IV Electrophysiology

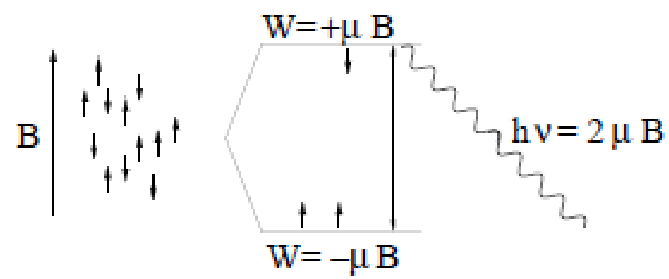
1) Non-invasive Methods
   a) Nuclear magnetic resonance imaging
   b) Electro- and magnetoencephalography
2) Electrophysiology
3) Some experiments of the Heidelberg MEG group

1 a Nuclear Magnetic Resonance Imaging

electron $\mu_B = e\hbar/(2m_e) = 5.8 \times 10^{-11} MeVT^{-1}$

proton $\mu_p = 1.4e\hbar/(2m_p) = 1.6 \times 10^{-14} MeVT^{-1}$

T = Tesla



statistical equilibrium:

$$\frac{N_+}{N_-} = \frac{e^{-W_+/(kT)}}{e^{-W_/(kT)}} = e^{-2\mu B/kT}$$

room temperature: $kT \approx 1/40eV$

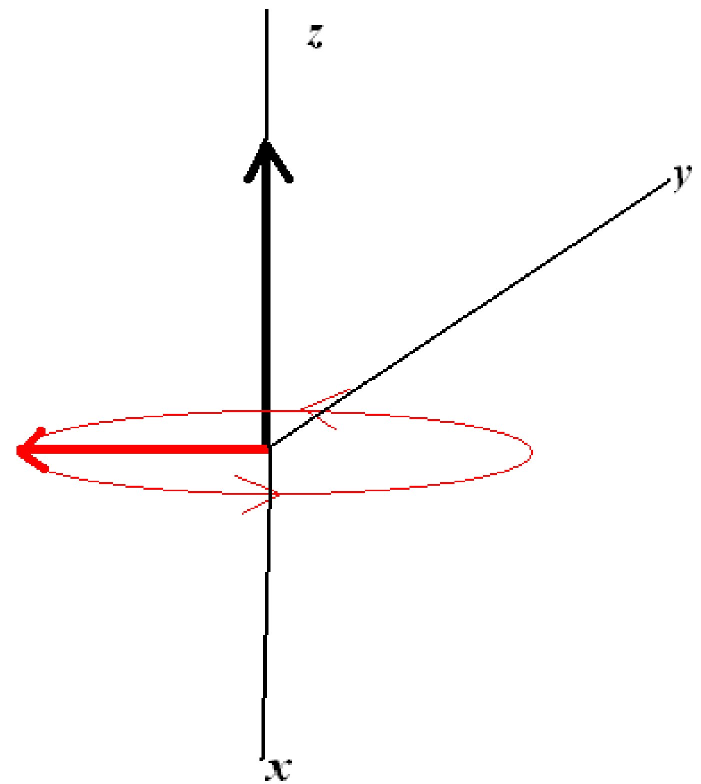
earth magnetic field: $e^{-6.410^{-11}} \approx 1 - 6.410^{-11}$

1 T = 10000 earth m. f: $e^{-6.410^{-7}}$

HF -field with frequency $h\nu = 2\mu B$ ⟶ deviation of statistical equilibrium.
Restoration by emission of radiation with this frequency.

The magnetic field at the resonating spin, normally of the proton, is also determined by the electrons of the surrounding chemical environment. It is special for water, e.g.

In equilibrium we have a polarization along the z axis given by $N_+ - N_-$ and no magnetization in the transverse $(x-y)$ plane. In disequilibrium after the irradiation with the HF the magnetization leads to equal values for N_+ and N_- and a magnetization in the transverse plane. Classically this corresponds to a flipping of the elementary magnets into the transverse plane and a precision. In the correct quantum mechanical description this is expressed by the density matrix:

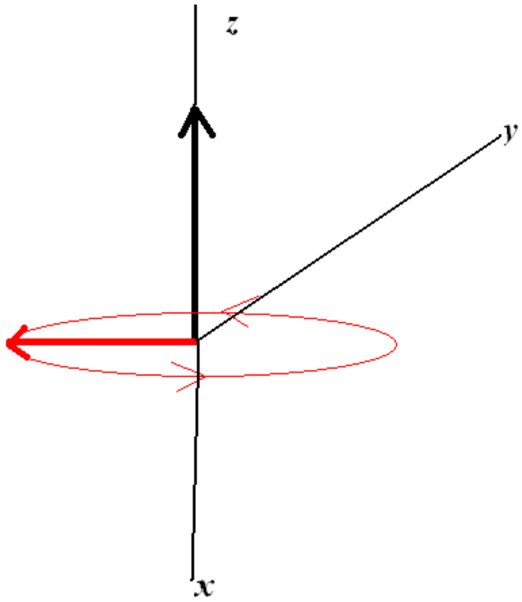


in the equilibrium $\rho_{eq} = \begin{pmatrix} N_+ & 0 \\ 0 & N_- \end{pmatrix}$

In the total disequilibrium: $\rho_{diseq} = \begin{pmatrix} N & \gamma \\ \gamma & N \end{pmatrix}$

This leads to the expectation values:

$\langle M_z \rangle = 0,\ \langle M_x \rangle = \mathrm{Re}\,\gamma,\ \langle M_y \rangle = \mathrm{Im}\,\gamma$



By interaction with the surrounding: $\rho_{diseq} \rightarrow \rho_{eq}$.

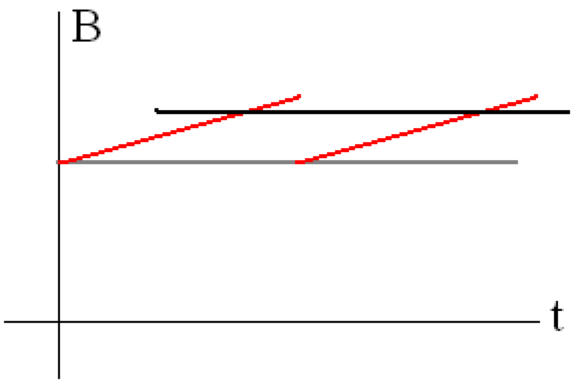
Decay of γ: T_2 (spin-spin relaxation, decoherence)

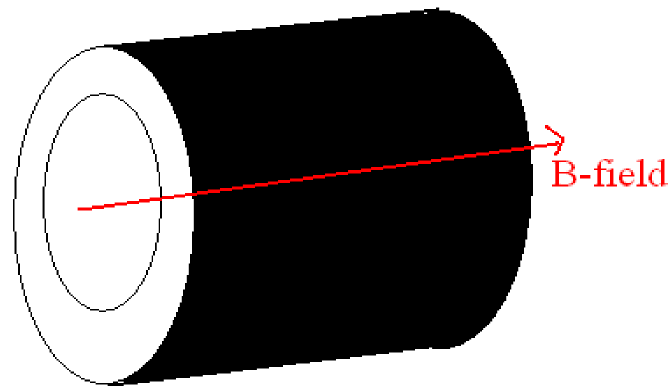
Restoration $N \rightarrow N_\pm$: T_1 (spin-lattice relaxation)

Normally $T_2 < T_1$

Essential ingredients for MRI:

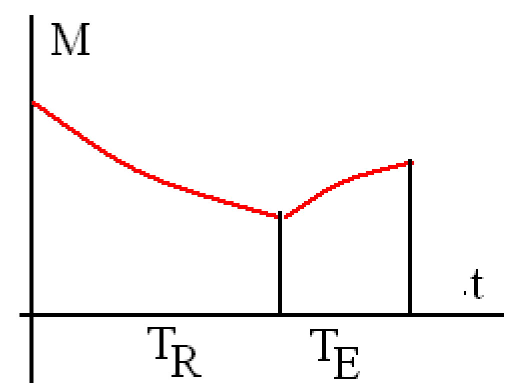
* Huge magnet in order to produce a magnetic field of several Tesla
* A HF generator with the appropriate frequency
* A time and space dependent magnetic field which guarantees that at a certain time the frequancy condition $h\nu = 2\mu B$ s satified for a fixed layer (tomography)
* Detection devices





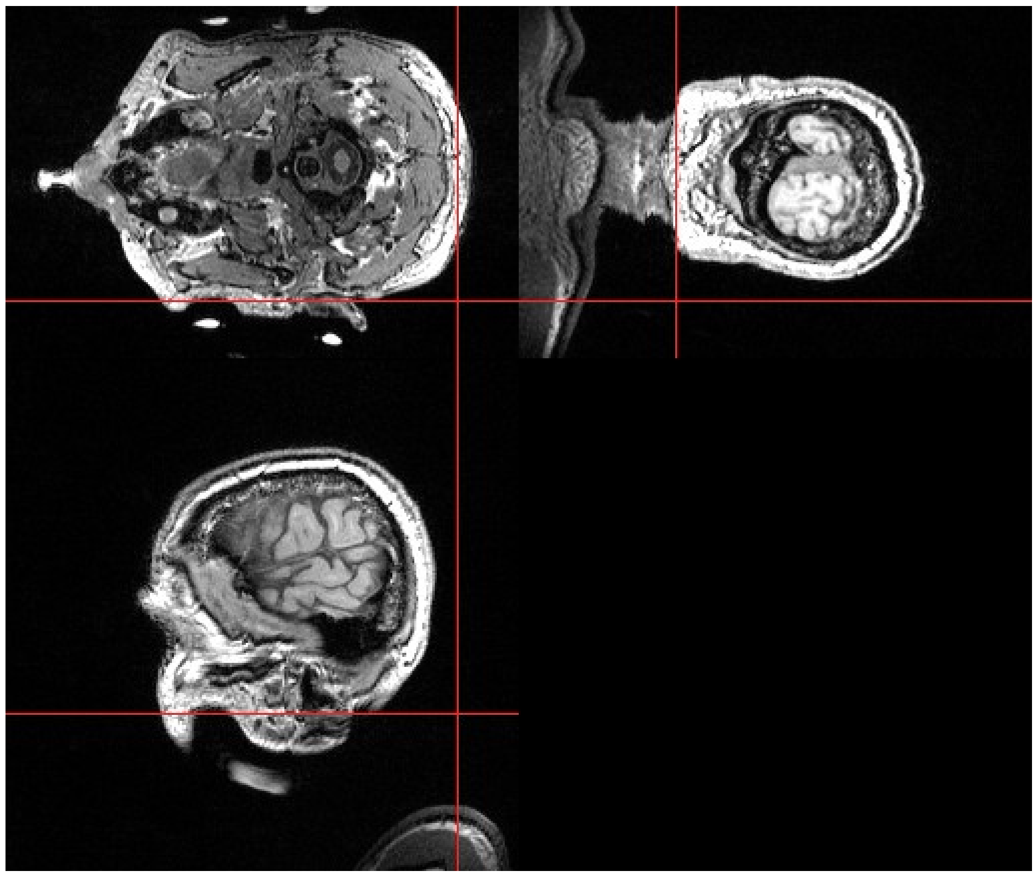
Inside:
Generator for gradient field
HF-emitters
HF receivers

One turns on the HF for time T_R and measures for time T_E
By choice of these times and other procedures (spin echo) one can give different weight to the restoration of the equilibrium magnetization T_1 weighted, or the decay of the transverse magnetization, T_2 weighted



Anatomical pictures of the brain: One chooses resonance for water:
Liquor: much water, black
neurons: medium water content, gray
glia cells: no water: white

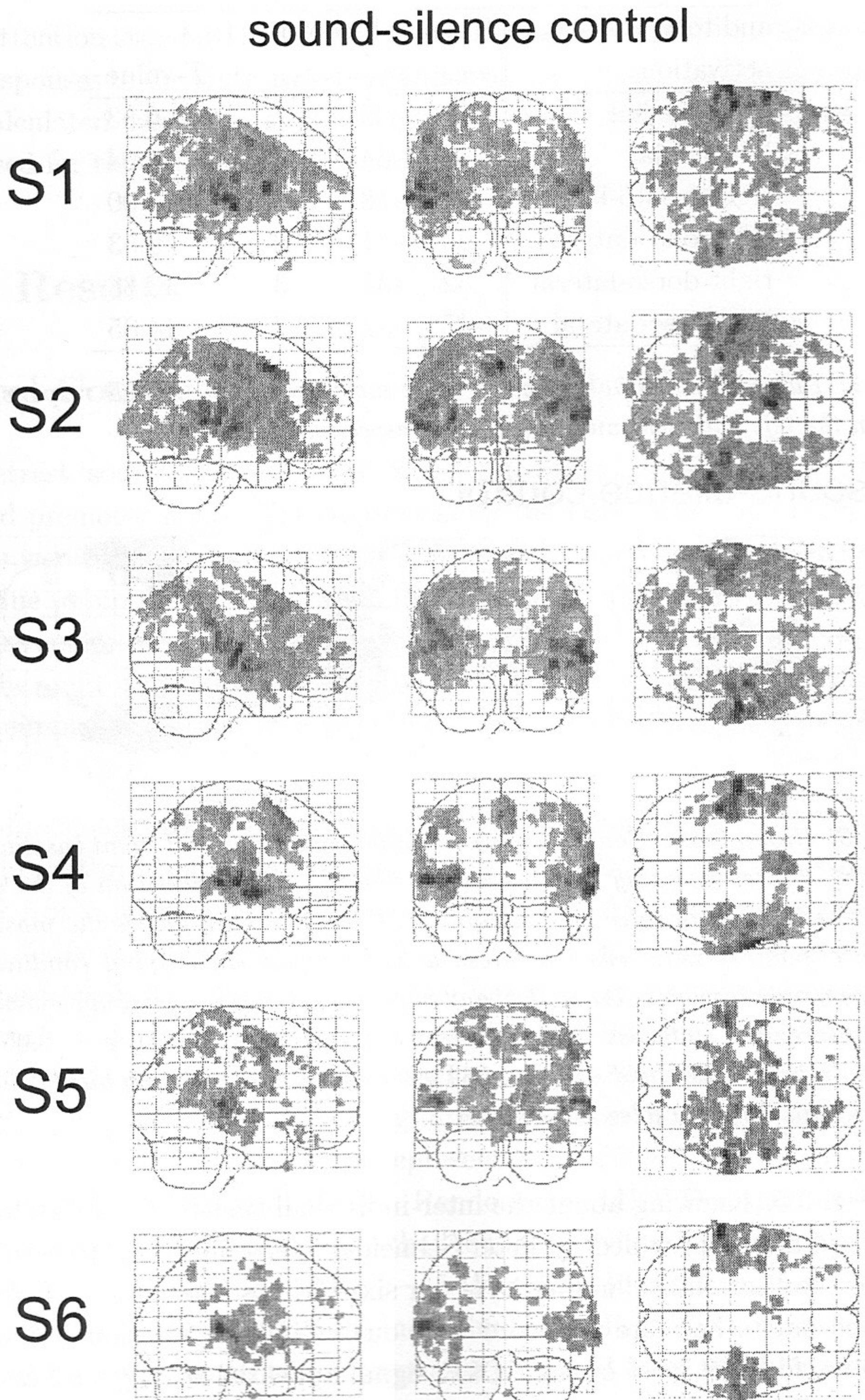
example: cortex-mri/HGD_Kopf/analyze/,,,,hdr



Functional magnetic resonance imaging

Neural activity   increased blood circulation
complicated: more blood, 2 s after activation increase of oxigenated blood (Hb, HbO2) at the expense of desoxigenated blood (HBr, dHB). In Hbr unpaired electrons, large spin-spin-relaxation, in HBO2 paired electrons, dimagnetic, weak spin-spin interaction. This yields some difference of radiation from regions with and without activation.
Delicate interpretation. errors due to subtraction of ``pictures'', depends on choosen threshold.

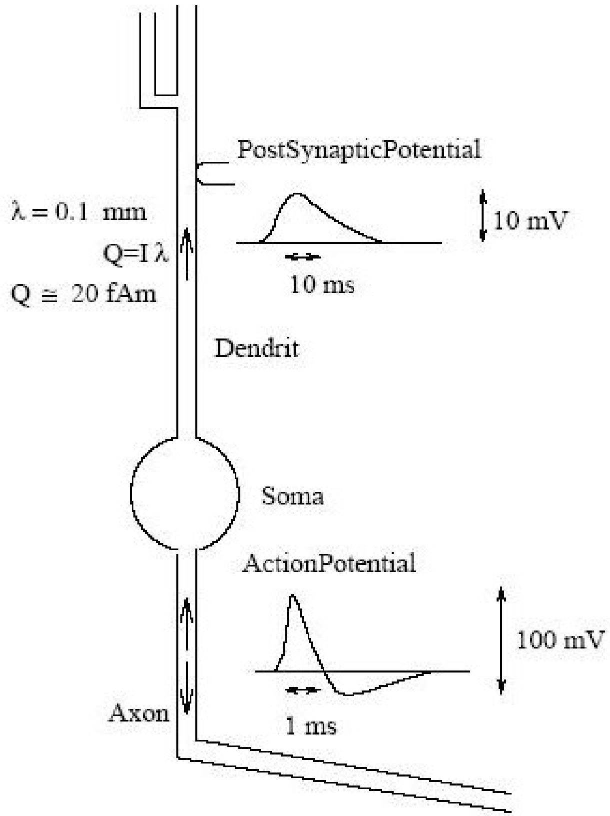
Positron Emission Tomography
In principle similar to FMRI, since it is sensitive to haemodynamics. Inject beta+ active source and determine region of increased glucose supply by measuring the gamma quanta from positron annihilation in coincidence.



FMRI for sound - silence
for 6 subjects

1 b Electro- and Magnetoencephalography (EEG and MEG)

More direct than FMRI and PET, since direct consequences of synaptic currents are measured.



