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

\[ T = \text{Tesla} \]

\[
\begin{align*}
\mu_B &= \frac{e\hbar}{2m_e} = 5.8 \times 10^{-11} \text{MeVT}^{-1} \\
\mu_p &= \frac{1.4e\hbar}{2m_p} = 1.6 \times 10^{-14} \text{MeVT}^{-1}
\end{align*}
\]

statistical equilibrium:

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

room temperature: \( kT \approx \frac{1}{40} \text{eV} \)

earth magnetic field:

\[
e^{-6.4\times10^{-11}} \approx 1 - e^{-6.4\times10^{-11}}
\]

HF field with frequency \( \hbar \nu = 2\mu B \) \( \rightarrow \) 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:

\[ \langle M_z \rangle = 0, \quad \langle M_x \rangle = \text{Re}\gamma, \quad \langle M_y \rangle = \text{Im}\gamma \]

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

Decay of \( \gamma \): \( T_2 \) (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 frequency condition \( h \nu = 2 \mu B \) is satisfied for a fixed layer (tomography)
* Detection devices

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

e.g., 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.
sound-silence control

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 \([\text{A m}]\)

- synaptic current \(20 \text{ fA m}\)
- 1 Million synapses \(20 \text{ nAm}\)
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 Josephson junction.

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

\[
\Phi_m = \frac{\hbar c 2\pi}{2e} \approx 4 \cdot 10^{-7} \text{ gauss cm}^2 = 4 \cdot 10^{-13} \text{ Wb} = 0.0001 \text{ ftcm}^2
\]
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.

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

\( \partial \cdot \vec{j} = 0 \), current conservation and b.c. \( \hat{n}_{\partial G} \cdot \partial \phi = 0 \) allow to calculate \( \phi(\vec{x}) \) as linear functional of \( \vec{j}_p(\vec{x}) \):

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

Ampere

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

\[
\phi(\vec{x}) = \int d^3x' \ \vec{L}(\vec{x}, \vec{x}') \cdot \vec{j}_p(\vec{x}')
\]

\[
B_\alpha(\vec{x}) = \int d^3x' \ \vec{L}_\alpha^m(\vec{x}, \vec{x}') \cdot \vec{j}_p(\vec{x}')
\]
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:

$$B_r(\vec{x}) \equiv \vec{B}(\vec{x}).\hat{x} = -\frac{1}{4\pi} \frac{\vec{Q} \cdot [\vec{x} \times \vec{x}_Q]}{|\vec{x} - \vec{x}_Q|^3}$$
\[ B_r(\vec{x}) = \frac{1}{4\pi} \frac{\vec{Q} \cdot [\vec{x} \times \vec{x}_Q]}{|\vec{x} - \vec{x}_Q|^3} \]
Heidelberg
Neuromag, 122 SQuIDs as Magneto-Gradiometers
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

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

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
headview EEG
Application in Neurophysiology:

Detection of activity:

One measures 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 seconds 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 acoustic signal, the vowel o, of the right hemisphere of a single subject. Position and direction of the dipole were fitted in the indicated time intervals. ca 200 averages.
Minimal Norm Estimate

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

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

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

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

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 $\mathcal{L}(x, x')$ 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:

$$0 = \int dx' \mathcal{L}(x_i, x') j_P^0(x')$$

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: $j_P = j_P + j_P^0$ and call $\hat{j}_P$ your estimate for $j_P$.

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

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

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

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

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 $\mathcal{L}(x_i, x')$ may 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 assumptions for $\sigma(x)$.
2 Electrophysiology
### Table 6.1: Listing of auditory evoked responses

<table>
<thead>
<tr>
<th>Response</th>
<th>Abbreviation</th>
<th>Latency (ms)</th>
<th>Animal analog</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochlear Responses</td>
<td>CM, SOAE, EOAE, Summing potential</td>
<td>5-15</td>
<td>Sp, Sp</td>
</tr>
<tr>
<td>Basilar Membrane Response</td>
<td>Waves I, II, III, IV, V, VI, VII</td>
<td>1-12</td>
<td>AP, 1, 2, 3, 4</td>
</tr>
<tr>
<td>ABR</td>
<td>FFR, CCF</td>
<td>0</td>
<td>CM</td>
</tr>
<tr>
<td>DPOAE</td>
<td></td>
<td>&lt;0</td>
<td>CM</td>
</tr>
<tr>
<td>SOAE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EOAE</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Diagram

- **N40**: Processing negativity
- **P3a**: Late Auditory Evoked Potential
- **P2**: N2 (-P2)
- **N1**: N10 (N100), N1c (N130)
- **AEP or ERP**: 40 Hz ERP
- **MLR**: Middle Latency Response
- **Na, Pa, TP4, N2, P2**: Slow negativity at 10 msec
- **MLR**: Frequency-following response
- **CCF**: Cross-Correlation Function
- **TEMPORAL Lobe**: Response
- **-10**: Vertex
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.
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
Structural and functional asymmetry of lateral Hesch’s gyrus reflects pitch perception preference


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

420 Teilnehmer, 144 Tonpaare
Grundtonhörer

Schlagwerk und Solo-Instrumente

Perkussion
Klavier
Trompete
Trompete

Blechbläser

Posaune
Posaune
Saxofon
Tuba
Klarinette
Fagott
Sopran
Sopran

Chor

Tenor
Bass

links: höhere Stimmlage

Streicher

Flöte
Oboe
Violine
Violine
Violine
Violine
Violine

rechts: tiefere Stimmlage

Dirigent

Publikum (Nichtmusiker)
Neuromagnetic responses reflect the temporal pitch change of regular interval sounds

Steffen Ritter,\textsuperscript{a,*} Hans Günter Dosch,\textsuperscript{b} Hans-Joachim Specht,\textsuperscript{c} and André Rupp\textsuperscript{a}

Spectra of presented stimuli: Huygens and anti-Huygens noise

\textsuperscript{a}401praat; ritterbsp12.collection
late latency responses

2 iterations gain positive

8 iterations gain positive

4096 iterations gain positive

delay

2ms

4ms

8ms

16ms

2 iterations gain negative

8 iterations gain negative

4096 iterations gain negative

2ms

4ms

8ms

16ms

nAm

0

20

0

100

200

300

400

time (ms)
Psychophysics by paired comparison

**MEG: N100m' latency**

- 2 iterations
- 8 iterations
- 4096 iterations

**Psychoacoustics: Relative Pitch Height**

- 2 iterations
- 8 iterations
- 4096 iterations

**Graphs:**
- X-axis: delay (ms)
- Y-axis: latency (ms) for MEG and relative pitch for Psychoacoustics
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 strobbed temporal integration. The position and height of the first peak at lag $\tau$ predict the perceived pitch.
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)
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
Grand average over all signals

Dipole fit

Sum over all MEG channels

Musical tone

spoken syllable ma1

praat401: ma1

horn
The vowel oe does not occur in Chinese

ma1 is meaningful whereas mu1 has no meaning