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Biomagnetism: Principles and Applications in the Study of the Human Brain

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and

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- Historical overview
- Biomagnetic fields and noise sources
- Modeling of bio-electric activity
- Instrumentation
- Applications to the study of the human [illegible]
- Perspectives

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L. Narici

4. Applications

4.1 Heart studies

4.2 Brain studies

4.2.1 spontaneous activity, epilepsy

4.2.2 evoked fields

5. Perspectives (for real time functional imaging)

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General references:

Proceedings of a NATO ASI on:

- Biomagnetism: an interdisciplinary approach. (Williamson, Romani, Kaufman, Modena Eds., Plenum Press, New York - London, 1983)
- Williamson & Kaufman, Biomagnetism, J. Magn. Magn. Mat. 22, 129-201, 1981
- Romani, Williamson & Kaufman, Biomagnetic Instrum. Rev. Sci. Instrum. 53, 1815-1845, 1982
- Romani & Narici, Principles and validity of the biomagnetic method, Medical Progr. through Technol., 11, 123-159, 1986

1.1 Historical overview

1963 – Measurement of the heart magnetic signal by non-superconducting instrumentation
(Baule & McFee, Am. Heart J. 66, 95-96, 1963)

1970 – First recording of a magnetocardiogram (MCG) using a SQUID inside a magnetically shielded room
(Cohen, Edelsack and Zimmerman, APL, 16, [illegible])

1974 – Practical use of a gradiometer in unshielded environments
(Opfer et al., IEEE Trans. Mag. MAG-9, 536-539, 1974)

1972 ÷ 80 – Widespreading of the technique, measurements of different biomagnetic fields, development of modelling

1981 ÷ 82 – First results applying the source localization procedure: heart conduction system, "tonotopic" organization of the human auditory cortex.
(Romani et al., Science, 212, 1339-1340, 1982)

1984 – First multichannel systems
- Helsinki (Ilmoniemi et al., EEG J., 58, 467, 1984)
- Roma (Romani, Phisica 126B, 70-81, 1984)
- NYU (Williamson et al., Proc. ICEC 10, 1984)

1986 ↓ – Functional localization

II Sources responsible for the presence of magnetic fields outside the human body:

- Ionic current flows inside and outside the membrane of excitable cells
- Magnetic contaminants in the lung
- Excess (or deficiency) of paramagnetic substances – revealed when exposed to an applied magnetic field – in some organs (liver, spleen, etc.) as a consequence of genetic diseases ([illegible])

I Sources of environmental "noise" ([illegible])

- Earth magnetic field
  - (vibrations of the sensor ⇒ strong signal

    $\Delta\theta = 10^{-8}$ rad ⇒ [illegible] fT
  - minor effects due to the spatial gradient of the earth's field, [illegible]

    $\Delta s = 10^{-3}$ m ⇒ [illegible] fT
- Micropulsations of the earth's [illegible] (interaction of the solar wind [illegible]
  - circadian variations (daytime [illegible]
  - $1/f$ behavior

– "Urban" noise

- instruments, fans, elevators, ... produce signals at specific frequencies + a typical contribution to the frequency spectrum at the power line frequency and its harmonics

2. Instrumentation

2.1 Sensors

- Induction coils
  - limit set by noise associated with the resistance of the windings. (inversely proportional to f)
  - Sensitivity of ~ 3 pT/$\sqrt{Hz}$ at ~ 10 Hz and room temperature operation, may be improved cooling the system)
- Flux-gate magnetometers

  - limit set by Barkhausen noise in the ferrite core

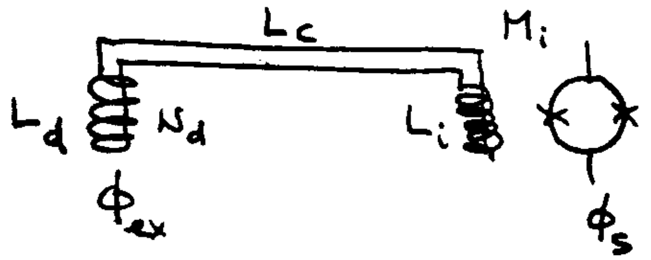
  the best sensitivity for laboratory prototypes in ambient field is of the order of a few pT/$\sqrt{Hz}$ above 1 Hz –

- Used for evaluation of lung contamination in a gradiometric configuration.