Current dipole moment: localized current times length of it [A m]

synaptic current	20 fA m
1 Million synapses	20 nAm

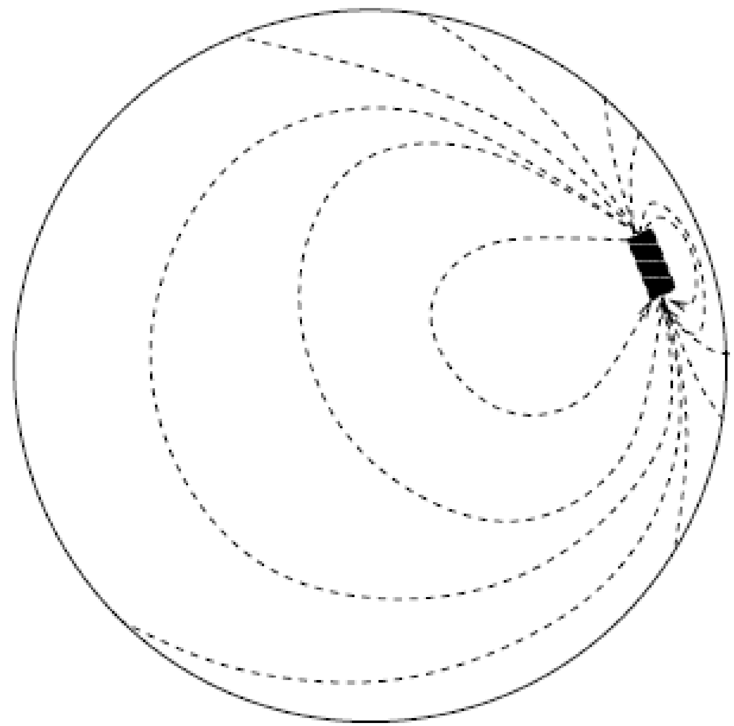


Abbildung 6.3: Current distribution in the brain initiated by a primary current in the black box; the dashed lines are the stream lines of the volume current.

The currents lead to electric potentials on the scalp (EEG) and to magnetic fields (MEG).

Strength of magnetic field: order of 100 fT (earth 10^8 stronger)

measuring device; SQuIDs

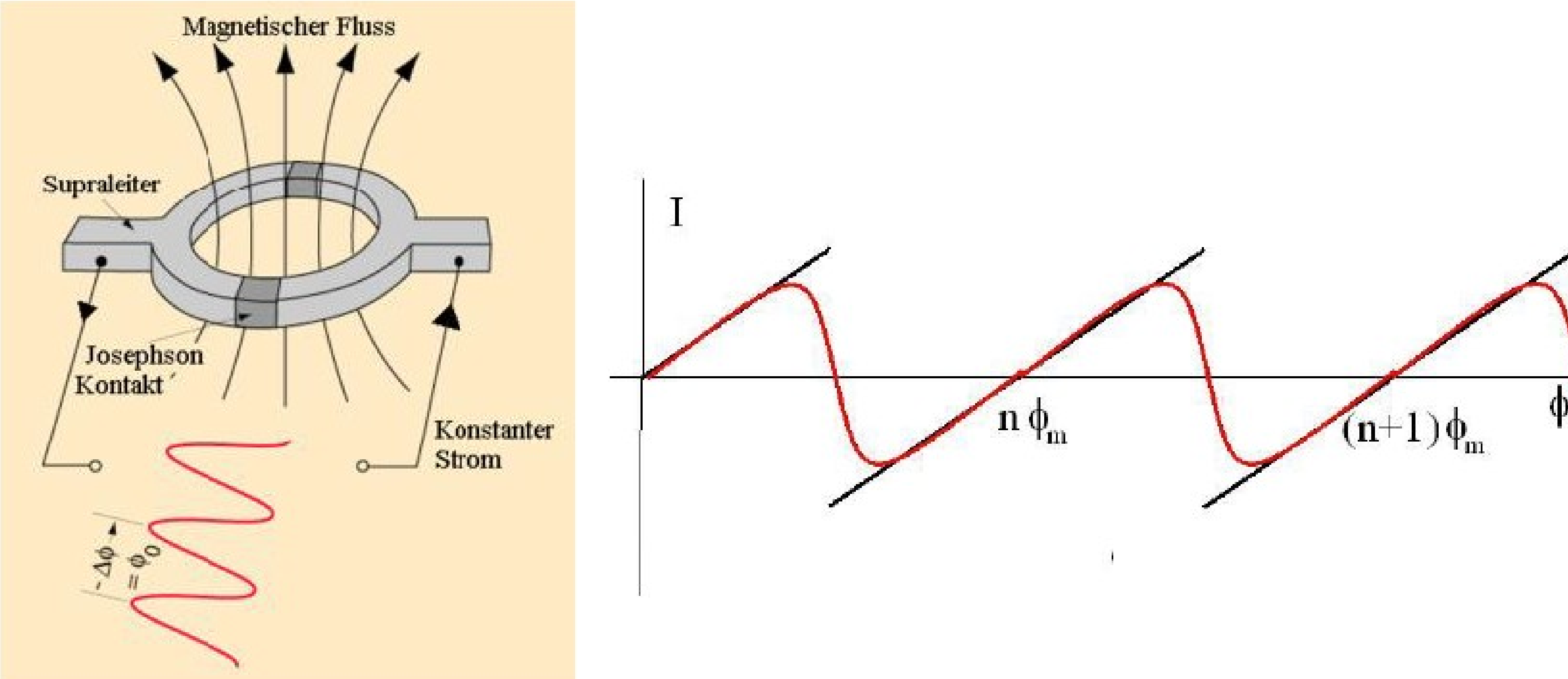


Abbildung 6.2: Construction principle of a SQUID

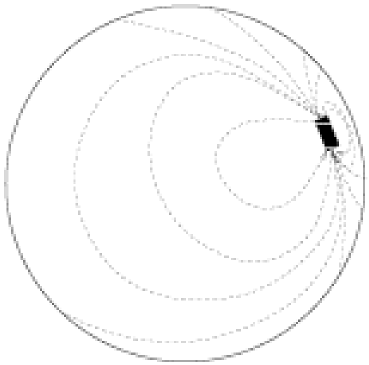
and the compensating currents, black theoretical, without Josephson junction, red with Josepson junction.

$$\Phi = \int_F \vec{B}.d\vec{f}, \quad \text{quantized in flux quanta:}$$

$$\Phi_m = \frac{\hbar c 2\pi}{2e} \approx 4 \cdot 10^{-7} \text{ gaus cm}^2 = 4 \cdot 10^{-15} \text{ Wb} = 0.0001 \; fT\, cm^2$$

Given $\vec{j}_p(\vec{x})$, the primary current and $\sigma(\vec{x})$ the conductivity inside the skull,

wanted the magnetic field $\vec{B}(\vec{x})$ and/or the electric potential $\phi(\vec{x})$ outside the skull



$$\vec{j}(\vec{x}) = \vec{j}_p(\vec{x}) + \vec{j}_v(\vec{x}) = \vec{j}_p(\vec{x}) - \sigma(\vec{x})\vec{\partial}\phi(\vec{x}).$$

← Ohm

$\vec{\partial}.\vec{j} = 0$, current conservation and b.c $\hat{n}_{\partial G}.\vec{\partial}\phi = 0$

allow to calculate $\phi(\vec{x})$ as linear functional of $\vec{j}_p(\vec{x})$

$$\vec{B}(\vec{x}) = \frac{1}{4\pi}\left[\vec{\partial} \times \int_G d^3x' \frac{\vec{j}(\vec{x}\,')}{|\vec{x} - \vec{x}\,'|}\right]$$

↑ Ampere

hence one can calculate the magnetic field as linear functional of $\vec{j}_p(\vec{x})$

$$\phi(\vec{x}) = \int d^3x' \, \vec{\mathcal{L}}(\vec{x}, \vec{x}\,').\vec{j}_p(\vec{x}\,')$$

$$B_\alpha(\vec{x}) = \int d^3x' \, \vec{\mathcal{L}}^m_\alpha(\vec{x}, \vec{x}\,').\vec{j}_p(\vec{x}\,')$$

Theorem: The magnetic field outside the head is uniquely determined by the component $B_n(\vec{x}) = \hat{n}_{\partial G}.\vec{B}(\vec{x})$ with $\vec{x} \in \partial G$, that is the normal component of $\vec{B}$ on the surface of the head.

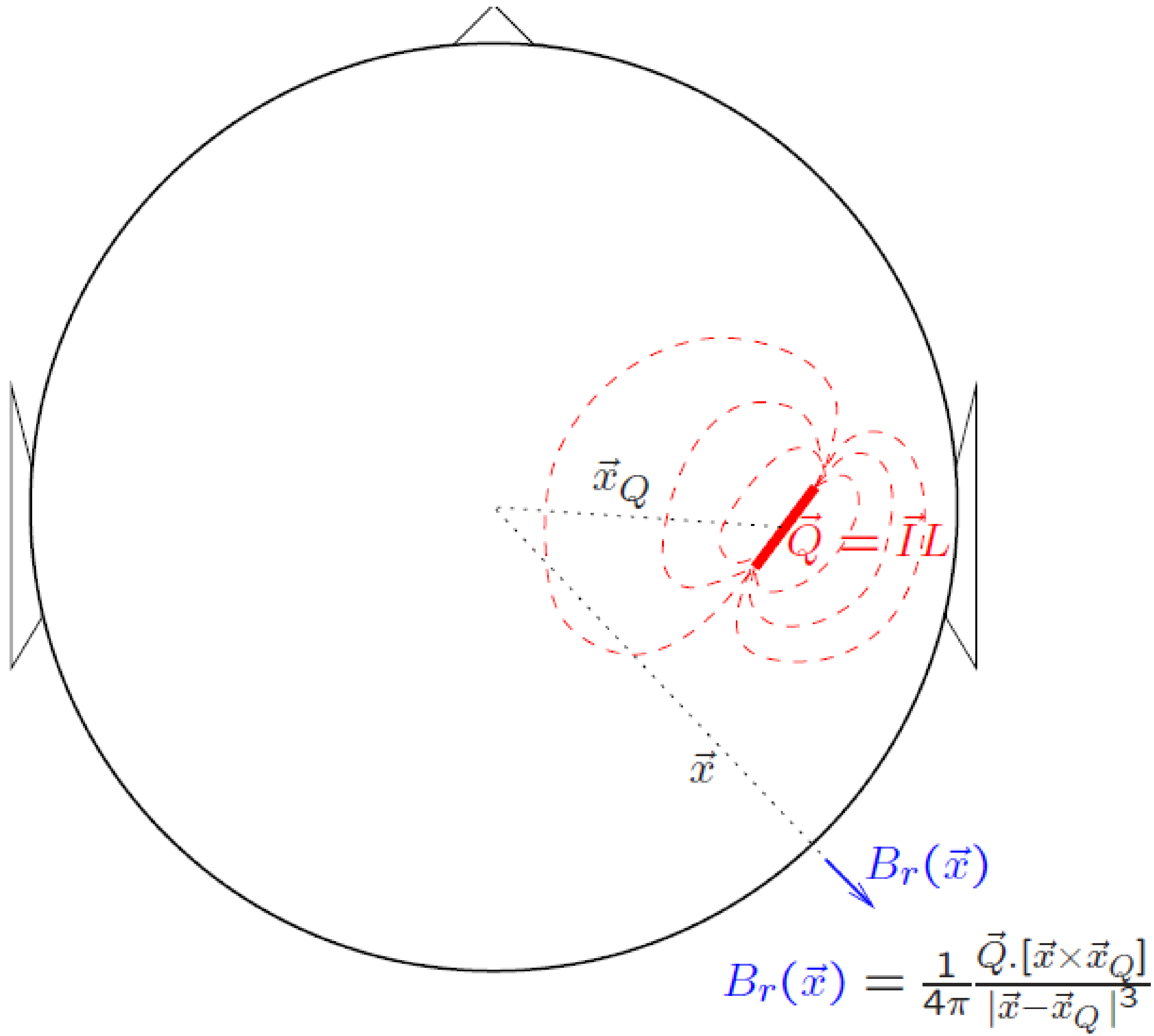
Proof by Neumann boundary condition.

Theorem If the head is a spherically symmetric system, that is $\sigma(\vec{x}) = \sigma(|\vec{x}|)$ and G is a sphere, the contribution of the volume current to the normal component of $\vec{B}$ on the surface of the head is zero.

$$\vec{j}_p(\vec{x}) \approx I\,\vec{l}\,\delta(\vec{x} - \vec{x}_Q) = \vec{Q}\,\delta(\vec{x} - \vec{x}_Q).$$

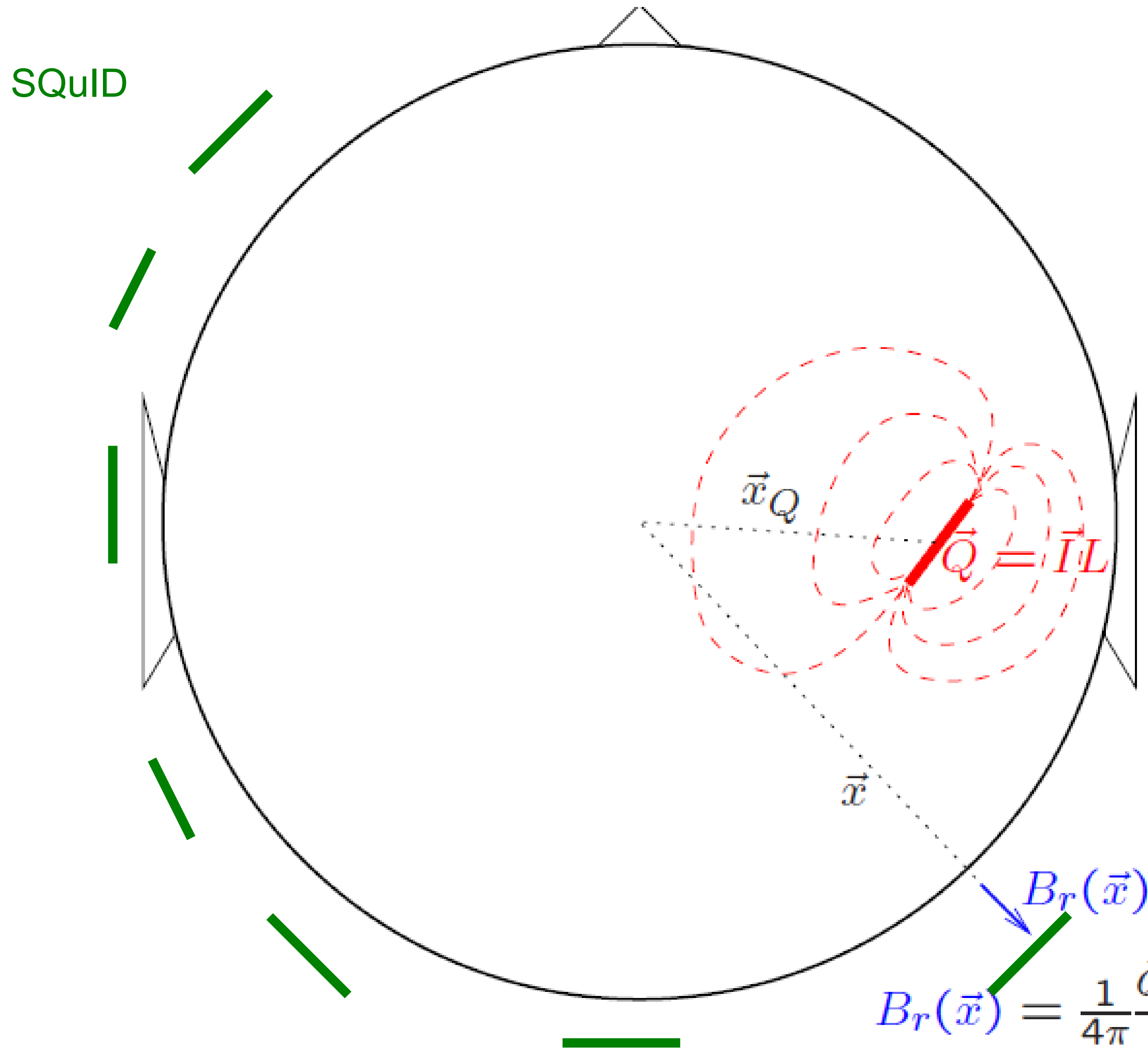
for a spherical head we obtain then:

$$B_r(\vec{x}) \equiv \vec{B}(\vec{x}).\hat{x} = -\frac{1}{4\pi}\frac{\vec{Q}.[\vec{x} \times \vec{x}_Q]}{|\vec{x} - \vec{x}_Q|^3}$$


$\vec{x}_Q$
$\vec{Q} = \vec{I}L$
$\vec{x}$
$B_r(\vec{x})$
$B_r(\vec{x}) = \frac{1}{4\pi}\frac{\vec{Q}.[\vec{x}\times\vec{x}_Q]}{|\vec{x}-\vec{x}_Q|^3}$

Summary MEG

Heidelberg
Neuromag, 122 SQuIDs as
Magneto-Gradiometers



$$B_r(\vec{x}) = \frac{1}{4\pi}\frac{\vec{Q}.[\vec{x}\times\vec{x}_Q]}{|\vec{x}-\vec{x}_Q|^3}$$


Neurc

Determine synaptic currents (Action potentials lead to quadrupole currents and fall off to fast)

Question: Can the currents be determined uniquely from the fields outside the scull? (Inverse Problem)

Answer: No (Helmholtz ca 1858)
Reason: There are current distributions which lead to fields which vanish outside or at the surface of the scull.

