural hearing loss
 - 20 dB HL \geq AC \leq 95 dB HL for at least one octave frequency, 250 to 8000 Hz
 - Mild: 20 dB HL \geq AC \leq 45 dB HL
 - Moderate-severe: AC $>$ 45 dB HL
 - 18 to 83 yrs (mean = 54.7 yrs, SD = 18.9 yrs)

SFOAE Stimuli

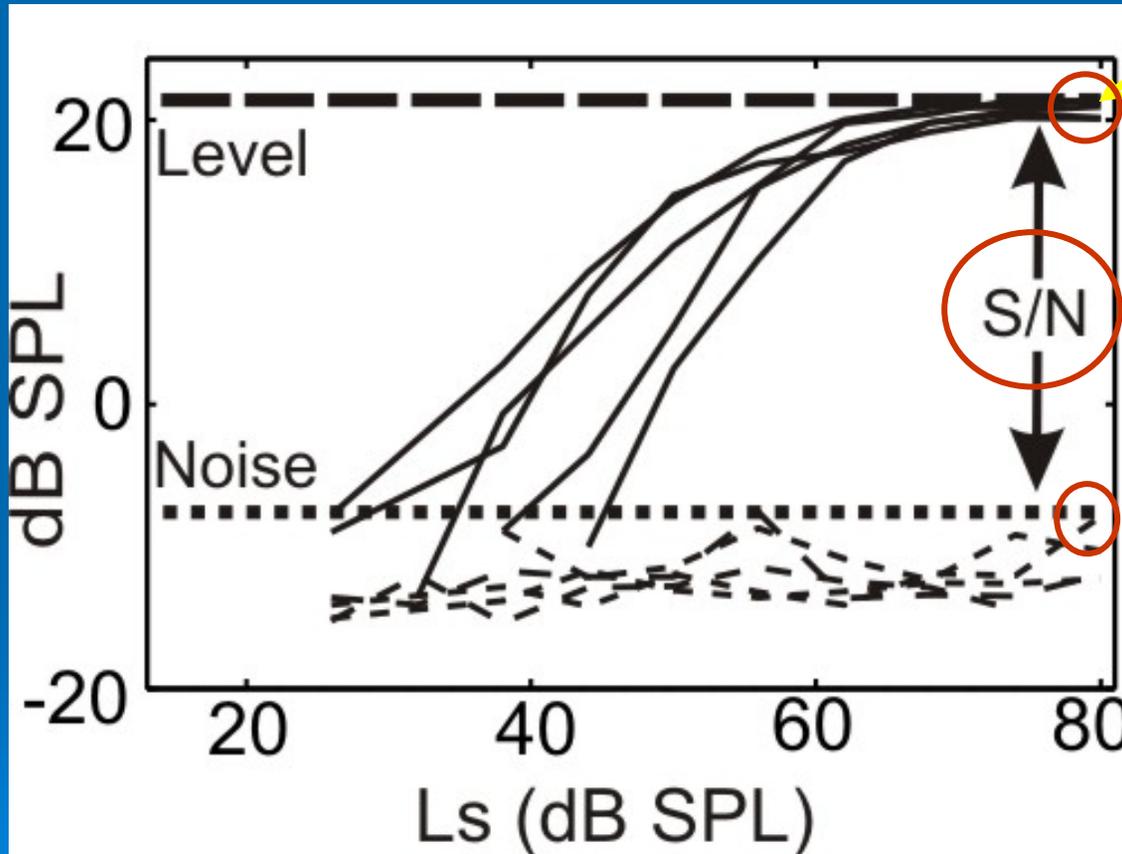
➤ Probe

- f_p = octave frequencies from 500 to 8000 Hz
- L_p = 70 to 20 dB SPL in 10-dB steps

➤ Suppressor at each f_p and L_p combination

- f_s varied 2 octaves below to 0.7 octaves above f_p
- L_s = 80 dB SPL to level at which response fell into noise floor in 6-dB steps
- Point: to find maximum suppression