- Energy sensitivity
- flux noise

best figure of merit: <u>field</u> <u>noise</u> when measuring an external field.

- <u>Requirements</u>: field sensitivity better than "brain noise" with acceptable 1/f behavior, corner fr. < 0.1 Hz
- The flux transporter



$M_i = k_i \sqrt{L_i L_{SQUID}}$

$$\frac{\phi_s}{\phi_{ex}} = \frac{N_d M_i}{(L_d + L_i + L_c)}$$

usually L_c is neglegible and $\frac{\phi_s}{\phi_{ex}}$ is maximum for $L_d \sim L_i$

- To increase N_d is convenient to space the turns of the detection coil, so to reduce their mutual inductance, and have $L_d \propto N_d$ rather than $L_d \propto N_d^2$

2.2 <u>Shielded</u> <u>rooms</u>

- electric and magnetic shielding by the use of alternated layers of high permeability and high conductivity materials.
- best achieved performances (BMSR):

Attenuation $> 10^5$ at d.c.
$> 10^7$ at 50 Hz

- commercially available rooms (about 300,000 US \$) A ~ 100 at 0.1 Hz, A > 10^4 at 50 Hz

inside volume ~ 30 m^3

- eddy current shielding (Zimmerman, 1977)
  pure Al walls, 5 cm thickness
  - no dc-shielding, A ~ 45 db at 60 Hz,
  - low cost.

2.3 Gradiometers and spatial discrimination

Based on the idea that "far" fields, i.e. produced by a distant source may be regarded as having a constant gradient.

- reduction in sensitivity as the energy is shared among the sub-coils of the gradiometer. The reduction increases with increasing order of the gradiometer.