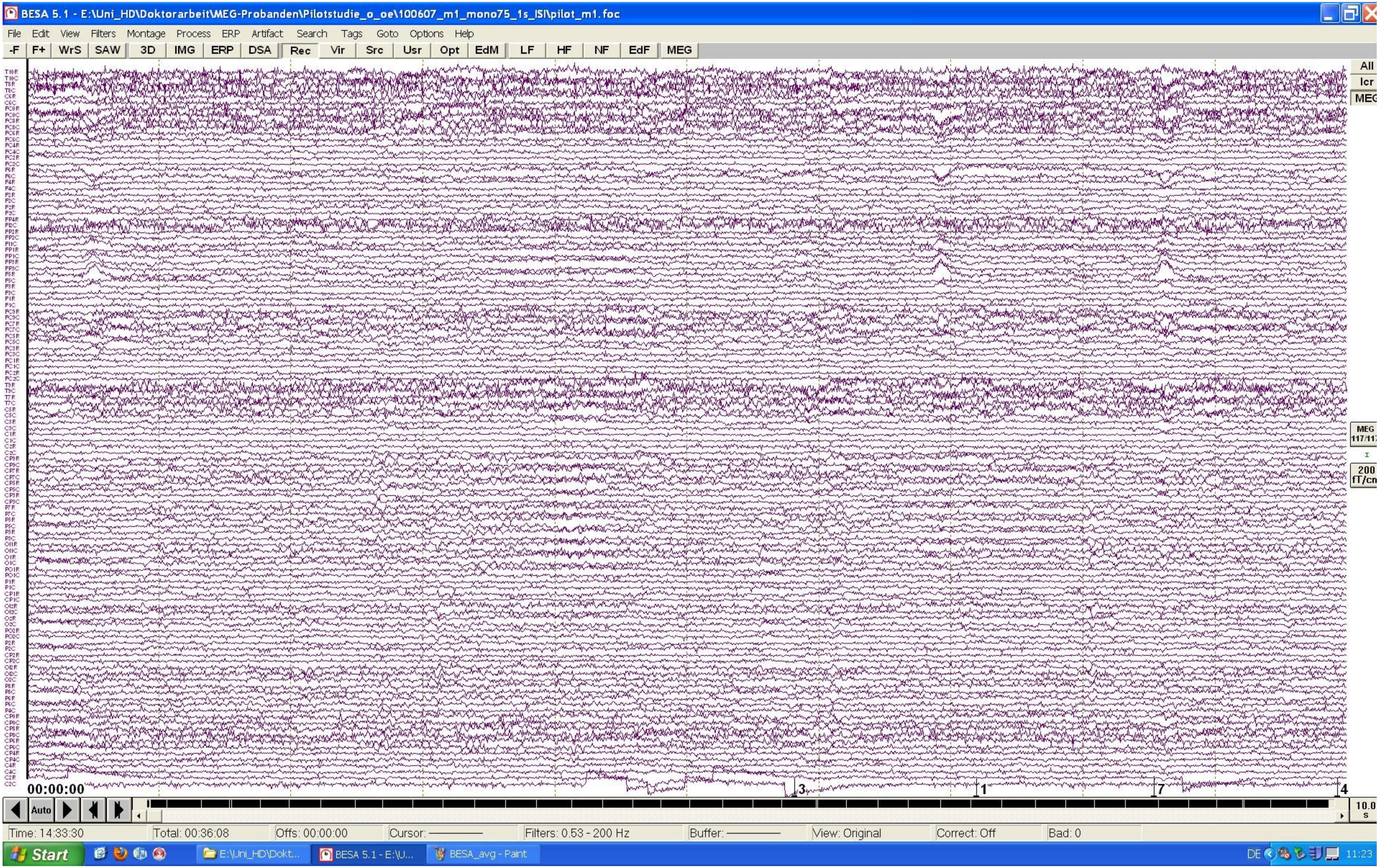
As can be seen e.g. from $B_r(\vec{x}) \equiv \vec{B}(\vec{x}).\hat{x} = -\frac{1}{4\pi}\frac{\vec{Q}.[\vec{x} \times \vec{x}_Q]}{|\vec{x} - \vec{x}_Q|^3}$

a current in radial direction, that is $\vec{Q} = |\vec{Q}|\hat{x}_Q$

leads to $B_r(\vec{x}) \equiv 0$

Problem relieved, but not resolved totally, by simultaneous EEG and MEG measurement.

Protocol of the raw data (magnetic field gradients) in all 122 channels

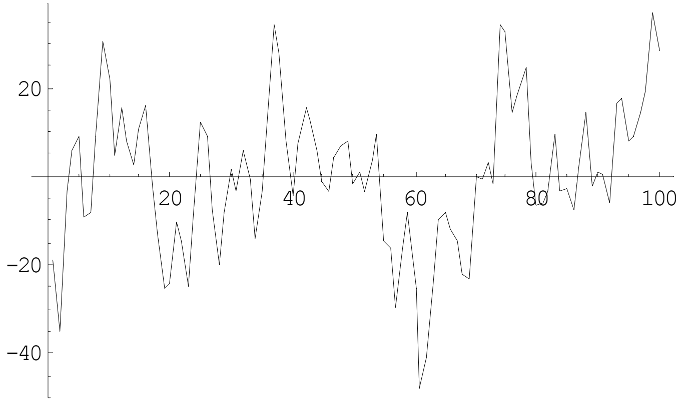


Other problem: Also the idle brain develops a lot of activity.
Energy consumption of an idle brain comparable to that of the calf of a marathon runner. Mental activity only increases energy consumption by about 20 %

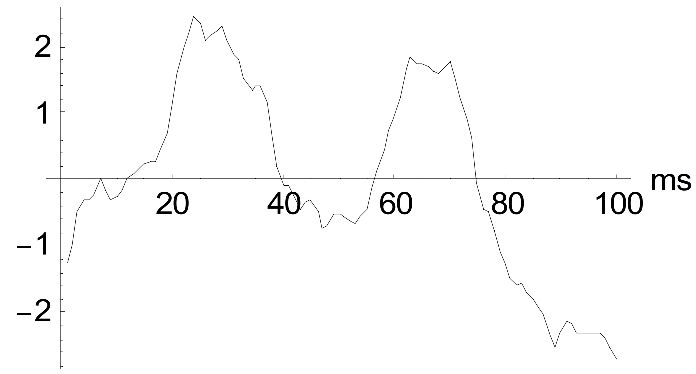
Therefore noise normally of equal strength as signal.

Way out: Many averages. Adding n probes of noise increases amplitude like square root of n. But n synchronized signals -- hopefully -- add, therefore signal-to-noise ratio increases as square root of n.

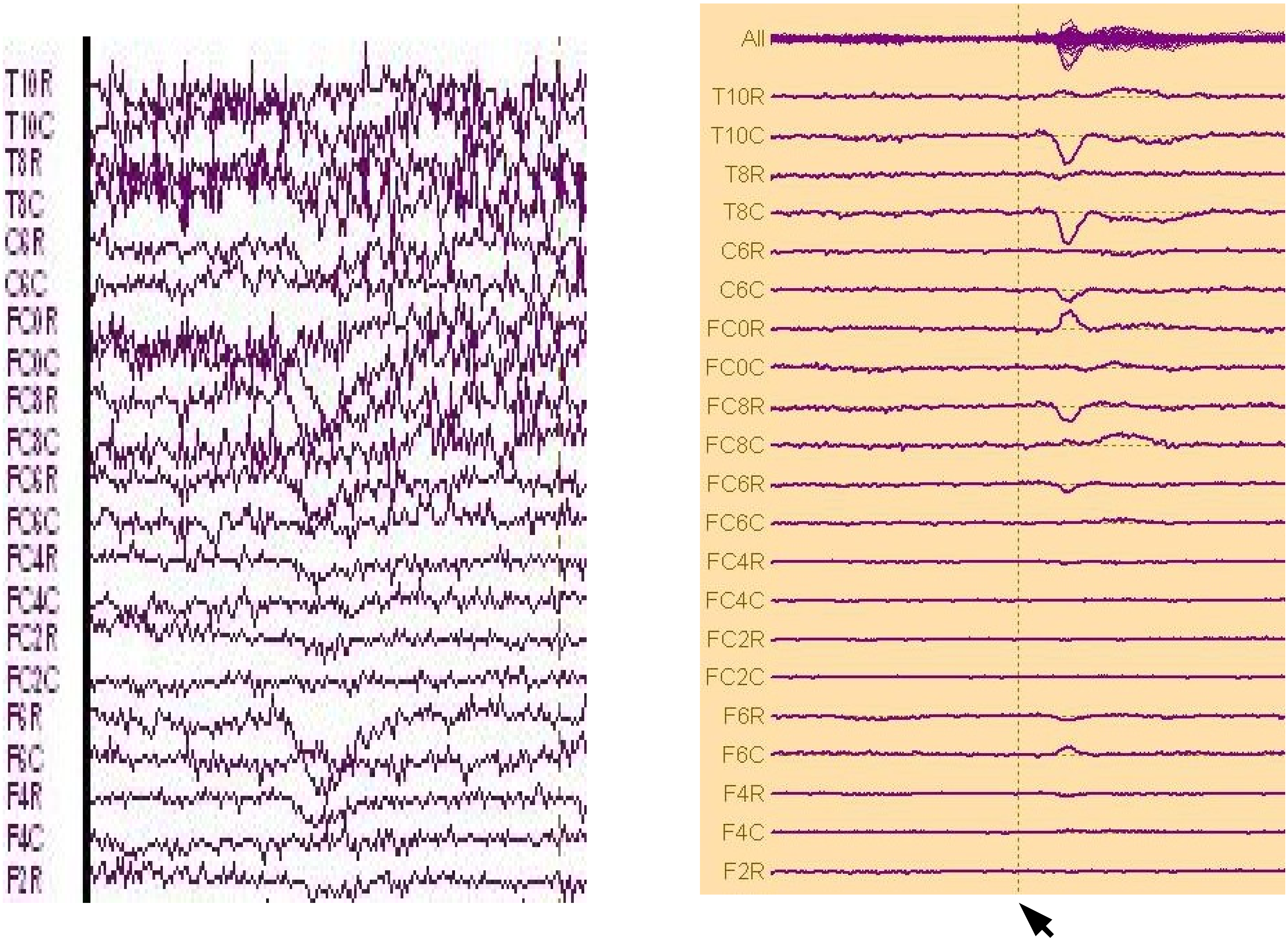
Brain activity as measured by MEG during silence