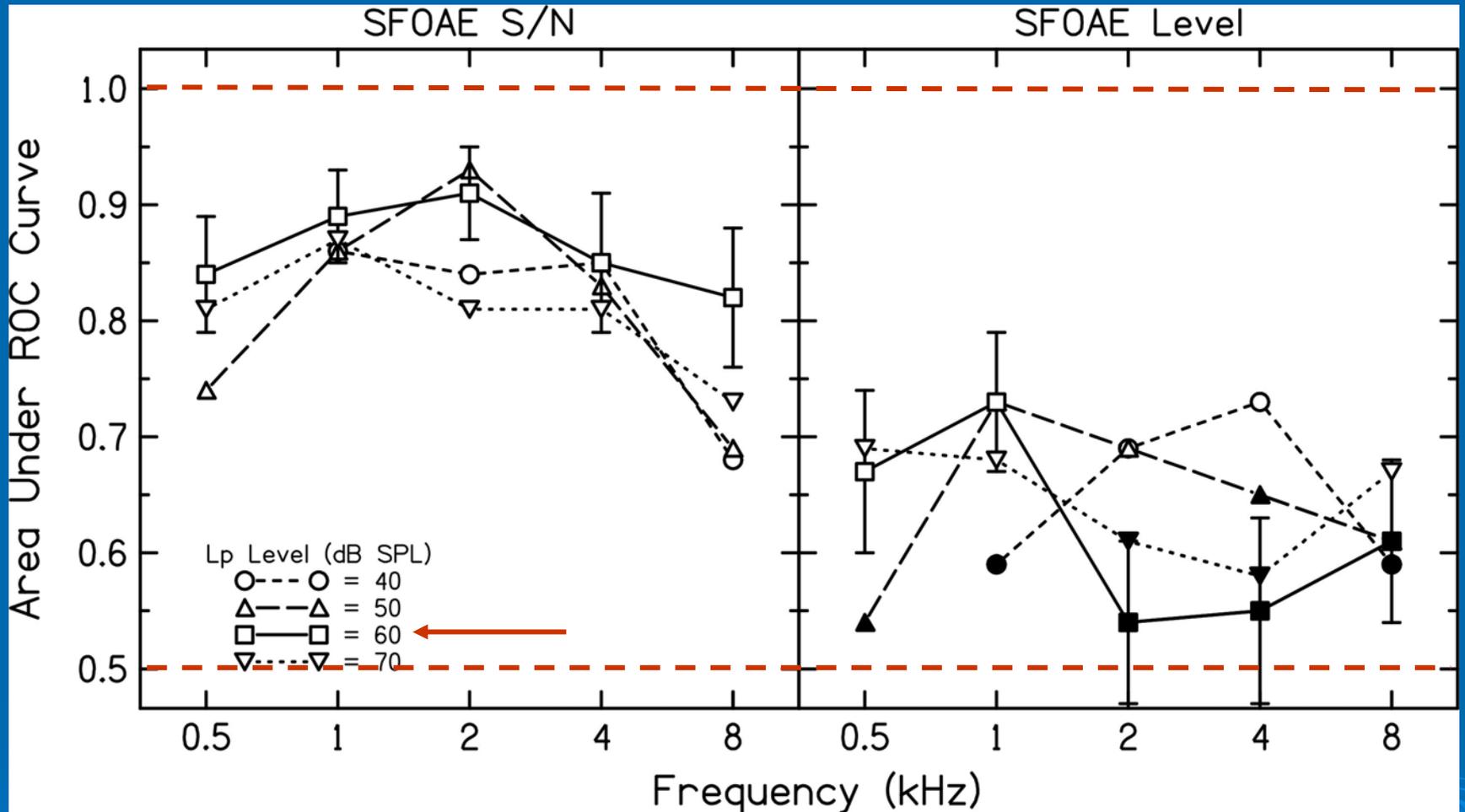
$f_p = 1000 \text{ Hz}$, $L_p = 60 \text{ dB SPL}$