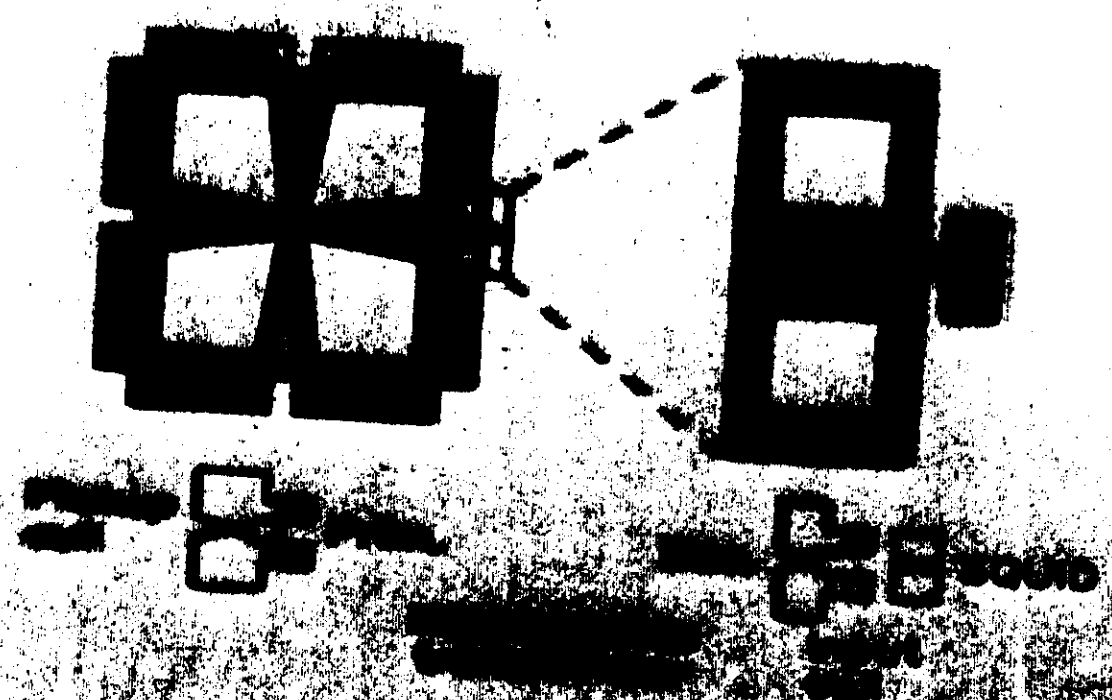
2.3.1 Vertical gradiometers

Wound-wire gradiometers require additional "balancing" systems, to achieve a satisfactory insensitivity to constant fields or fields with constant gradient (at least a few p.p.m. in field- and 1/10⁴ in gradient-balancing.

2.3.2 Planar gradiometers (Ketchen et al., 1978) (Carelli & Foglietti, 1983) [illegible] balance [illegible]

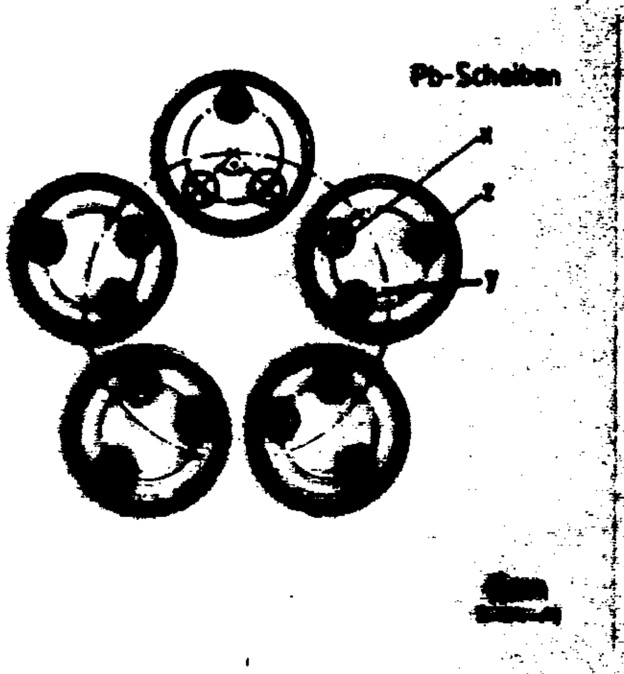
Advantages:
- no superconducting connections
- direct integration in a silicon chip
- enhanced sensitivity to higher spatial frequencies

Disadvantages:
- enhanced complexity of detected patterns
- lack of symmetry for source rotation



P.T.I. at IENA <u>no shielded room</u>

5 detecting channels $B_N \leq$ [illegible]
(II-order gradiometers)