An episode of 100 ms

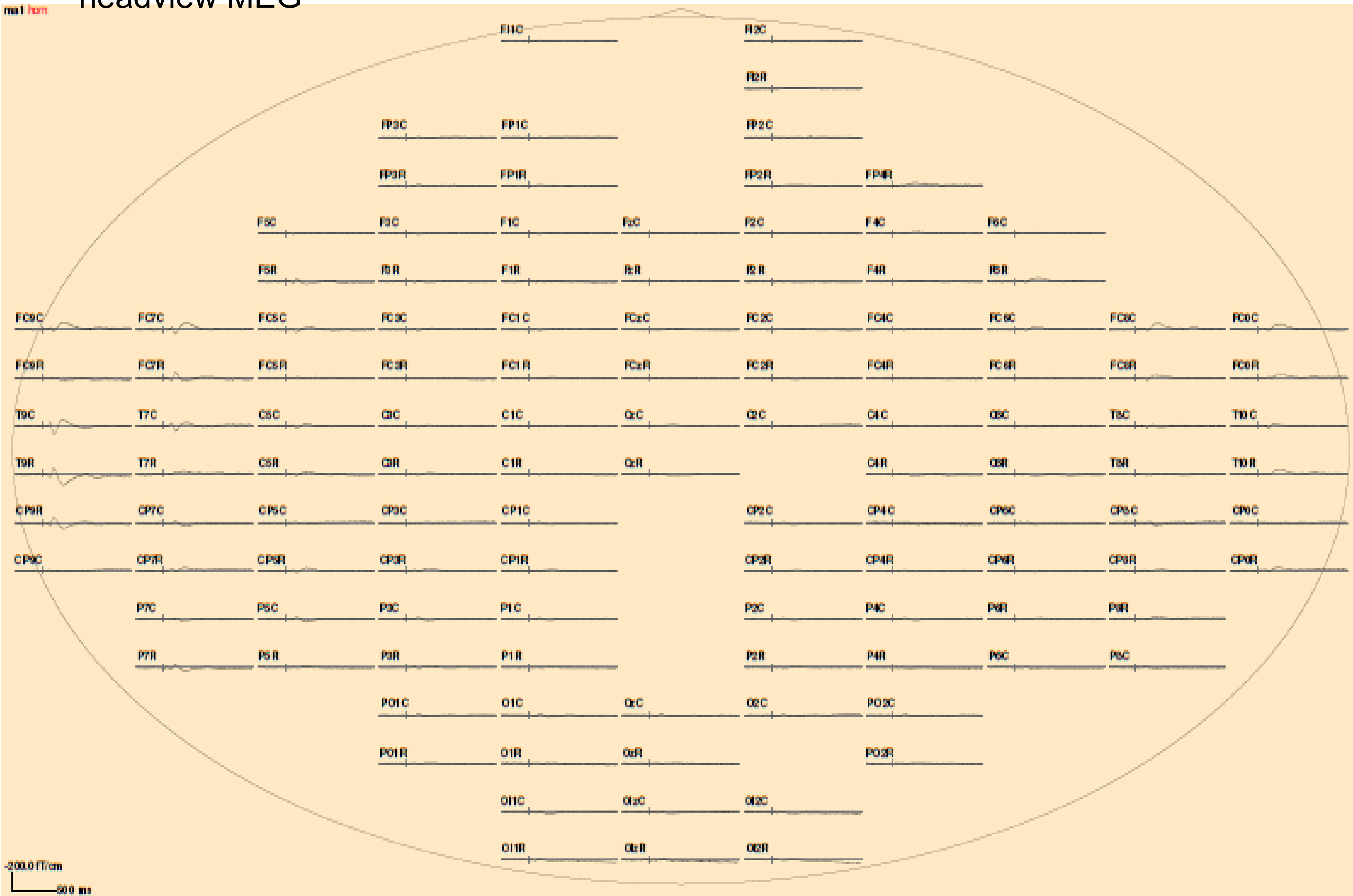


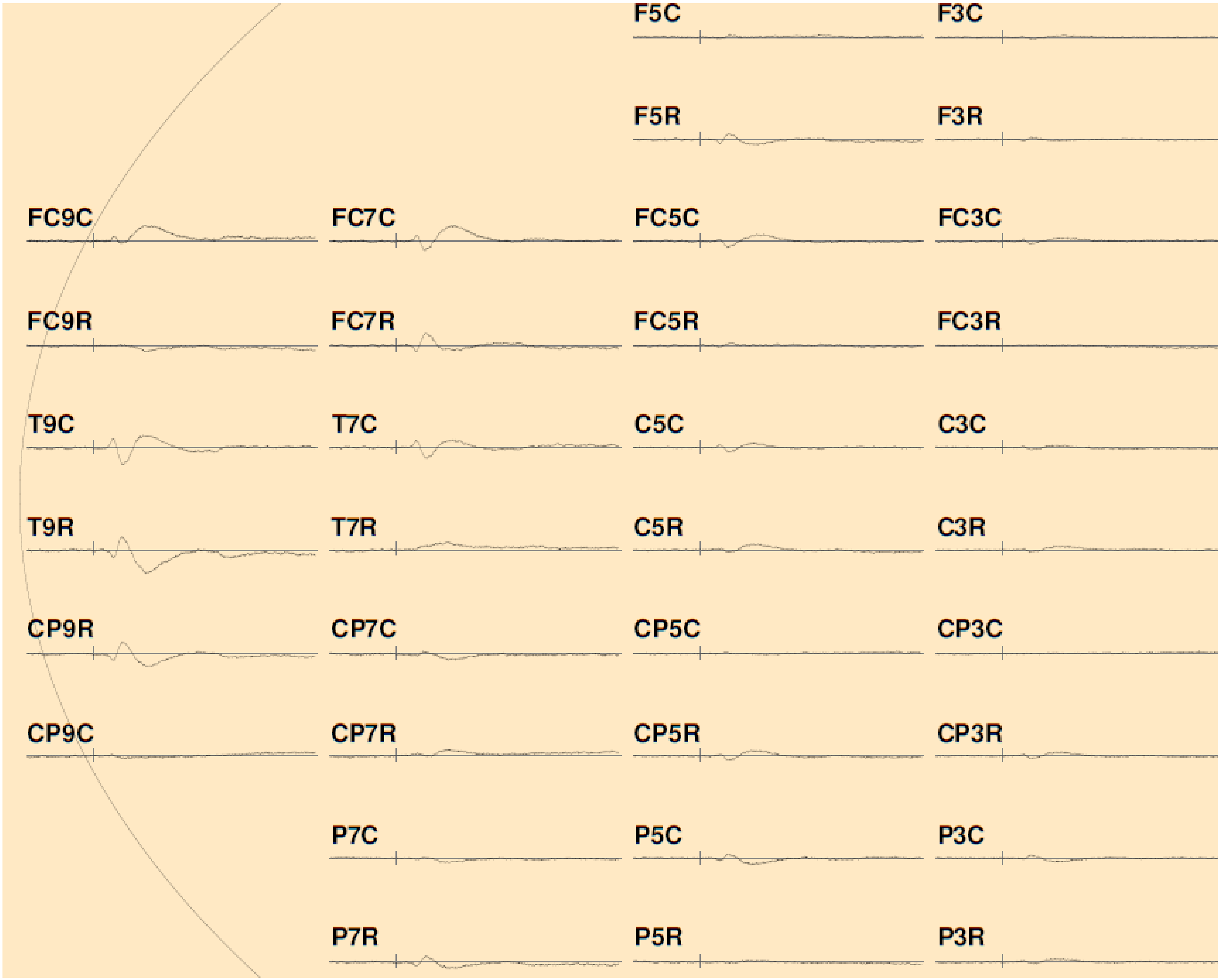
Average over 100 episodes



Raw data and data averaged, synchronized at stimulus onset

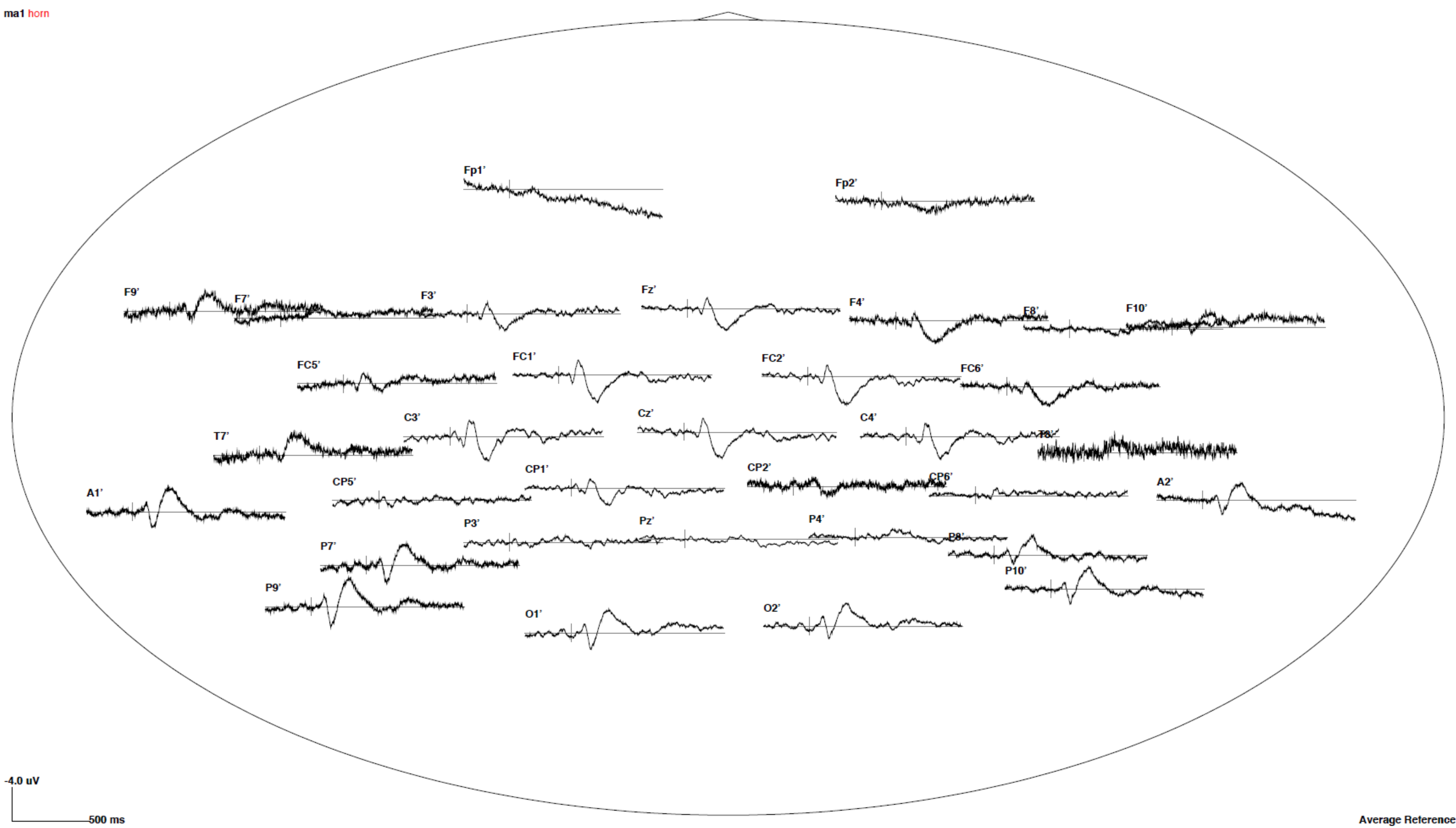
headview MEG





F5C
F3C
F5R
F3R
FC9C
FC7C
FC5C
FC3C
FC9R
FC7R
FC5R
FC3R
T9C
T7C
C5C
C3C
T9R
T7R
C5R
C3R
CP9R
CP7C
CP5C
CP3C
CP9C
CP7R
CP5R
CP3R
P7C
P5C
P3C
P7R
P5R
P3R

headview EEG



Application in Neurophysiology:

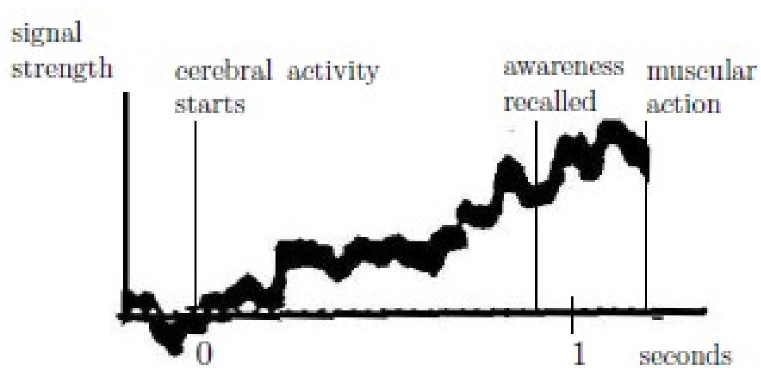
Detection of activity:

One mesures the field at few positions, normally for EEG, (minimal one reference and one measuring electrode) to see if there is activity at all.

Many classical experiments have been performed in this way.

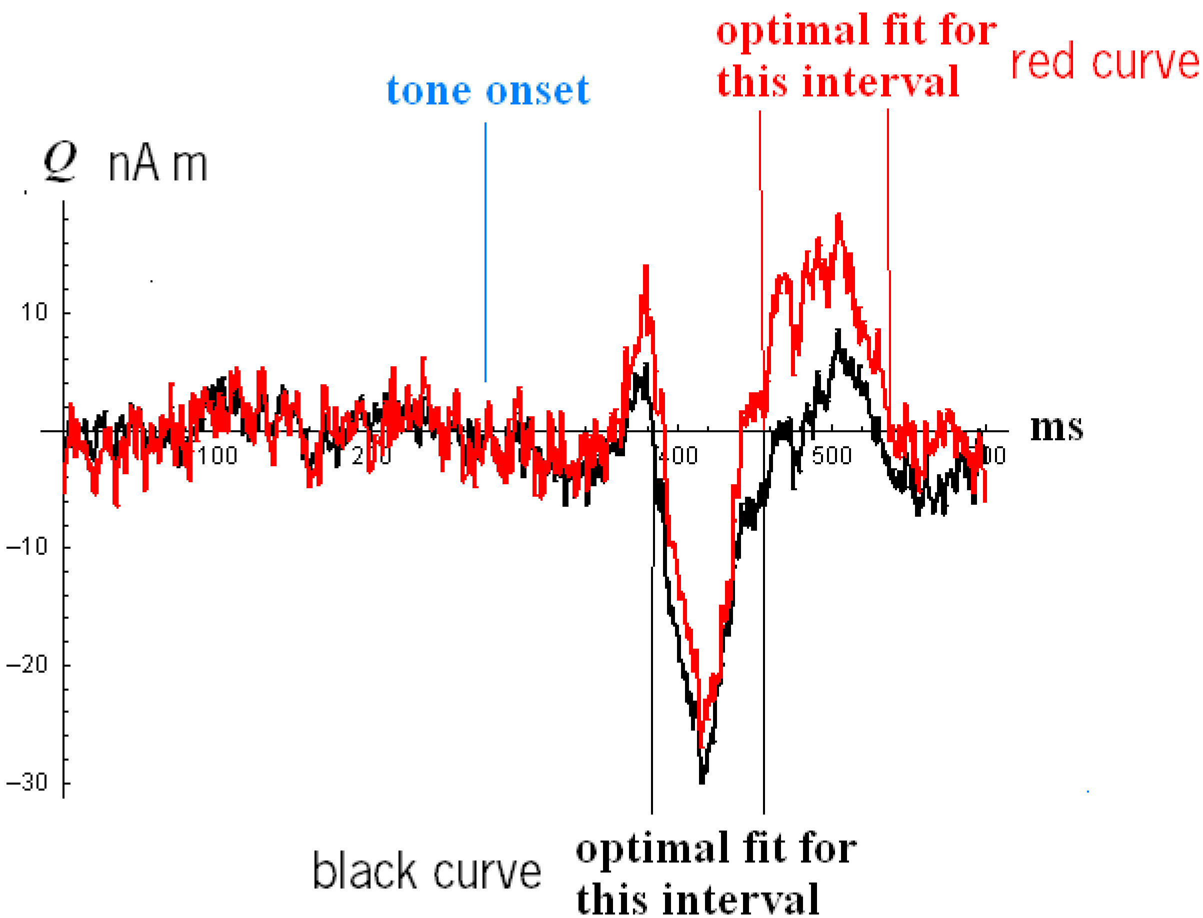
e.g. prepotentials: There is neural activity nearly a second before muscular activity

Libets experiment: The person is aware of the action ca 0.3 seonds after the prepotential has started.

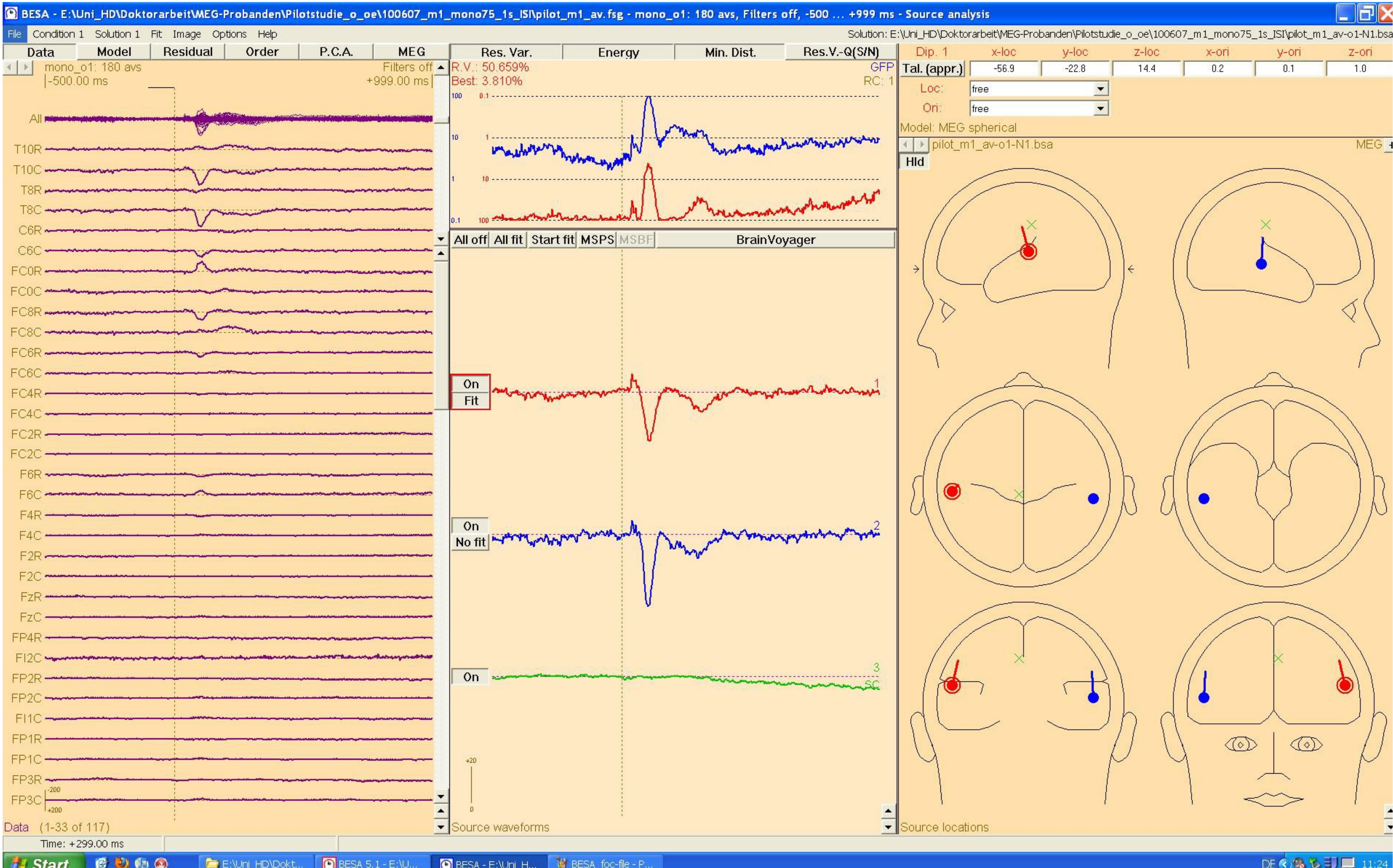


Dipole fit:

One assumes a fixed number of dipoles in the head and fits their position, strength and direction to get optimal agreement of the resulting fields with the measured ones.



resulting dipole current evoked by an acoustical signal, the vowel o, of the right hemsiphere of a single subject. Position and direction of the dipole were fitted in the indicated time intervals.
ca 200 averages.


BESA - E:\Uni_HD\Doktorarbeit\MEG-Probanden\Pilotstudie_o_oe\100607_m1_mono75_1s_ISI\pilot_m1_av.fsg - mono_o1: 180 avs, Filters off, -500 ... +999 ms - Source analysis
File Condition 1 Solution 1 Fit Image Options Help
Solution: E:\Uni_HD\Doktorarbeit\MEG-Probanden\Pilotstudie_o_oe\100607_m1_mono75_1s_ISI\pilot_m1_av-o1-N1.bsa
Data Model Residual Order P.C.A. MEG
Res. Var. Energy Min. Dist. Res.V.-Q(S/N)
mono_o1: 180 avs
Filters off
-500.00 ms
+999.00 ms
R.V.: 50.659%
Best: 3.810%
GFP
RC: 1
Dip. 1 x-loc y-loc z-loc x-ori y-ori z-ori
Tal. (appr.) -56.9 -22.8 14.4 0.2 0.1 1.0
Loc: free
Ori: free
Model: MEG spherical
pilot_m1_av-o1-N1.bsa
MEG
Hld
All
T10R T10C T8R T8C C6R C6C FC0R FC0C FC8R FC8C FC6R FC6C FC4R FC4C FC2R FC2C F6R F6C F4R F4C F2R F2C FzR FzC FP4R FI2C FP2R FP2C FI1C FP1R FP1C FP3R FP3C
All off All fit Start fit MSPS MSBF BrainVoyager
On
Fit
On
No fit
On
Data (1-33 of 117)
Source waveforms
Source locations
Time: +299.00 ms
Start
BESA 5.1 - E:\U...
BESA - E:\Uni_H...
BESA_foc-file - P...
DE
11:24

Minimal Norm Estimate

To get idea of the total current ditribution in the brain.

Given Head model: Form and conductibility $\sigma(x)$.

Wanted: Postsynaptic current distribution $\vec{j}_P(x)$.

ED:
$\vec{B}(x) = \int dx' \mathcal{L}_m(x,x') j_P(x')$;
$\Phi(x) = \int dx' \mathcal{L}_e(x,x') j_P(x')$;

Be V_i, $i = 1, \ldots, N$ the signals registered at position x_i, i.e. $V_i = \Phi(x_i)$ or say $B_n(x_i)$. Then that is

$$V_i = \int dx' \mathcal{L}(x_i, x') j_P(x')$$

where $\mathcal{L}(x_i, x')$ depends on the head model, for EEG crucially on $\sigma(x)$

We want now to reconstruct from the measured signals V_i the distribution of the primary currents j_P. There are two Problems:

1) Fundamental, inverse Problem: There are primary currents, which give no signals, that is:

$$0 = \int dx' \mathcal{L}(x_i, x') j_P^0(x') \quad \text{and noise (errors)}$$

2) Technical: Only finite Number of signals V_i.

For the inverse problem, there is no cure, only remedy: Ignore those currents!
Set: $j_P = \hat{j}_P + j_P^0$ and call $\hat{j}_P$ your estimate for j_P.

Then we make for $\hat{j}_P$ the ansatz:

$$\hat{j}(x) = \sum_{k=1}^{N} w_k \, \mathcal{L}(x_k, x) \tag{6.32}$$

This is the best we can do, since solutions, which cannot be expressed in that way, e.g. j_P^0, cannot be determined anyhow.

We insert the ansatz and obtain now the system of linear equations:

$V_i = \int dx' \mathcal{L}(x_i, x') \, \hat{j}(x') = \int dx' \mathcal{L}(x_i, x') \, \sum_{k=1}^{N} w_k \, \mathcal{L}(x_k, x')$

$V_i = w_k K_{ik}, \quad K_{i,k} = \int dx' \mathcal{L}(x_i, x') \, \mathcal{L}(x_k, x')$

Theoretically clear: Linear equations, easy to solve.