23 dB SPL

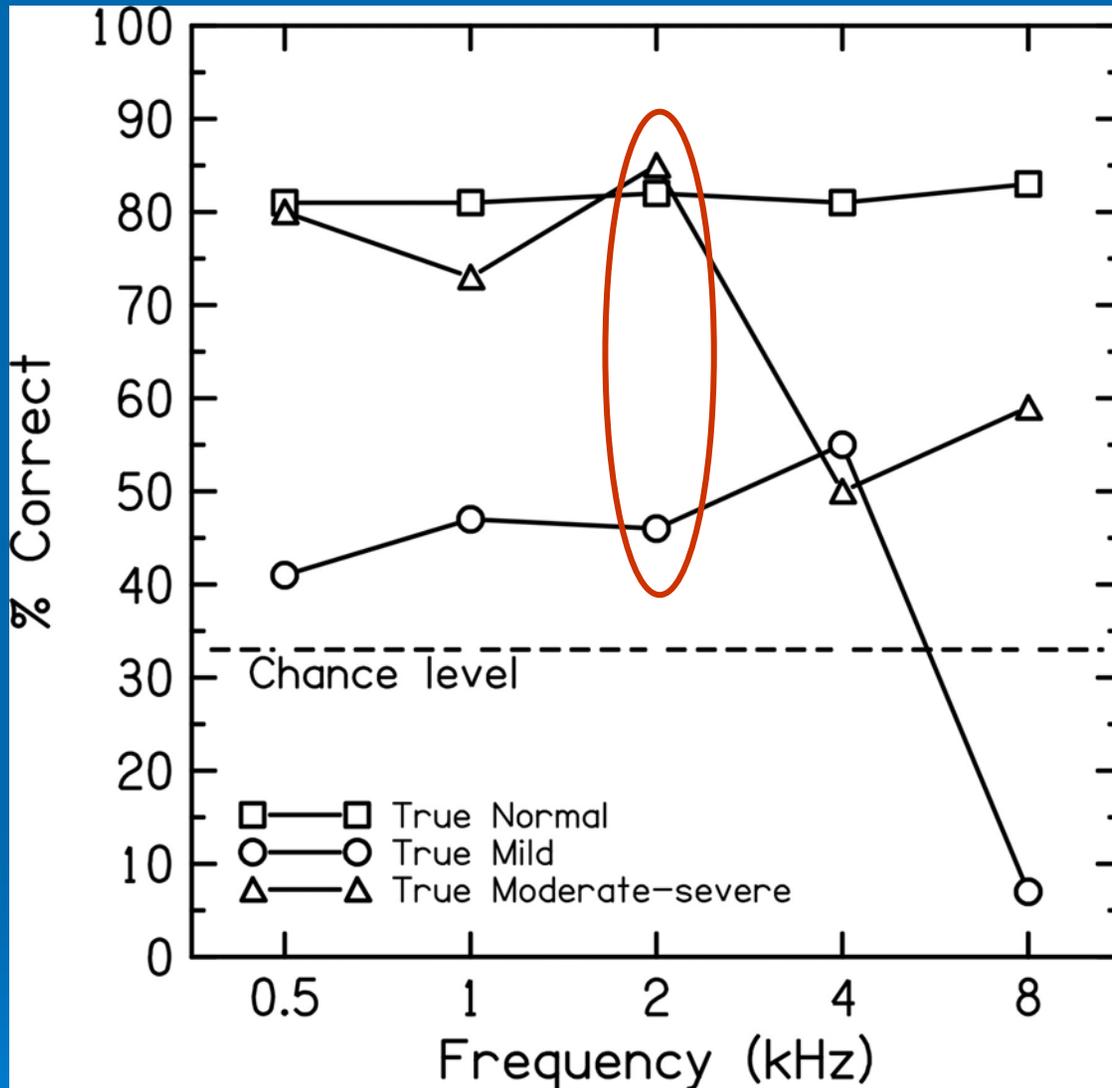
Total suppressed SFOAE: = largest SFOAE SPL produced by an f_s and L_s combination

Fig. 1 from Ellison and Keefe 2005



Performance in predicting presence/absence of hearing loss
 Filled symbols = non-significant for predicting hearing loss