(BTI) "Gemini" at Bellevue Hospital

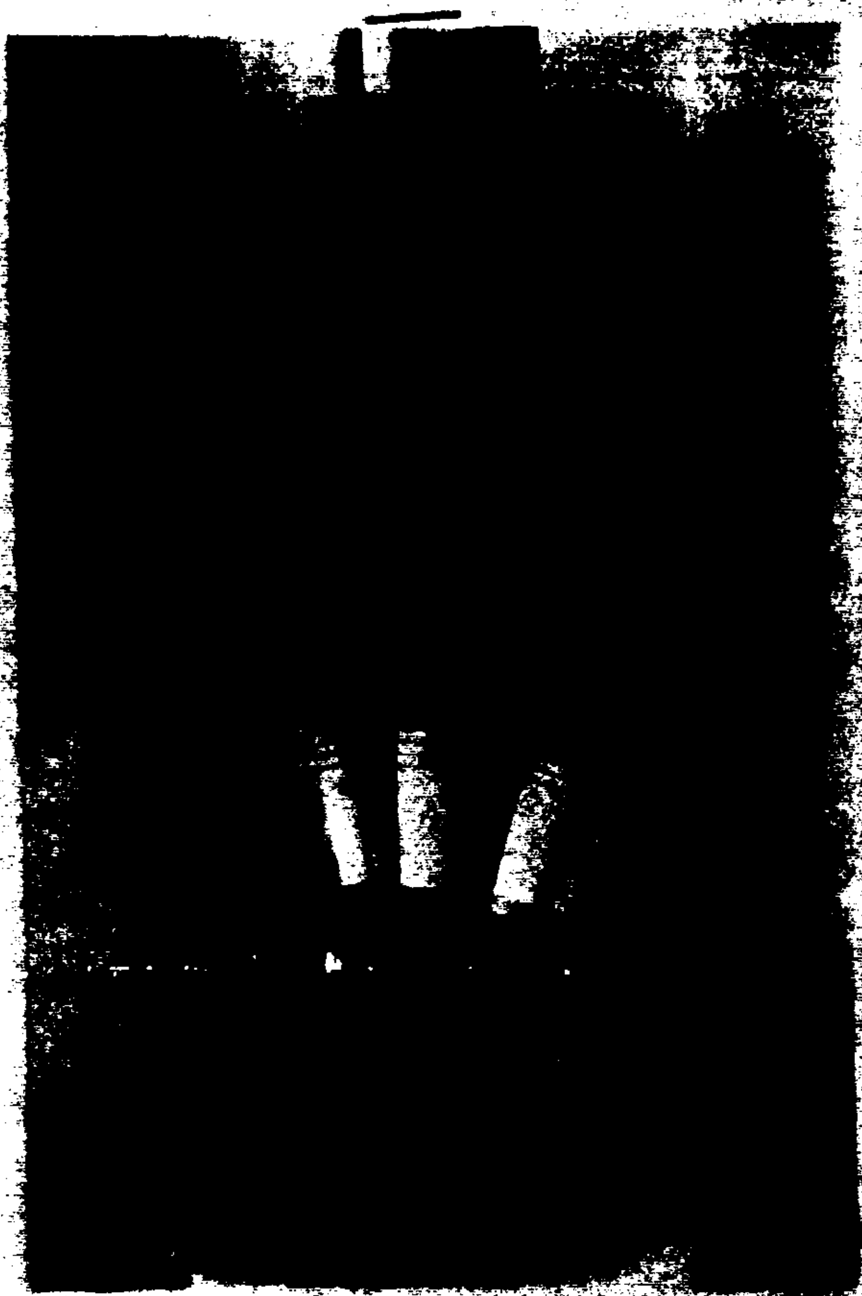
2× 7 detecting channels $B_N < 15\ fT/\sqrt{Hz}$
(II-order gradiometers)

(BTI, 7 channel at PTB in Berlin)
(I-order gradiometers ⟹ $B_N \sim 7\ fT/\sqrt{Hz}$)

<u>shielded room</u>

L.T.L. at HUT

Shielded



7 detecting channels
(I. order gradiometer)

systems

- "few" channel systems (4 ÷ 7 sensors) (many commercial)
- best performances achieved inside shielded rooms. $B_N \sim 5\ fT/\sqrt{Hz}$
- reduce errors due to positioning
- reduce recording time
- do not eliminate the lack of simultaneity

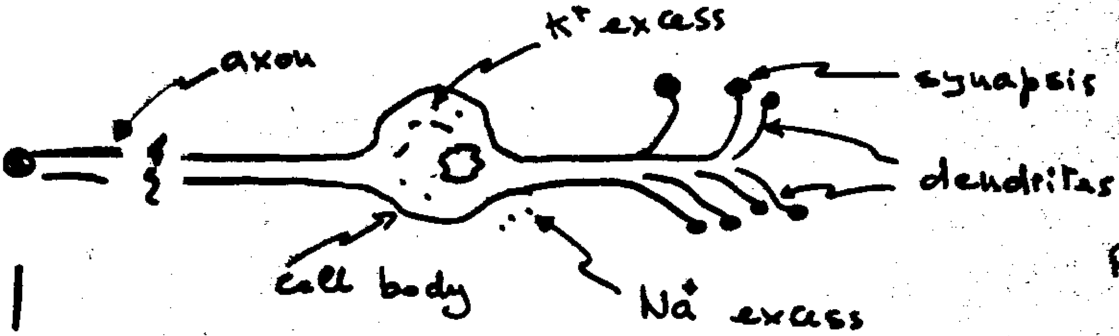
3. MODELING AND SOURCE LOCALIZATION

3.1 The forward and inverse problem

- Forward problem: to calculate the distribution of magnetic fields and electric potentials from a given distribution of charges and currents inside the body
- Inverse problem: To identify a distribution from a measured pattern of fields and potentials at the body surface
- The inverse problem has not a unique solution.
- Need for a choice of a model source that is physiologically meaningful and yet mathematically tractable.