$w_k = \sum K_{ki}^{-1} V_i$

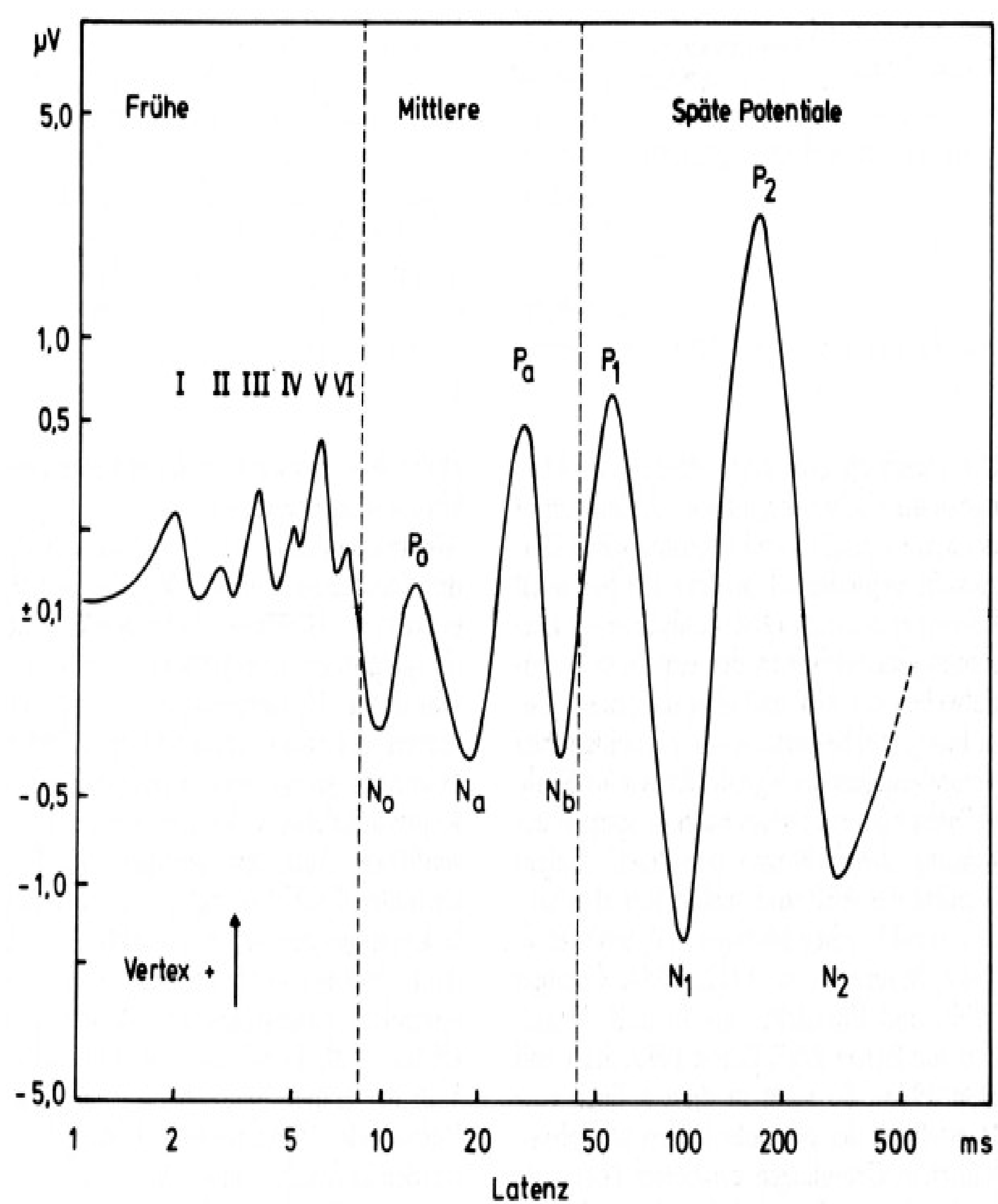
If we have the w_k we can obtain $\hat{j}_P$ from 6.32, since $\mathcal{L}(x_k, x)$ are known functions.

But there is a serious problem: Small errors in V_i or $\mathcal{L}(x_i, x')$ my lead to huge errors in w_k. Errors in V_i are measuring errors, errors in $\mathcal{L}(x_i, x')$ are model errors, for instance entering through the simplification of the asumptions for $\sigma(x)$.

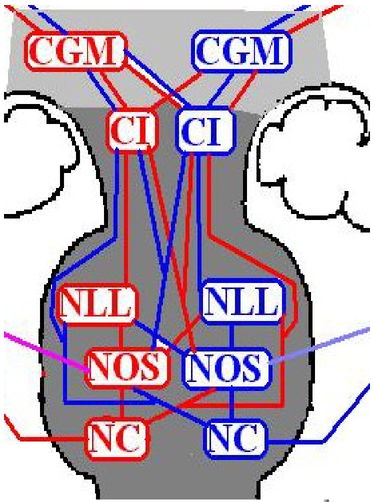
2 Electrophysiology

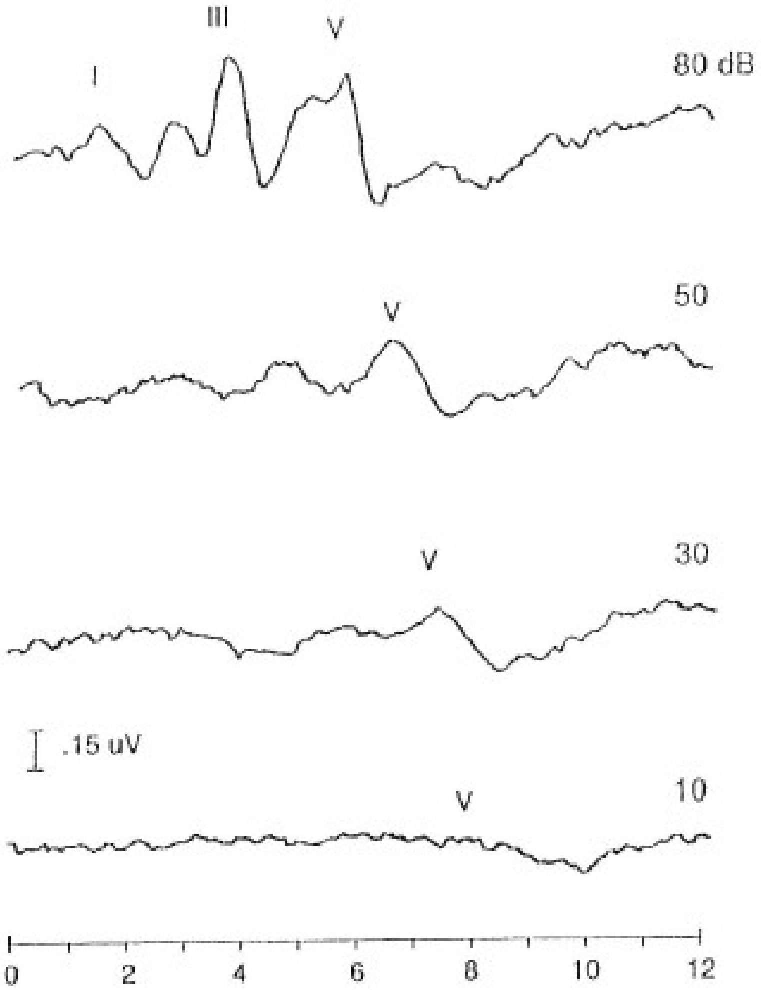
TABLE 6.1. Listing of auditory evoked responses.

Response	Abbreviation	Latency (msec)	Animal analog
Cochlear Responses			
Cochlear microphonic	CM	0	CM
Summating potential	SP	0	SP
Otoacoustic emissions	OAE		
Spontaneous	SOAE	>0	
Evoked	EOAE	5–15	
Transient			
Continuous			
Distortion product	DPOAE	>0	
Brainstem Responses			
Auditory Brainstem Response	ABR	1–12	AP, 1, 2, 3, 4
Waves I, II, III, IV, V, VI, VII			
Frequency following response	FFR	6	
Cross-Correlation Function	CCF		
Amplitude-Modulated Following Response	AMFR		
Slow negativity at 10 msec	SN10, Na	10	
Middle Latency Response	MLR		
Na, Pa, TP41, Nb, Pb (P1)		10–60	Temporal lob response midline respo
40 Hz Response	40 Hz ERP		
Late Auditory Evoked or Event Related Potentials	AEP or ERP		
N1, N1b (N100), N1c (N150)		80–250	
P2		200	
N2			
Sustained negativity			
Cortical Auditory Evoked Potential	CAEP		
Elicited with oddball paradigm			
Mismatch negativity	MMN	150–275	
Nc		400–700	
Processing negativity	Nd	60–700	
P300, P3a, P3b		250–350	P3a-like
Cortical Discriminative Response	CDR		
N400		400	

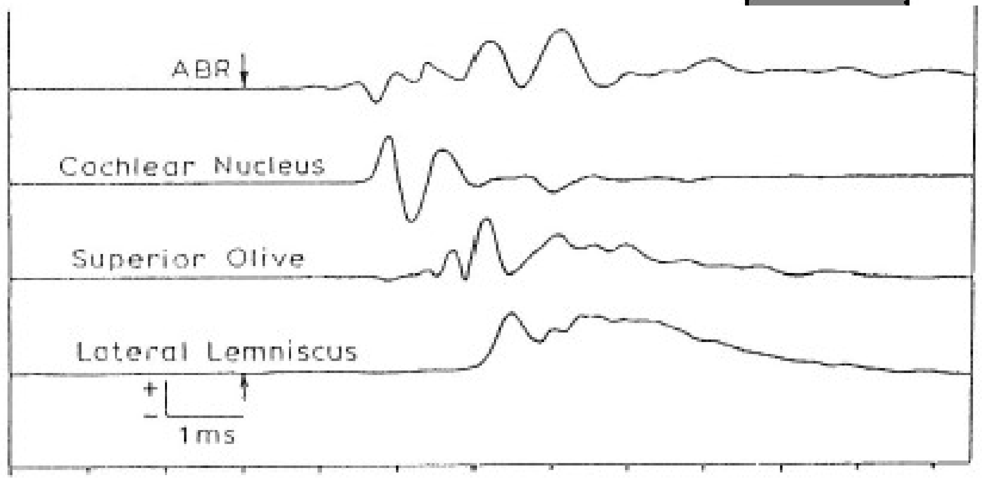


Auditory brain stem responses, early





ABR of a human (EEG) at different SP levels



ABR of an anesthetized cat: uppermost curve EEG
the lower curves are taken invasively at different stages of the auditory pathway.

MEG not possible, since currents mainly radial.

Mid Latency responses

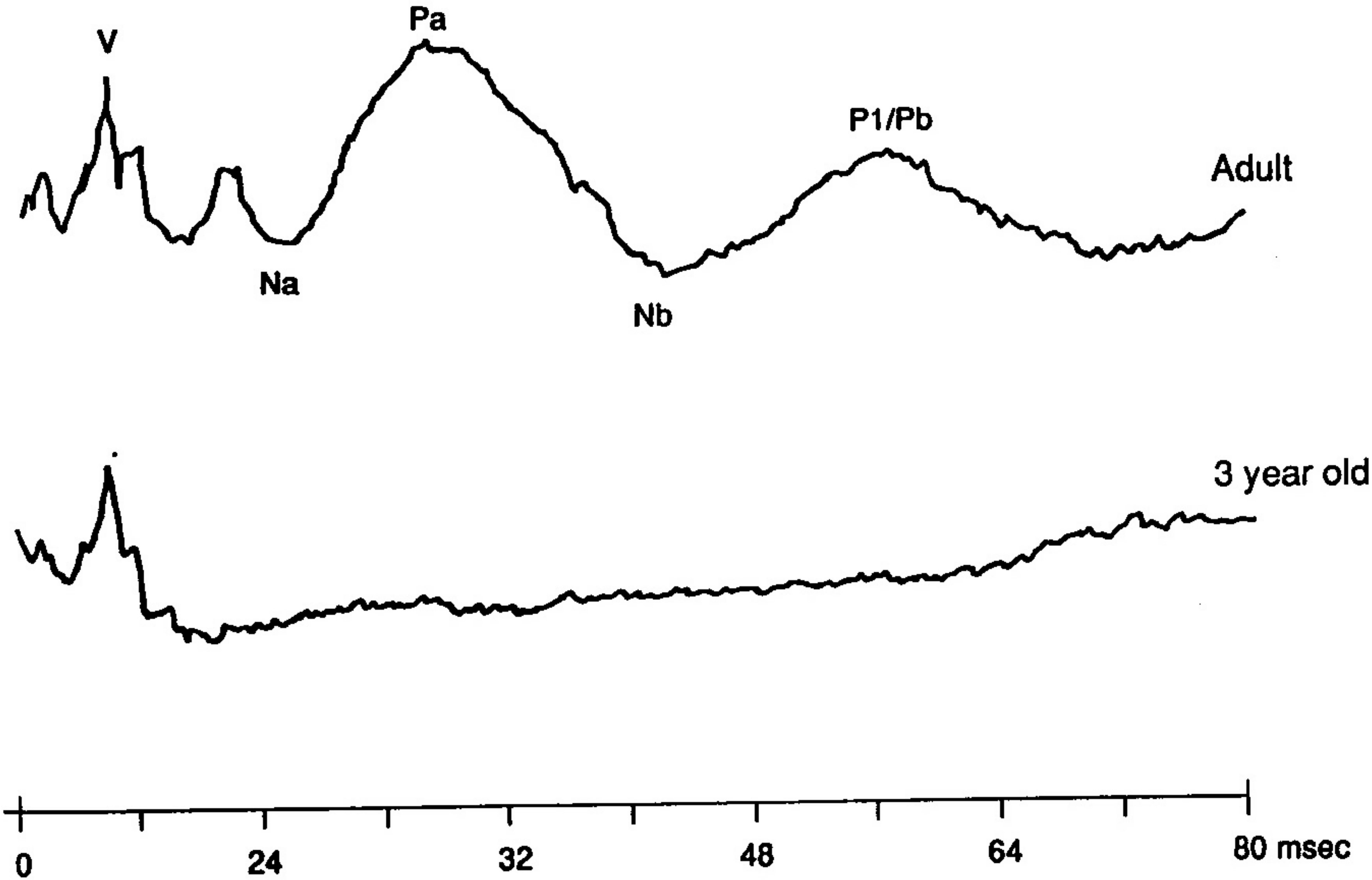


FIGURE 6.5. Representative MLR components recorded from a normal adult subject. Bottom: All MLR components can be absent during certain sleep stages in normal children.

Some Work by the MEG Group Heidelberg

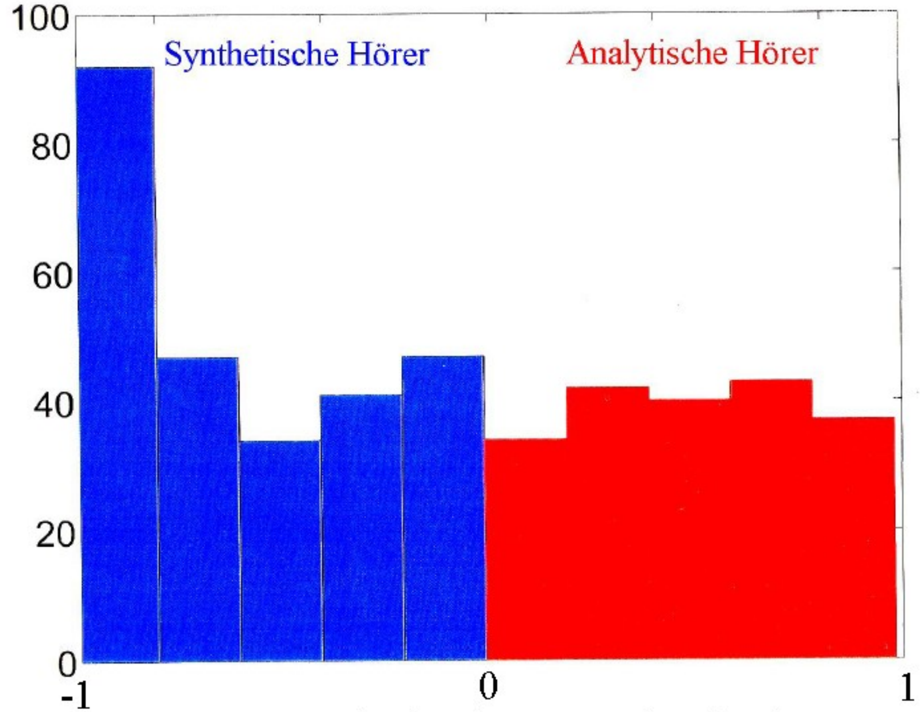
Systematische Untersuchung der Psychoakustik, Neurophysiologie und Anatomie

Structural and functional asymmetry of lateral Hesch's gyrus reflects pitch perception preference