Fig. 2 from Ellison and Keefe 2005



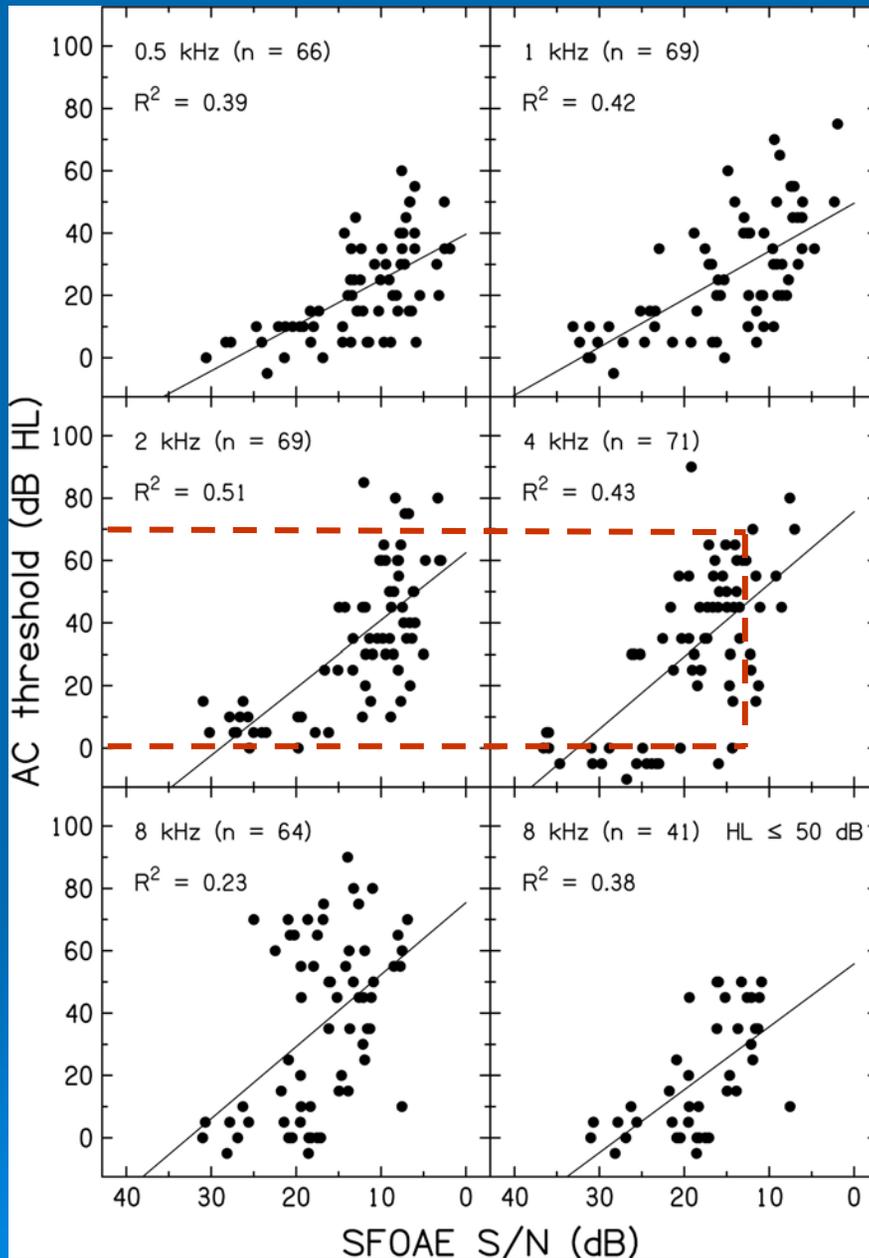
$L_P = 60$ dB SPL except at 1000 Hz where best performance was $L_P = 50$ dB SPL