Two distinct phenomena contribute to scalp potentials and magnetic fields:

- postsynaptic currents (relatively slow events: 10 - 500 ms)
- action potentials (fast events < 10 ms)



Resting potential
$V \approx -80$ mV

- due to the time scale it is reasonable to consider the intra- and extra-cellular pattern as approximately quasi-static for postsynaptic currents.

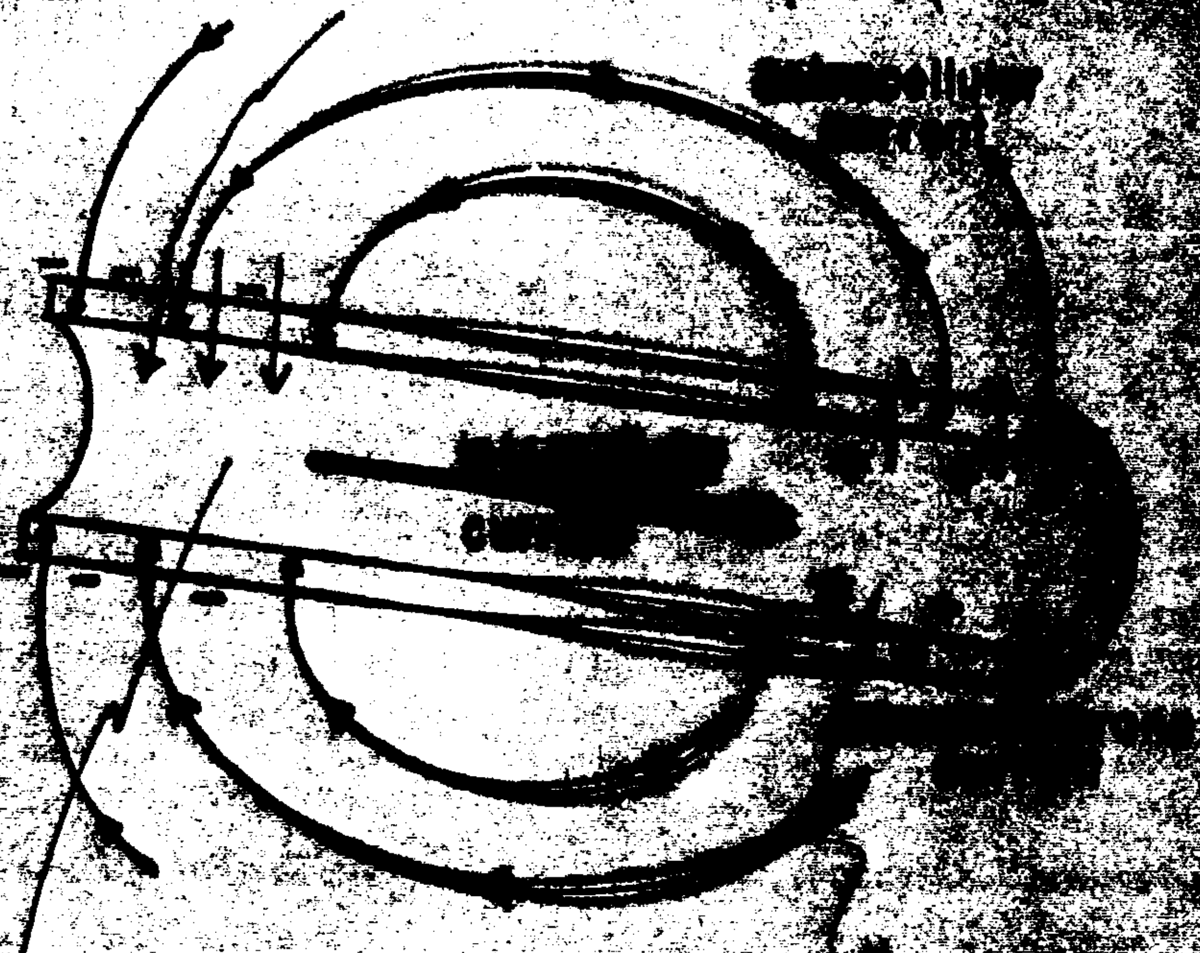
3.2 The current dipole