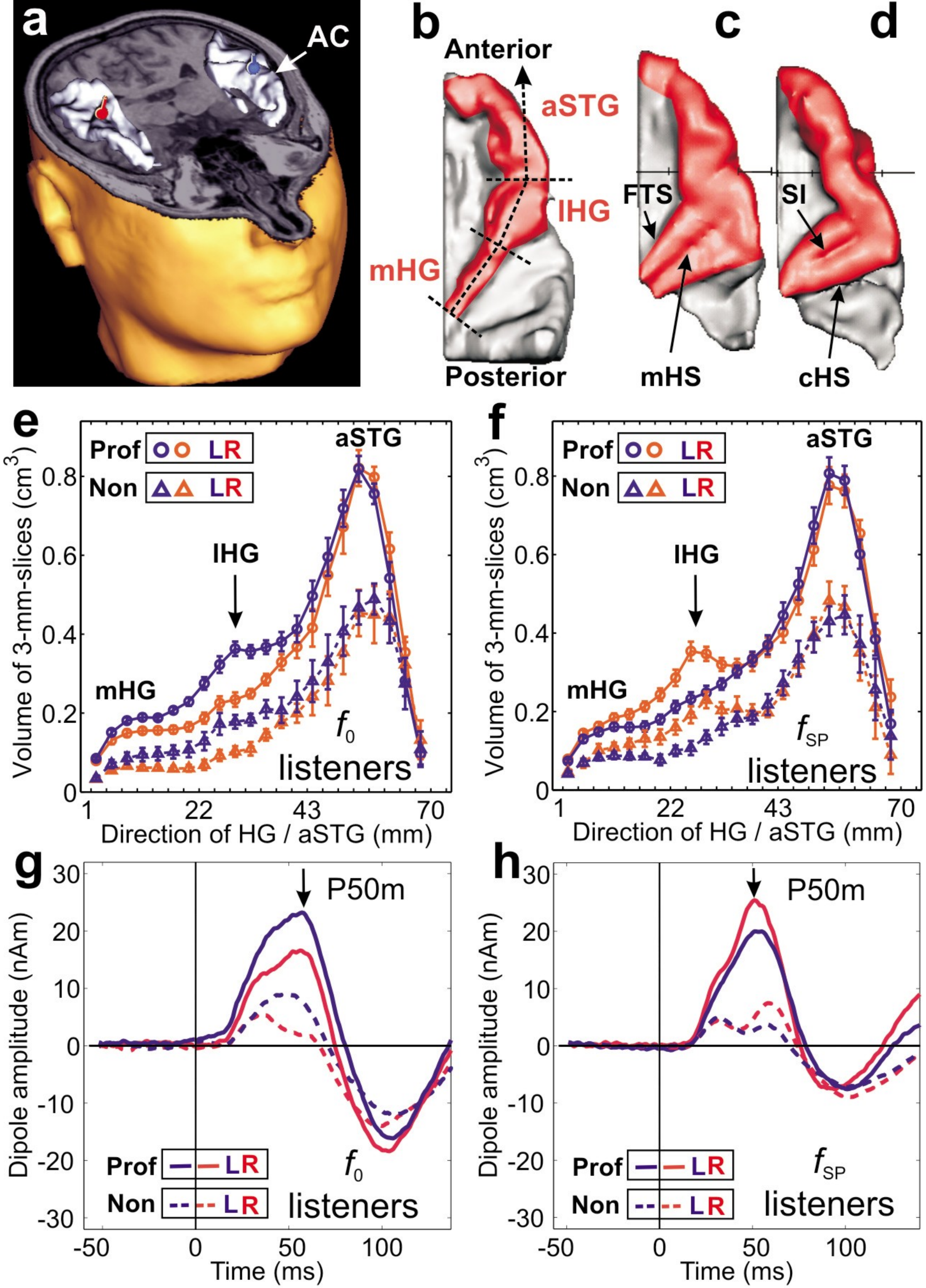
P.Schneider, V. Sluming, N. Roberts, M. Scherg, R. Goebel, H.J. Specht, H.G. Dosch, S. Bleeck, C. Stippich, A. Rupp

nature-neuroscience, **8** (2005) 1241-1247

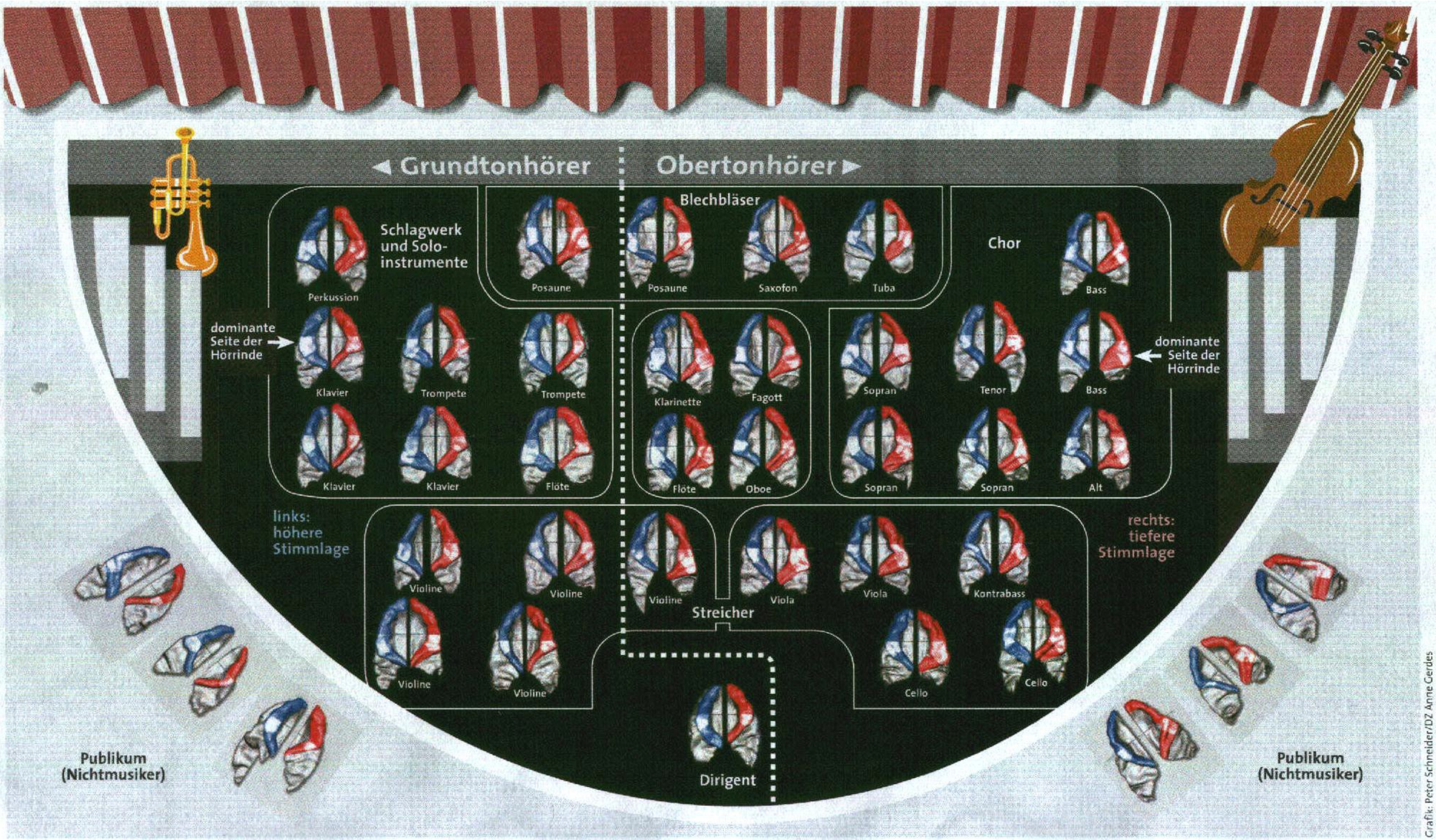
420 Teilnehmer, 144 Tonpaare



$$\delta_P = \frac{\text{analytisch} - \text{synthetisch}}{\text{analytisch} + \text{synthetisch}}$$



Schneider_fig_2



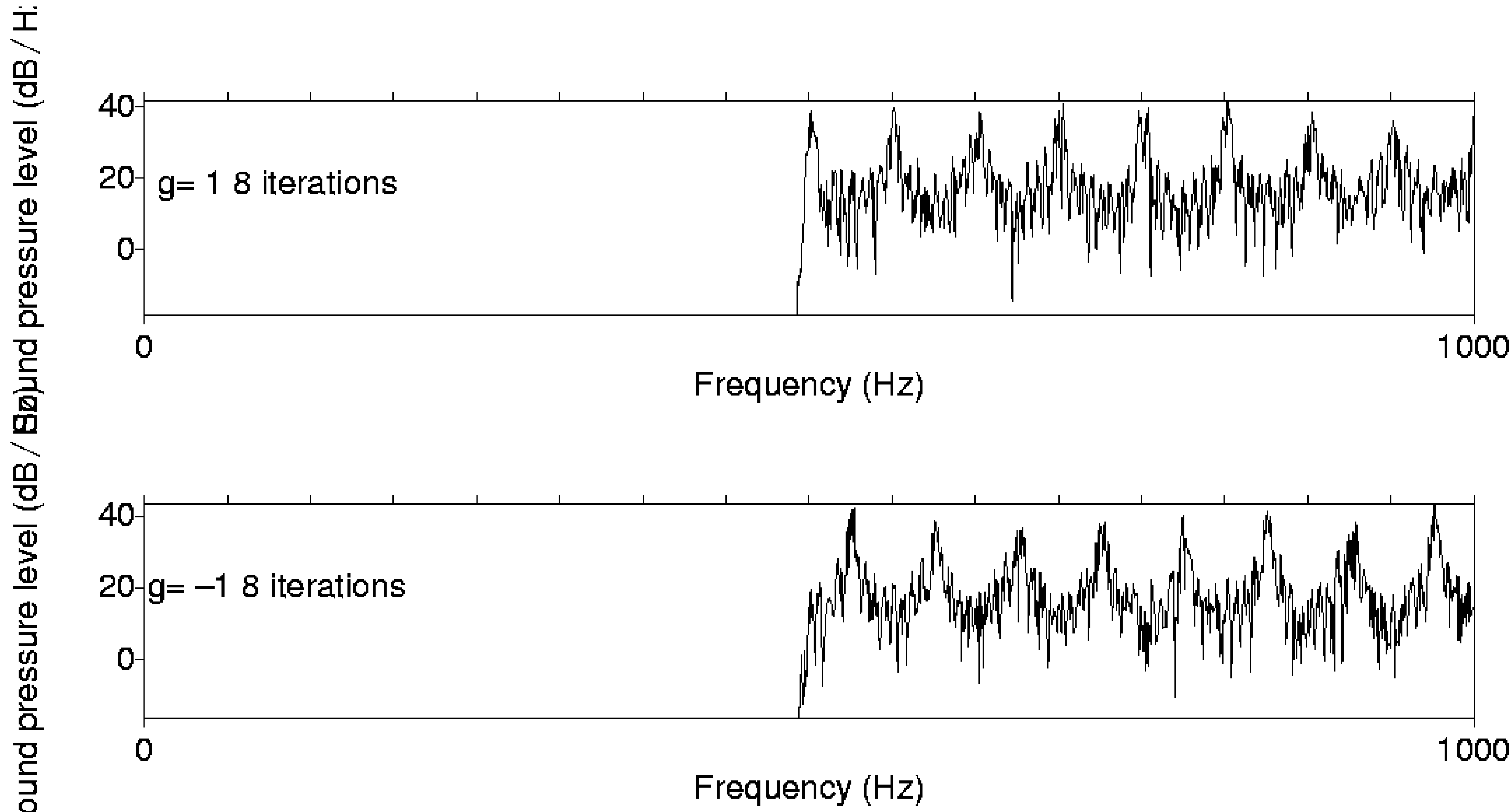
Grundtonhörer
Obertonhörer
Schlagwerk und Soloinstrumente
Blechbläser
Chor
Perkussion
Posaune
Posaune
Saxofon
Tuba
Bass
dominante Seite der Hörrinde
Klavier
Trompete
Trompete
Klarinette
Fagott
Sopran
Tenor
Bass
dominante Seite der Hörrinde
Klavier
Klavier
Flöte
Flöte
Oboe
Sopran
Sopran
Alt
links: höhere Stimmlage
rechts: tiefere Stimmlage
Violine
Violine
Violine
Viola
Viola
Kontrabass
Streicher
Violine
Violine
Cello
Cello
Publikum (Nichtmusiker)
Dirigent
Publikum (Nichtmusiker)
Grafik: Peter Schneider/DZ Anne Gerdes

Neuromagnetic responses reflect the temporal pitch change of regular interval sounds

Steffen Ritter,[a,*] Hans Günter Dosch,[b] Hans-Joachim Specht,[c] and André Rupp[a]

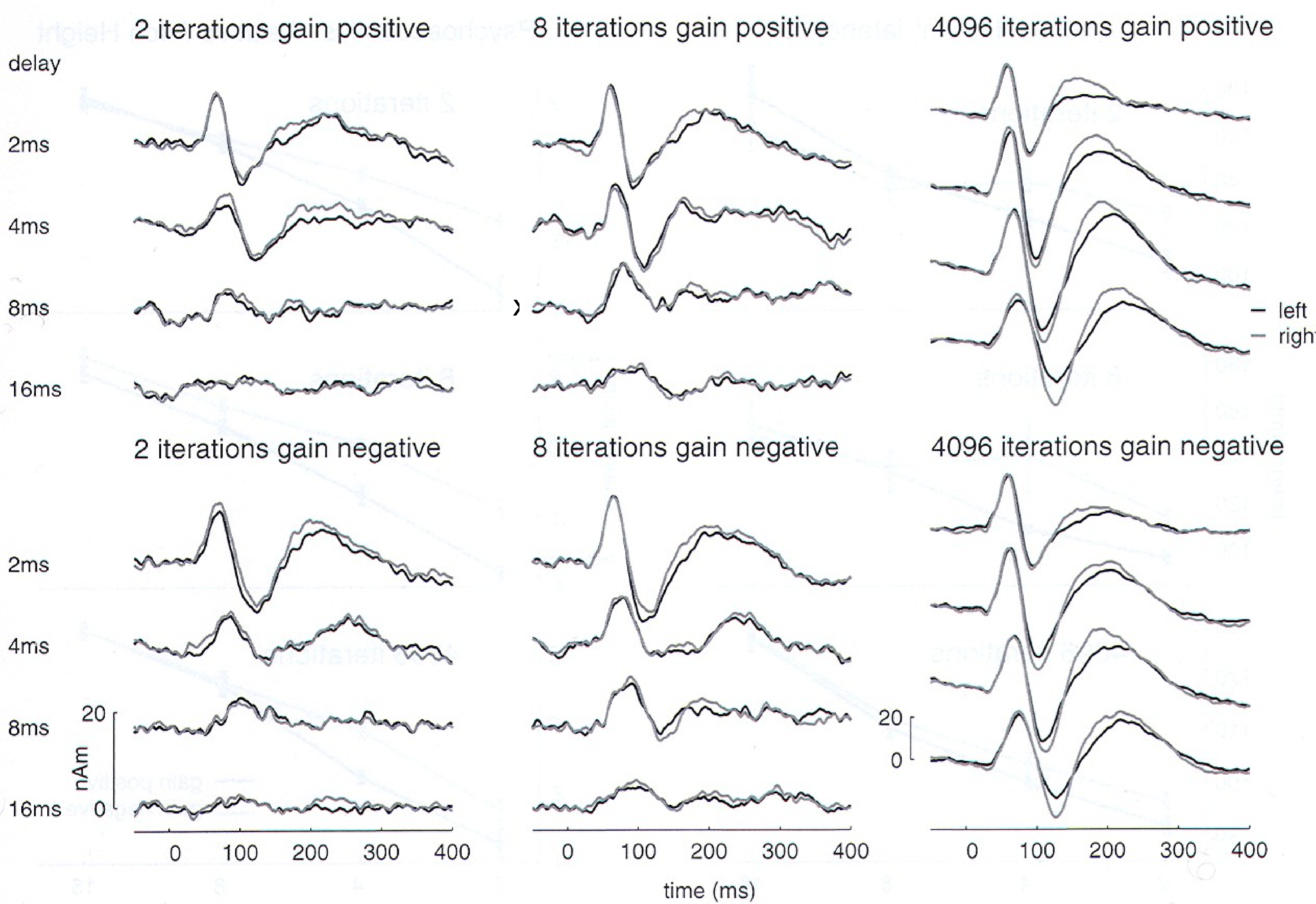
Spectra of presented stimuli: Huygens and anti-Huygens noise