Fixed specificity at 80% to separate normal vs. impaired, find SFOAE SNR

Fixed specificity at 75% to separate mild vs. moderate-severe, find SFOAE SNR

Percent of ears correctly identified in each of 3 categories based on SFOAE SNR

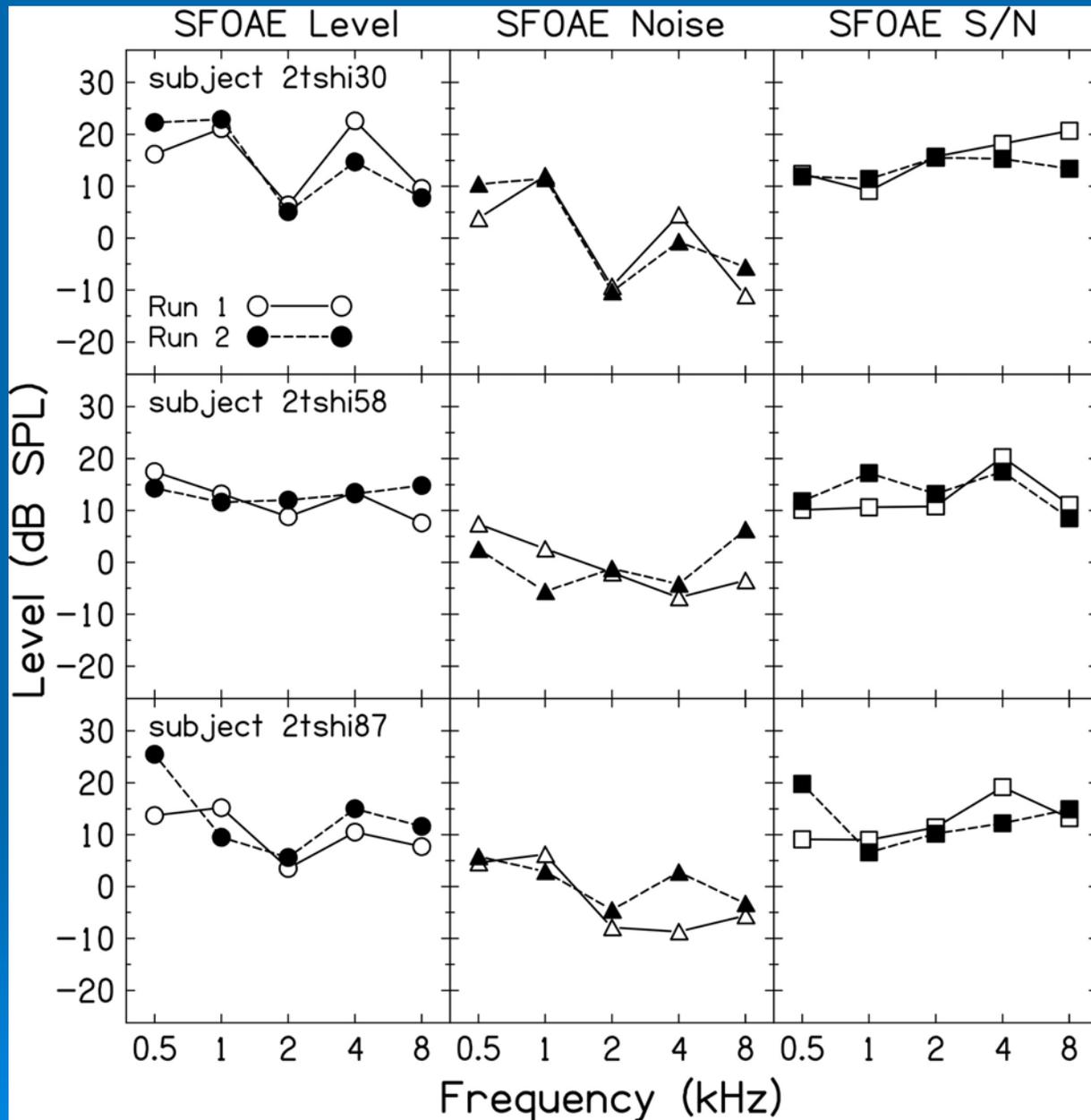
Fig. 3 from Ellison and Keefe 2005



$L_p = 60$ dB SPL except
at 2000 Hz, where L_p
 $= 50$ dB SPL

Amount of variability in AC
thresholds at a particular
SNR preclude the ability to
predict a specific AC
threshold using SFOAE SNR