- a short element of current I of length L and negligible cross-section
- "Moment" $Q = IL$ (A.m)
- actually $\vec{Q}$ is a vector pointing in the direction of I

1 dipole may account for postsynaptic currents

2 dipoles (successive and opposed) for action potentials

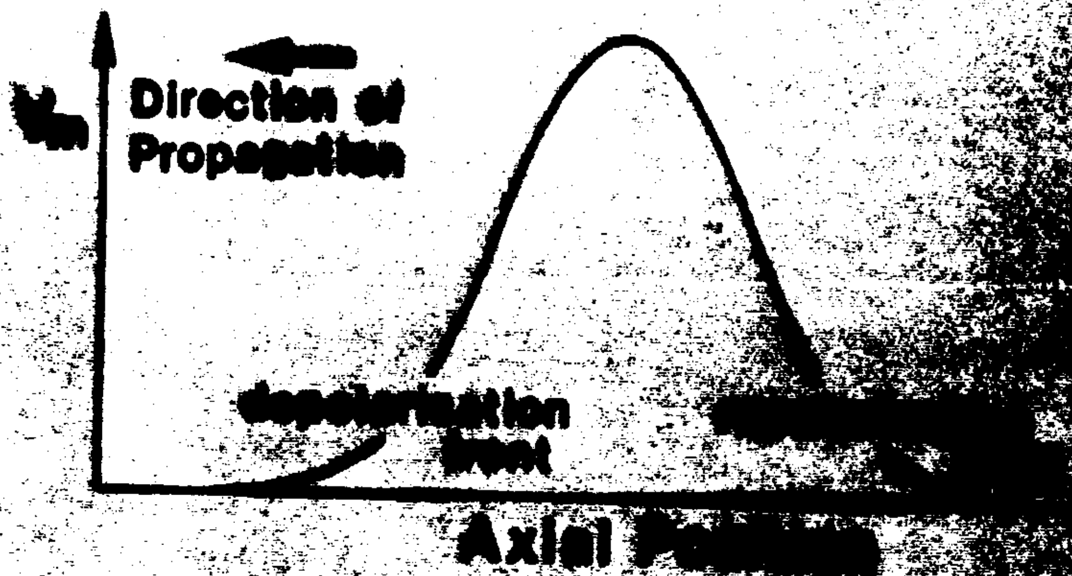
- Using the Biot-Savart law it is possible to calculate the magnetic field B produced by a current dipole at a distance a change in permeability (...) allows a slow inflow of the