401praat: ritter-bsp12.collection

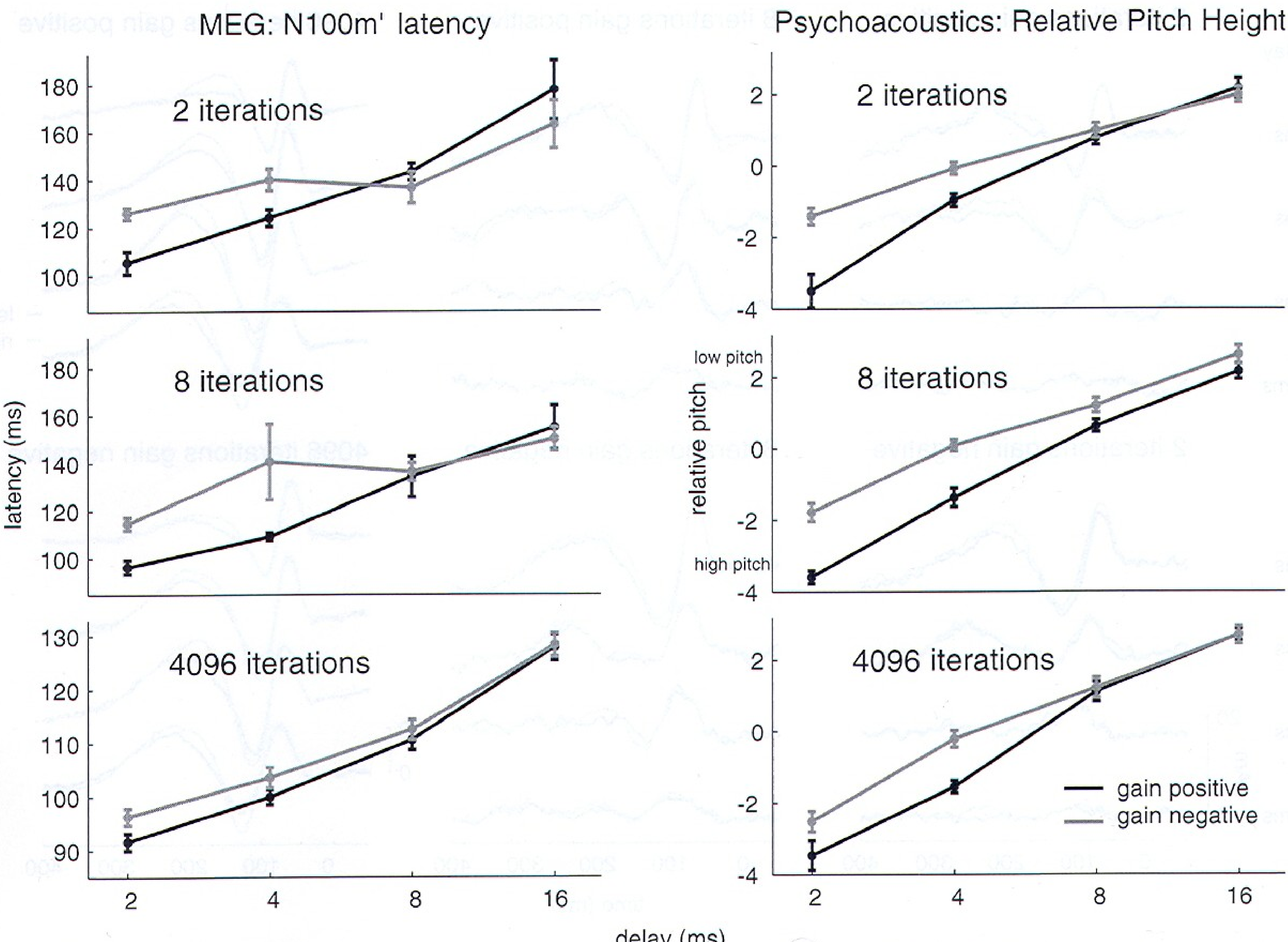


late latency responses

S. Ritter et al. / NeuroImage 27 (2005) 533–543



Psychophysics by paired compairison



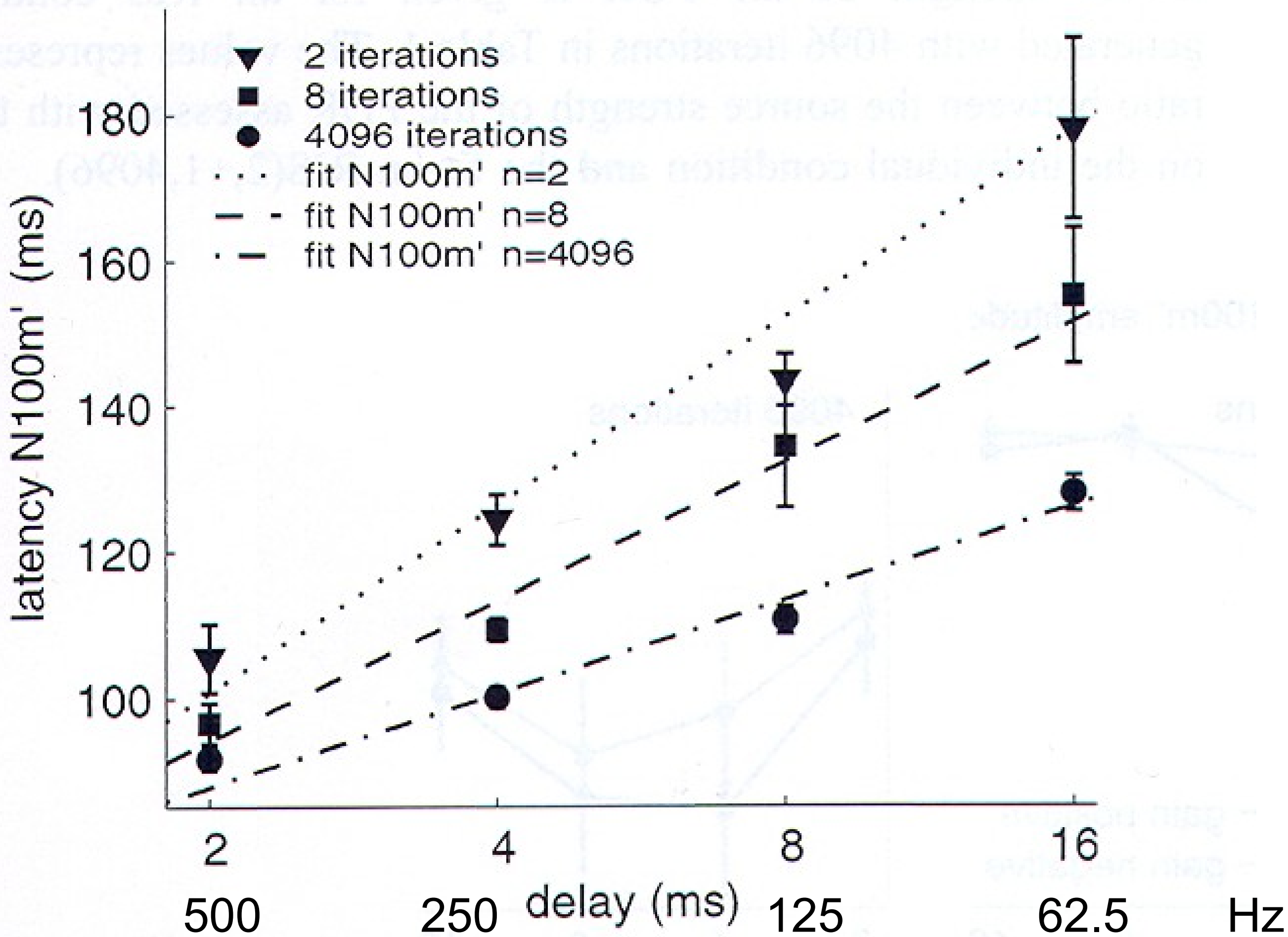


Fig. 7. Latency of pitch responses evoked by RIS with positive gain, different delay times d and different number of iterations n. The dashed lines correspond with the fit formula described in the text that depends on d and n.

Note relations:
lower fr. longer latency
lower iteration longer lat.

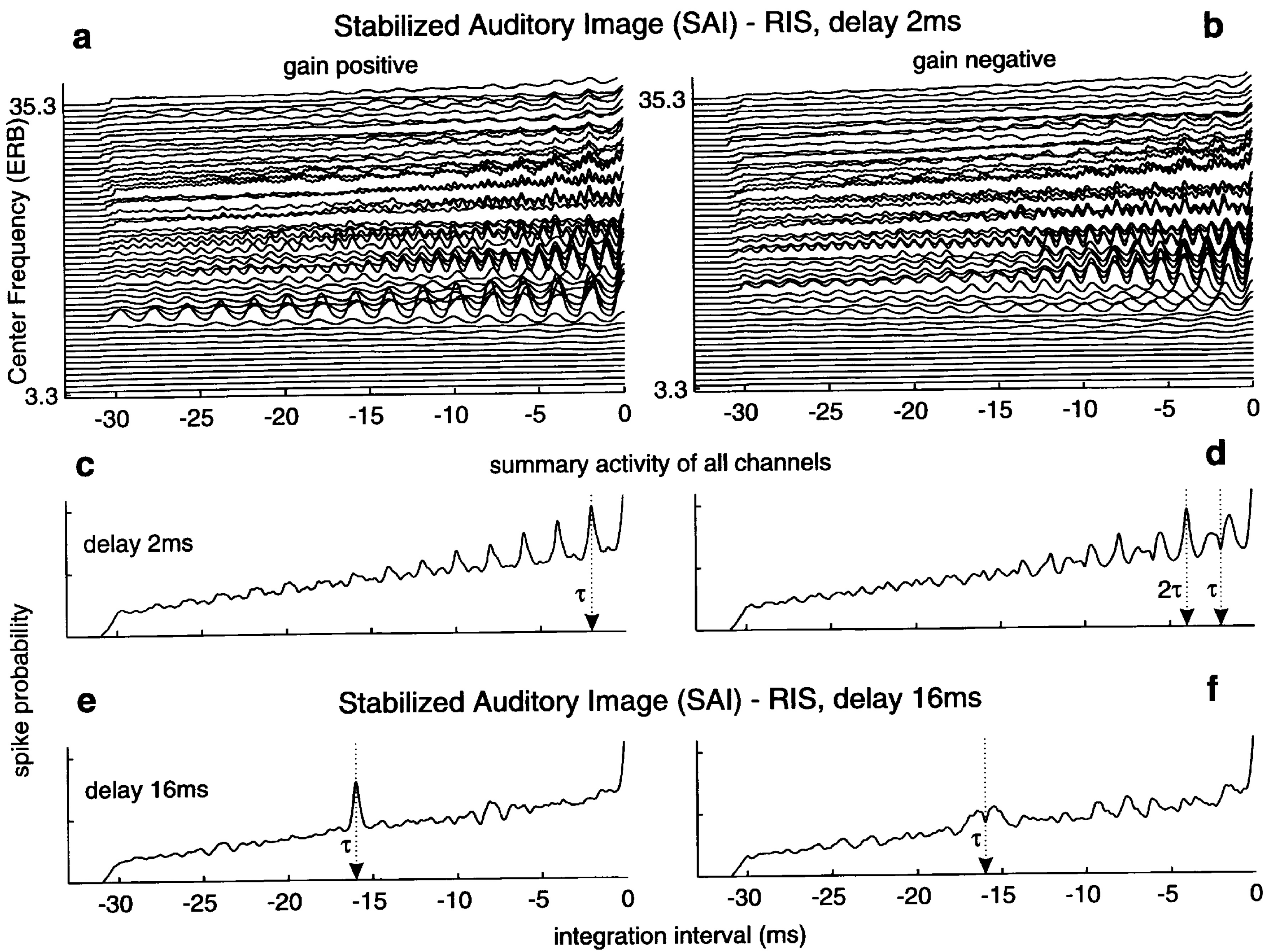


Fig. 11. Auditory image model (AIM; Patterson et al., 1995) for RIS(d,g,n). Stabilized auditory images (SAIs) are created from the neural activity pattern by strobed temporal integration. The position and height of the first peak at lag τ predict the perceived pitch.

Additional neuromagnetic source activity outside the auditory cortex in duration discrimination correlates with behavioural ability

N. Sieroka,[a,b,*] H.G. Dosch,[b] H.J. Specht,[c] and A. Rupp[a]

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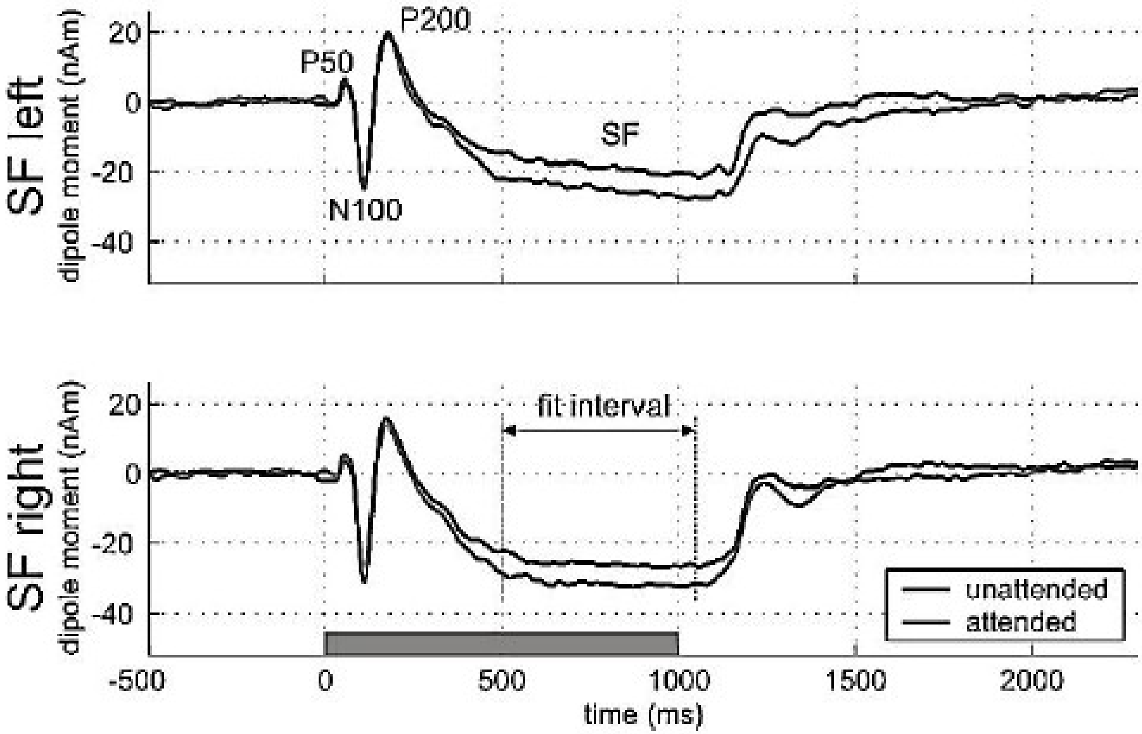
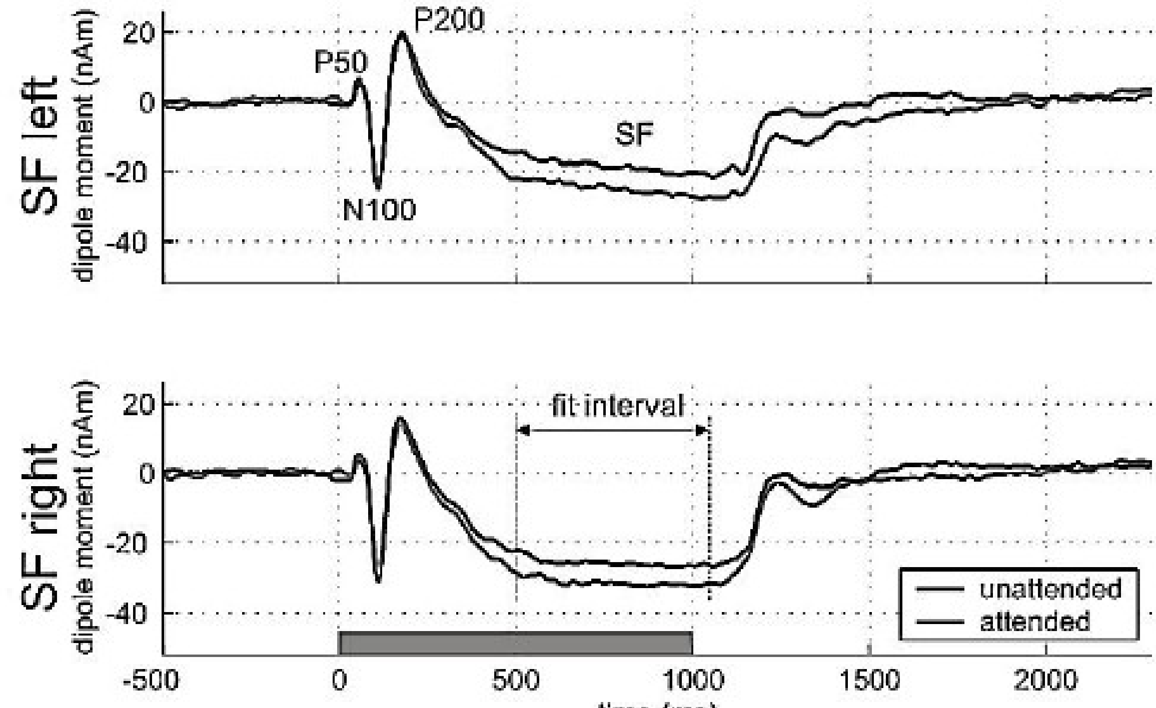
Two tones presented, one frequently of 1 s duration (standard), one rarely with 1.2 sec duration (deviant)
Session unattended: watching silent movie
Session attended : pushing a button if deviant occurs (very absorbing)

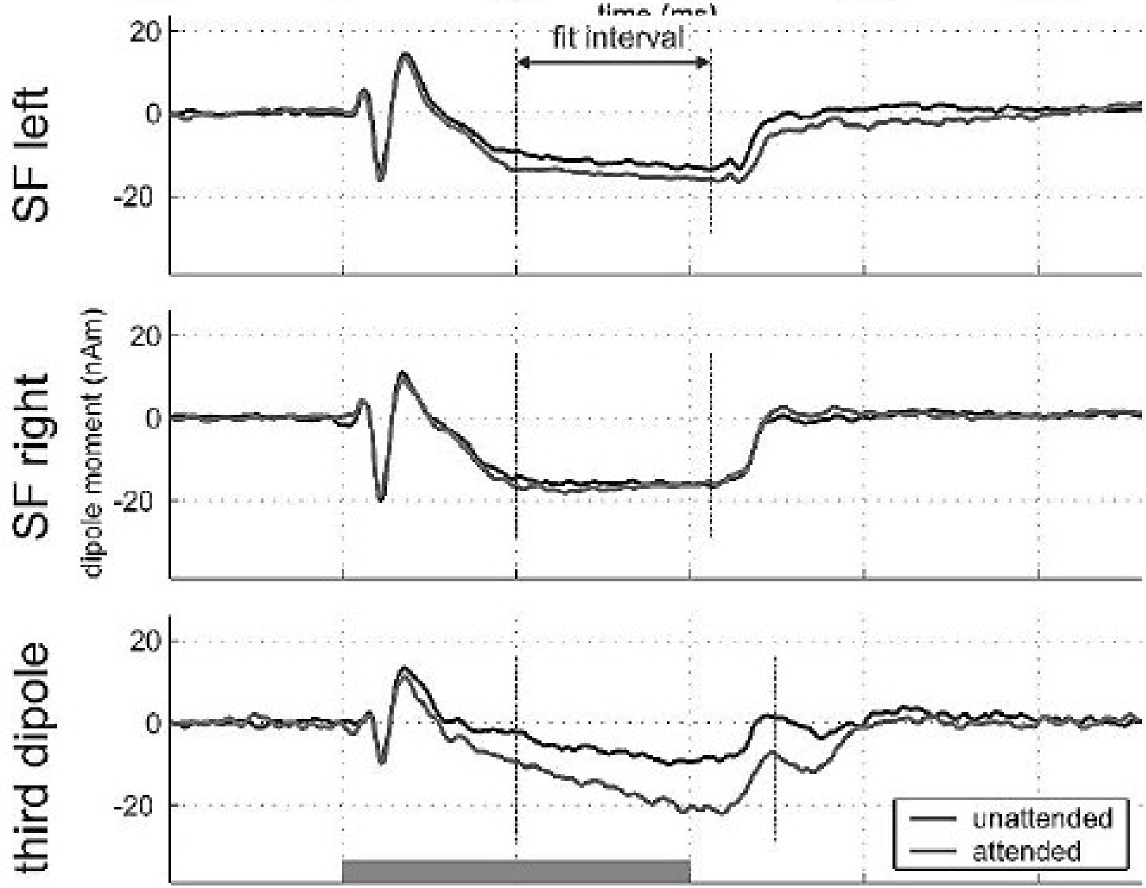
401praat: 1sec. 1.2sec



two dipole fit, one dipole in each hemisphere, turn out to be situated in the auditory cortices



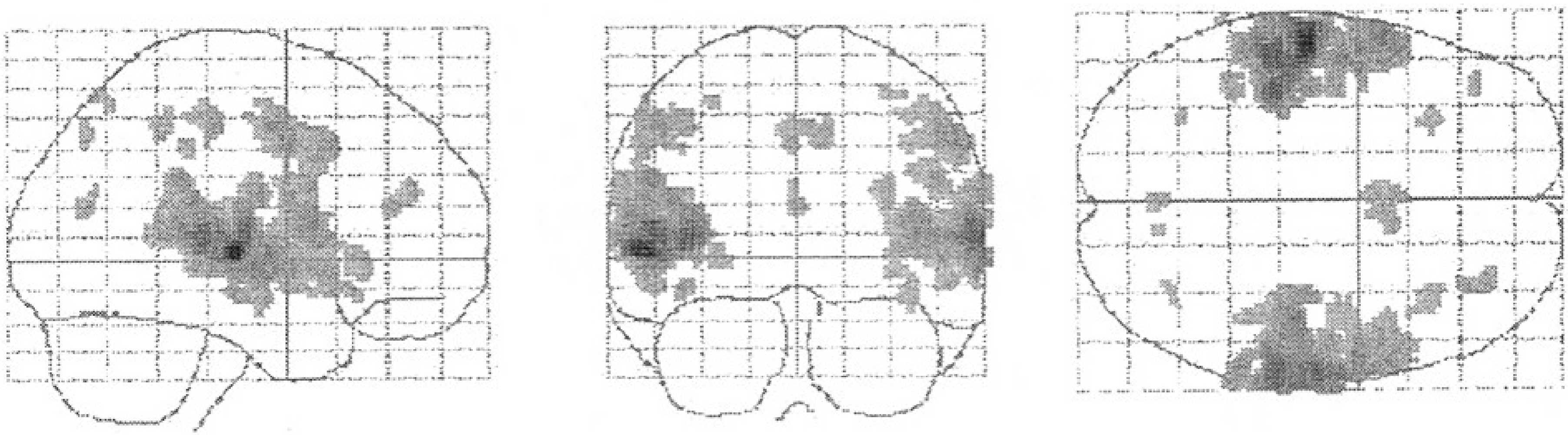
two dipole fit, one dipole in each hemisphere, turn out to be situated in the auditory cortices



three dipole fit, two in the auditory cortices, and one additional free.