Fig. 4 from Ellison and Keefe 2005

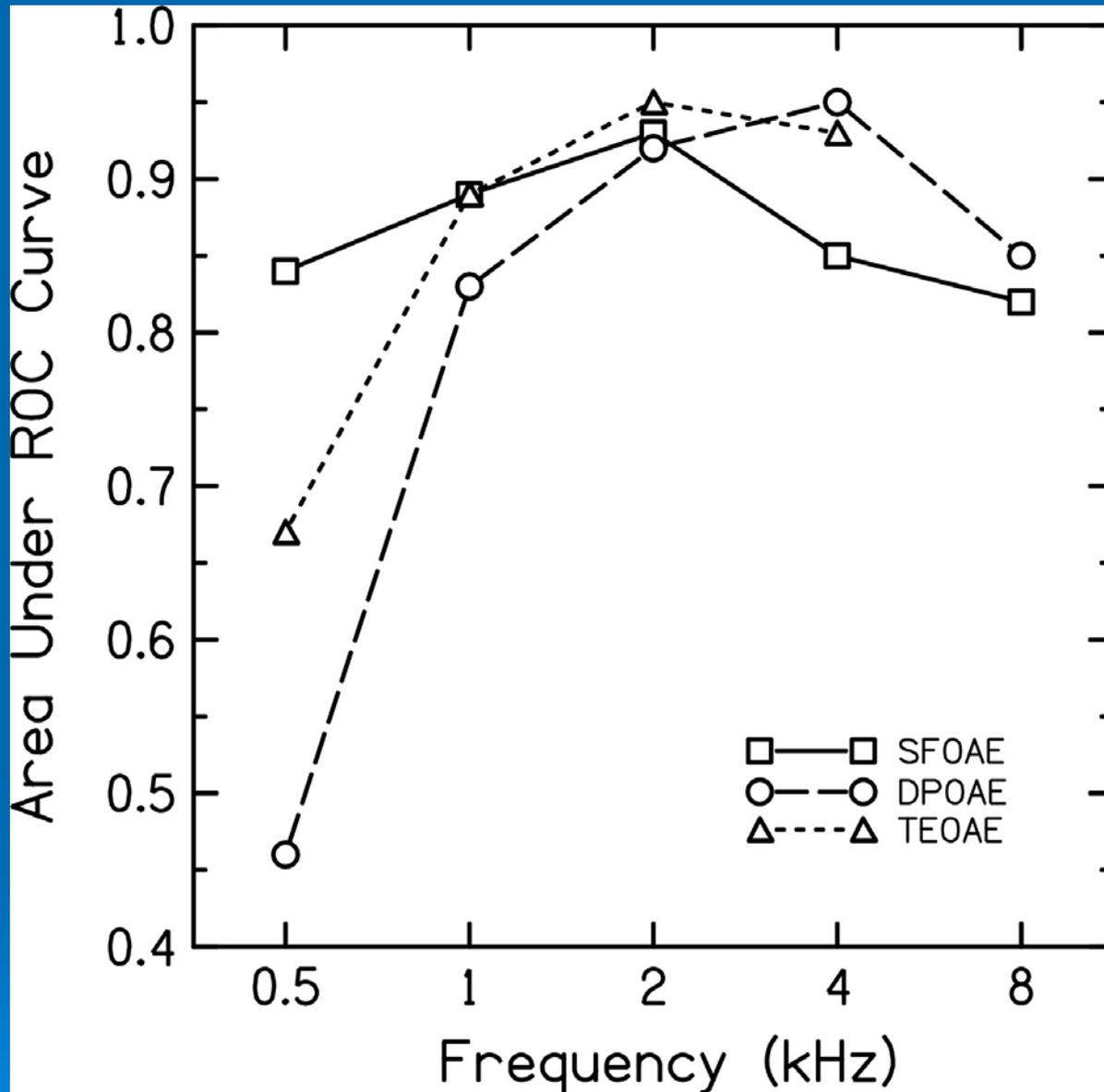


145 days
between visits
for 2tshi30,
and 26 days
for 2tshi58 and
2tshi87

$L_p = 60$ dB
SPL

SFOAE SNR
repeatability
overall within
3.5 dB

Fig. 5 from Ellison and Keefe 2005



500 Hz DPOAE data from Gorga et al., 1993, JASA, 93, 2050-2060

1000 to 8000 Hz DPOAE data from Gorga et al., 1997, Ear Hear, 18, 440-455

TEOAE data (one-octave band) from Prieve et al., 1993, JASA, 93, 3308-3319

Fig. 7 from Ellison and Keefe 2005

Conclusions for study 3

- Can use SFOAE SNR to
 - Classify ears as normal or impaired at all test frequencies
 - Classify impaired ears as mild or moderate-severe from 500 to 4000 Hz

Conclusions for study 3

- SFOAEs significantly correlated with AC thresholds from 500 to 8000 Hz using SNR as the predictor....
 - ...but cannot be used to predict a specific threshold due to variability
- SFOAEs performed better than DPOAE and CEOAEs in predicting thresholds at 500 Hz

Full Citations

- Ellison, J. C. and Keefe, D. H. (2005). Audiometric predictions using stimulus-frequency otoacoustic emissions and middle-ear measurements. *Ear Hear* 26, 487-503.
- Ruggero, M. A., Rich, N. C., Recio, A., Narayan, S. S., and Robles, L. (1997). Basilar-membrane responses to tones at the base of the chinchilla cochlea. *J. Acoust. Soc. Am.* 101, 2151-2163.
- Schairer, K. S. Fitzpatrick, D., and Keefe, D. H. (2003). Input-output functions for stimulus-frequency otoacoustic emissions in normal-hearing adult ears. *J. Acoust. Soc. Am.* 114, 944-966.
- Schairer, K. S. and Keefe, D. H. (2005). Simultaneous recording of stimulus-frequency and distortion-product otoacoustic emission input-output functions in human ears. *J. Acoust. Soc. Am.* 117, 818-832.