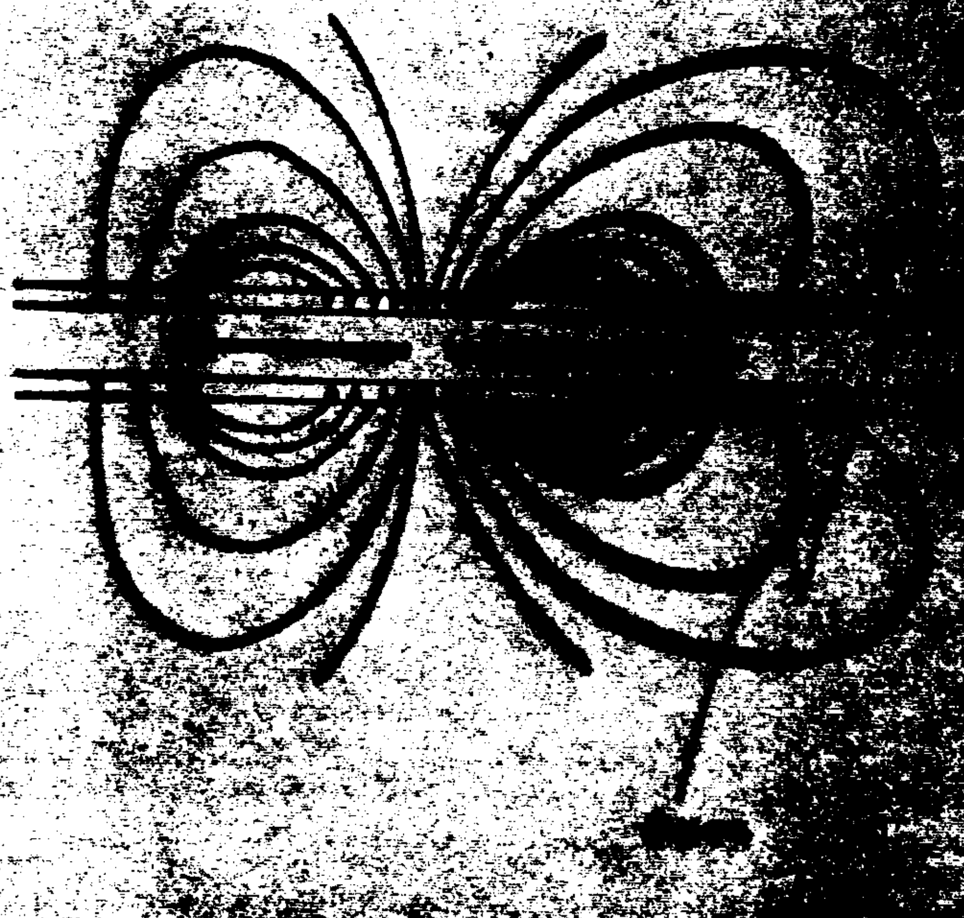


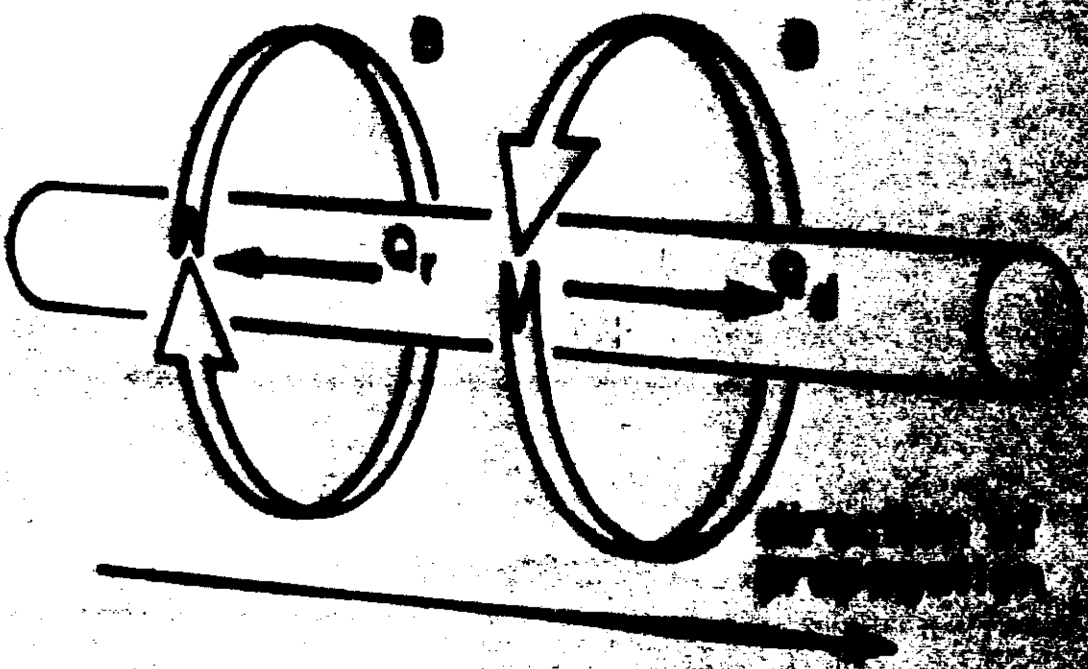
dendritic tree

the re-equilibrium state will be reached after several tens or milliseconds thanks to the Na-K pump