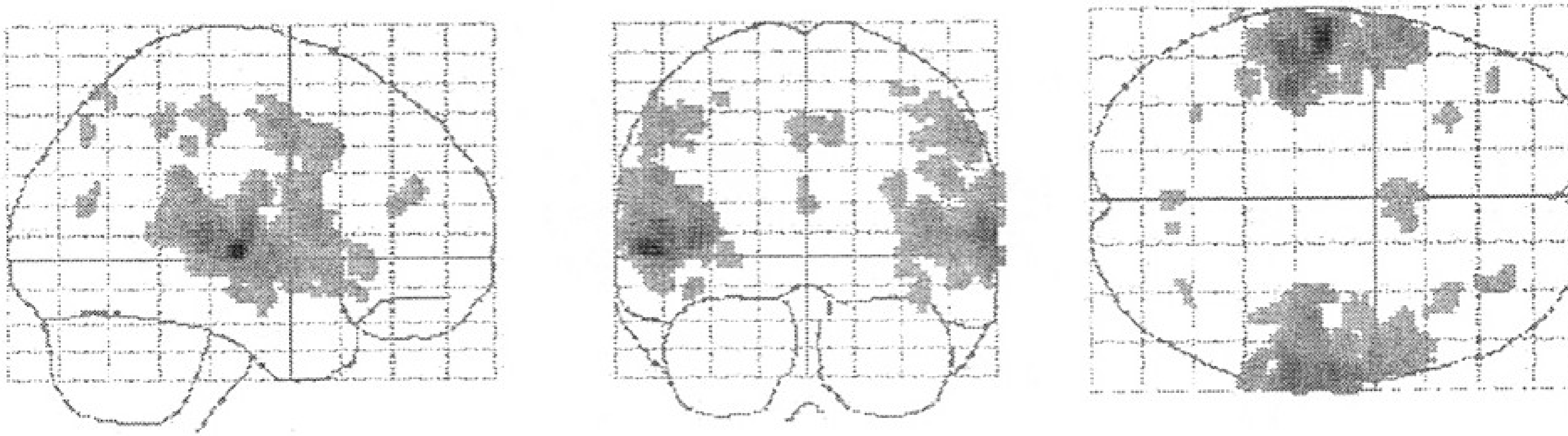
Check with FMRI

sound-silence control

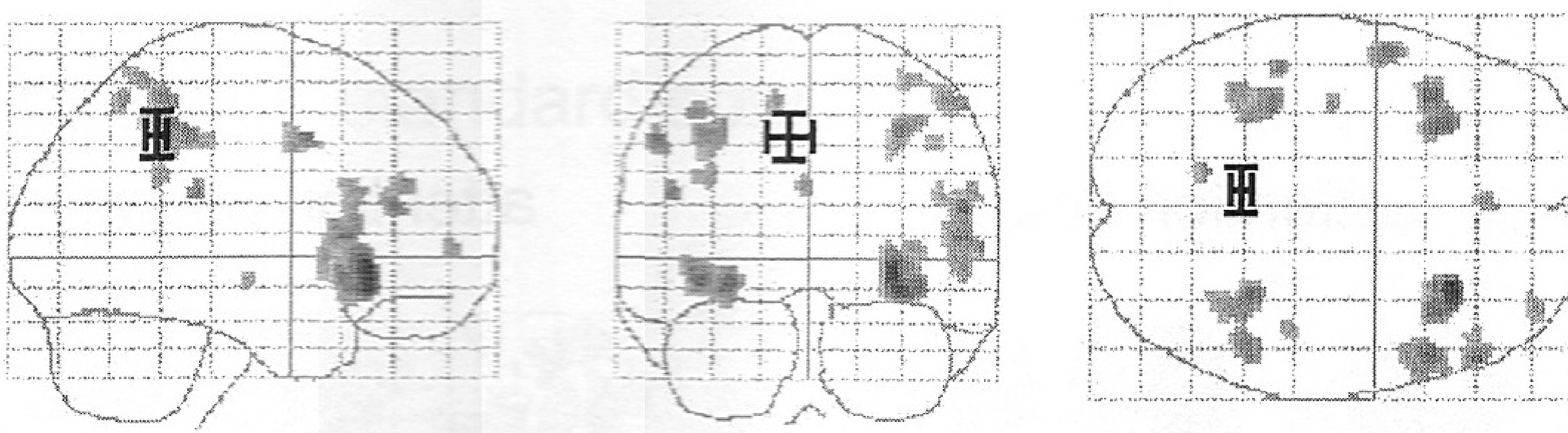


Check with FMRI

sound-silence control

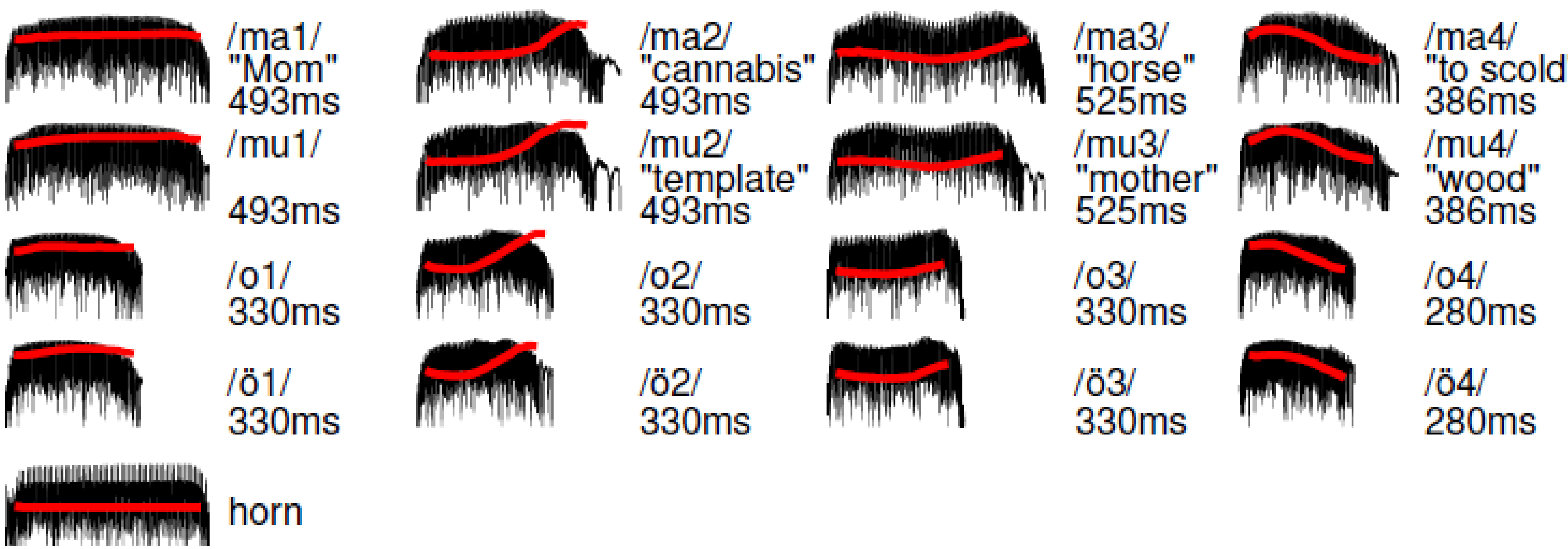


attention sound



Sustained Responses as Neurophysiological Parameter for the Assessment of Phonological and Semantic Processing

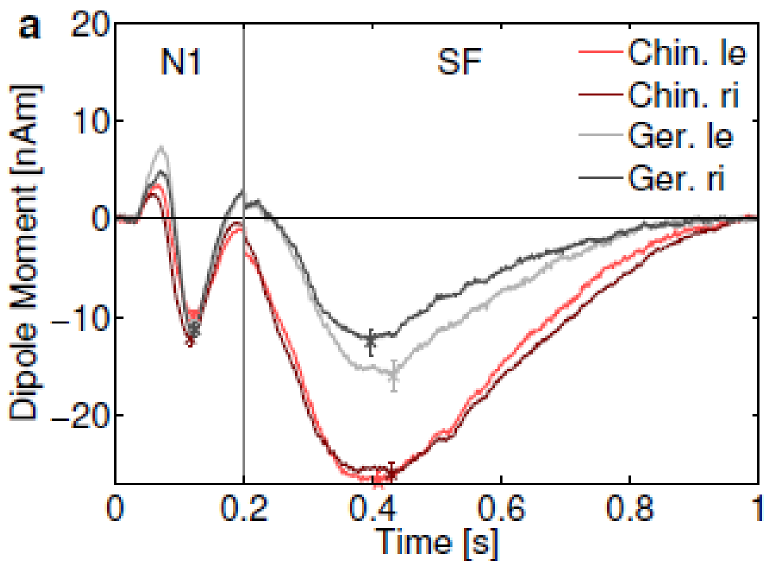
Christina Fan, Xingyu Zhu, Hans Günter Dosch, Christiane von Stutterheim, Andre Rupp



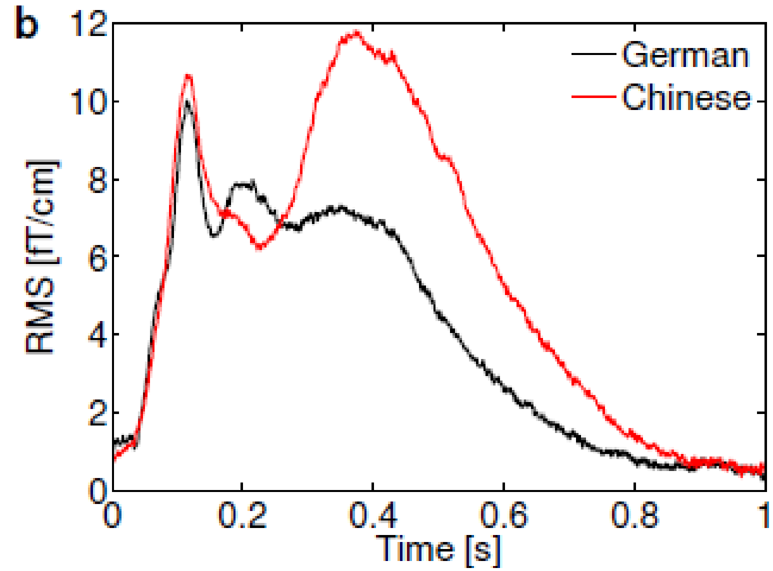
401praat: ma_1,ma_2,ma_2,ma4

Grand average over all signals

Dipole fit



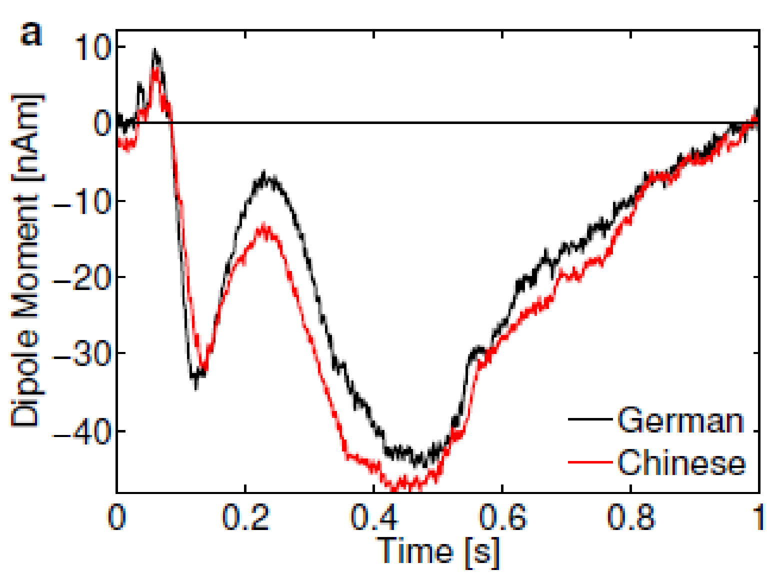
Sum over all MEG channels



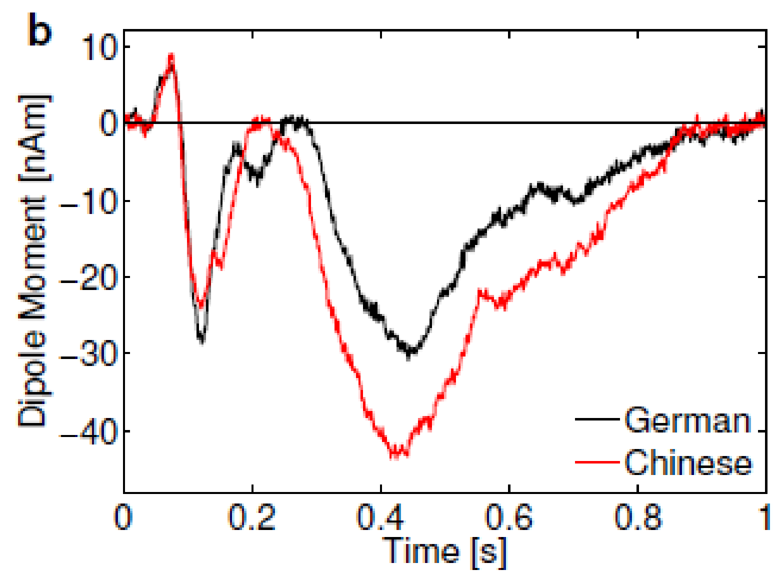
praat401: ma1

horn

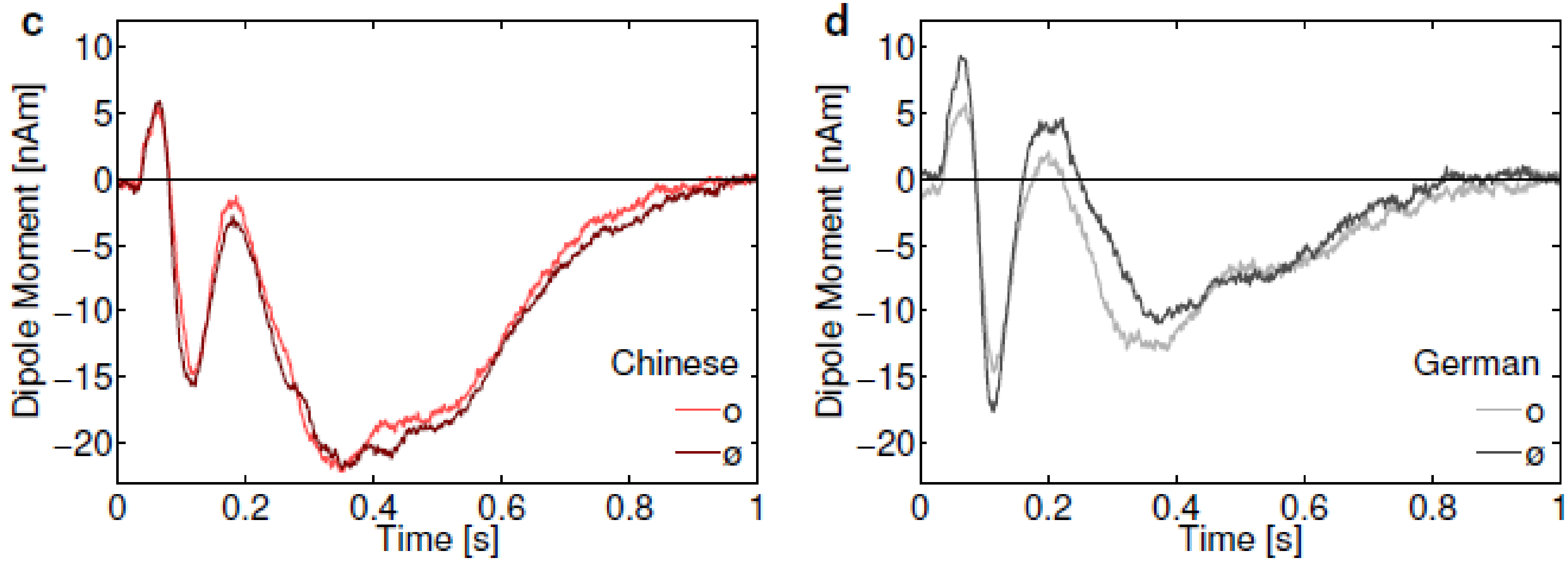
Musical tone



spoken syllable ma1



The vowel oe does not occur in Chinese



ma1 is meaningful whereas mu1 has no meaning