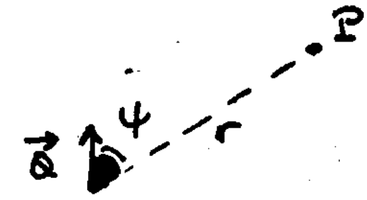
- in this case a complete depolariz[illegible] achieved (in about 1ms), immedi[illegible] by a repolarization process.







$$\vec{B} = \frac{\mu_0}{4\pi} \frac{\vec{Q} \wedge \vec{r}}{r^3}$$



- The field strength of a current dipole decreases as the square of the distance

- It has been estimated that the moment Q of an (apical) dendrite of a pyramidal neuron in the cortex may have the value

$$Q \sim 10^{-13} \text{ A.m}$$

Under this hypothesis, if we measure the field outside the scalp at ~ 4 cm distance, the maximum field would be $B \sim 6 \times 10^{-18}$ T. This value, when compared with the amplitude of a typical evoked field $B_m \sim 200$ fT suggests that at least $\frac{200}{0.006} \sim 3 \times 10^4$ neurons might be involved in the generation of an evoked signal from the cortex.

- Current dipole immersed in an infinite medium with homogeneous conductivity.
  - Only the primary (intracellular) current contributes to the field (other contributions provide zero net field for symmetry reasons)
  - Both primary and secondary (extracellular) currents contribute to the electric potentials

- current dipole in bounded media (half-space, sphere)

- The boundary produces a distortion of the current patterns, and the previous statement is no longer valid.

- Nevertheless, if the medium is an half-space with homogeneous conductivity, or a sphere with homogeneous conductivity or with conductivity homogeneous in concentric shells, the component of the field normal to the surface is independent of volume currents

- this statement is true in the ideal case but is substantially valid also for a real head, the contribution to the net field by volume currents being small

(Grynszpan & Geselowitz, 1973)
(Cohen & Hosaka, 1976)
(Williamson & Kaufman, 1987)

- a current dipole, oriented normally to the surface produces no net field.

- More complex current configurations require more sophisticated models (current quadrupole)

5.4 Procedure for source localization (brain)

- Measure the magnetic field distribution over the scalp (with regard to a specific ...)
- Measure head's parameters and fit the best sphere to the subject's head
- In case of a dipolar-like distribution perform a least squares fit between the measured field values and the ones from the model source ...
- Identify the three-dimensional location of the equivalent generator

4. APPLICATIONS

4.1 Heart studies

- standard MCG
- heart conduction system (His-bundle)
- accessory branch of activation (WPW)
- evaluation of sudden death risk
- follow-up of transplanted heart for rejection prediction

4.2 Brain studies

- spontaneous activity and epilepsy
- evoked fields (to study fundamental mechanisms of brain functioning)

[illegible]

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	HCG
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	+	-	+	+/-	+/-	+	+
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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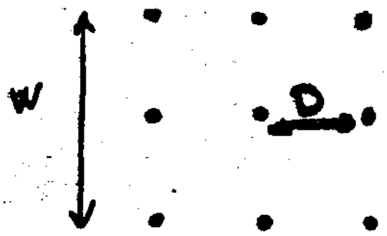
- Large multichannel systems
  - able to detect simultaneously the whole distribution of the magnetic field associated with a specific event. (class "100" sensors)
- dewars, cryo coolers
- choice of the gradiometric sensors (vertical or planar)
- choice of the array configuration



The recording grid spacing D determines the spatial sample rate and affects the higher spatial frequencies, whereas the total width W affects the lower spatial frequencies.

In other words D and W establish the optimum range of depth for a source to be detected.

It has been shown (Romani & Leoni, 1985) that for a dipolar source with a distance from the detection coil $d \gtrsim 2$ cm, the grid spacing should be $D > 2.5$ cm

- Goal: real time functional imaging
- estimated time for achievement: $4 \div 5$ years