Biomagnetism

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Progress in ultrasensitive magnetic measurements has made it possible to study weak magnetic fields produced by the bioelectric activity of biological tissues. Such measurements are made now in biophysics and medical science and have also clinical applications.

About two hundred years ago an Italian physician Luigi Galvani made a number of experiments on the interdependence of electricity and the contraction of the leg muscle of a frog. He noticed that some unexpected contractions occurred in synchronism with the sparking of a nearby electric instrument. In 1971, Galvani published his work De viribus electricitatis in motu musculari commentarius.

Alessandro Volta, professor of physics, repeated Galvani’s experiments. He questioned the biological generation of electrical phenomena and in 1786 showed that only the contact of two dissimilar metals with an electrolyte was necessary for the production of electric currents. Some 30 years after Galvani’s discoveries the first galvanometers became available. Evidence was then found that electric currents were produced by muscular activity and ever since, studies of such bioelectric phenomena have been very important for the basic understanding of many biological processes.

Registrations of electrocardiograms (ECG), electroencephalograms (EEG), electroretinograms (ERG) etc. are widely used in clinical practice while various types of bioelectric measurement are utilized in biophysics and medical science. The purpose of such measurements is to learn of electric currents (or potentials and charges) associated with the functioning of the biological systems studied. As is seen in Table 1, the frequencies involved are relatively low and the amplitudes of the signals in electric surface potential measurements are of the order of 1 mV or less (and about 100 mV in intracellular registrations).

Most bioelectric fields are caused by the same current distributions that create the electric potentials in the biological volume conductor. As Table 1 shows, bioelectric fields are weak, and small compared with the external magnetic noise. Registrations of magneto cardiograms (MCG), magnetoencephalograms (MEG), magnetoretinograms (MRG) etc. have become possible only during the past two decades. It has been proved both theoretically and experimentally that biomagnetic measurements are able to yield information on the sources which is complementary to the data obtained from electric measurements.

In Table 1, are also cited signals which are caused by pure magnetization such as ferromagnetic contamination of the lung tissue. Such phenomena naturally do not have any electric counterpart.

The Inverse Problem

From the point of view of its electromagnetism, a typical biological specimen can be illustrated as in Fig. 1. A volume conductor of electric current \( v' \) is bounded by an outer surface \( S' \) outside which the electric conductivity is zero. The sources of electric current density \( j_p \) are assumed to be confined within a subvolume \( v'' \). The actual current sources work at the cellular level and we measure the result of their total action: either the electric surface potential \( V(r) \) or the magnetic field \( B(r) \) close to \( S' \). In addition, \( V' \) could contain material with magnetization \( M(r') \). The question is which information on \( j_p \) and \( M \) can be obtained from such electromagnetic measurements in a quasistatic situation.

Unfortunately, the inverse problem of determining the sources of electromagnetic fields from external measurements has no unique solution. However, these quasistatic fields can be expanded into multipole contributions, whose equivalent generators are the multipole moments of the electric and magnetic multipole sources. These moments can be uniquely determined from external measurements but they do not determine the source distributions in real space. In addition, the multipole expansions are valid only outside a sphere containing all the sources of the field. In Fig.

Table 1 — Some bioelectromagnetic phenomena, their approximate frequency bands, maximum signal amplitudes and pioneering recordings.

<table>
<thead>
<tr>
<th>BIOELECTROMAGNETIC PHENOMENA</th>
<th>APPR. BANDWIDTH (Hz)</th>
<th>MAGNETIC SIGNALS</th>
<th>ELECTRIC SIGNALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogram</td>
<td>0.05 - 100</td>
<td>MCG 50 µT (Baule et al. 1963)</td>
<td>ECG 1 mV (Waller 1887)</td>
</tr>
<tr>
<td>Fetal Cardiogram</td>
<td>0.05 - 100</td>
<td>FMCG 10 µT (Kariniemi et al. 1974)</td>
<td>FECG 50 µV (Cromer 1906)</td>
</tr>
<tr>
<td>Myogram</td>
<td>DC - 2000</td>
<td>MMG 10 µT (Cohen 1972)</td>
<td>EMG 1 mV (Adrian 1929)</td>
</tr>
<tr>
<td>Encephalogram</td>
<td>0.05 - 30</td>
<td>MEG 1 µT (Cohen 1965)</td>
<td>EGG 50 µV (Berger 1924)</td>
</tr>
<tr>
<td>Evoked Potential/Field</td>
<td>DC - 100</td>
<td>VEF 0.2 µT (Cohen 1975)</td>
<td>VEP 10 µV (Walter et al. 1946)</td>
</tr>
<tr>
<td>Retinogram</td>
<td>0.1 - 30</td>
<td>MRG 0.1 µT (Aittoniemi et al. 1978)</td>
<td>ERG 100 µV (Holmgren 1865)</td>
</tr>
<tr>
<td>Lung Contamination</td>
<td>DC</td>
<td>FC 1 µT (Cohen 1973)</td>
<td>—</td>
</tr>
<tr>
<td>Susceptibility</td>
<td></td>
<td>MSPG (Wikswo et al. 1974)</td>
<td>—</td>
</tr>
<tr>
<td>Plethysmography</td>
<td></td>
<td>(Harris et al. 1978)</td>
<td>—</td>
</tr>
<tr>
<td>Human Iron Stores</td>
<td></td>
<td>(Harris et al. 1978)</td>
<td>—</td>
</tr>
</tbody>
</table>

Fig. 1 — To facilitate the calculation of bioelectric and biomagnetic fields we assume that the electric conductivity \( \sigma \) of a bioelectric volume conductor \( v' \) is constant and that the primary current sources \( j_p \) are confined to a subvolume \( v'' \). The volume currents \( j_{v''} \) are not shown in detail.
this sphere should enclose totally the volume $v'$.

In real studies of say the human body, for practical reasons, the measurements are not made outside the complete sphere because of the parasitic influences. A further problem is the inhomogeneous and often anisotropic electric conductivity of the human body. In addition, signals from other parts of the system may interfere with signals of interest. For example, in studies of some part of the human brain, interfering signals are produced by the heart, the eye and other parts of the brain whose functioning cannot be stopped during the time of the experiment! Evidently the solution of the inverse problem is difficult and is only obtained by using equivalent generators for the sources or by using a suitable simplified model for the volume conductor or both.

**Modelling**

A starting point for a simple model is to consider the current sources such as $J_p$ in Fig. 1 immersed in an infinite and homogeneous conductor. The expressions for the electric and magnetic potentials in an infinite volume are:

$$V_{\infty}(r') = -\frac{1}{4\pi\sigma} \left[ \nabla \cdot \left( J_p(r') \right) \right] \, dv''$$

and

$$A_{\infty}(r') = \frac{\mu_0}{4\pi} \left| J_p(r') \right| \, dv''$$

The influence of the boundaries has already been investigated by Helmholtz who considered a hypothetical potential double layer, placed at the surface $S'$ of the conductor. The double layer was chosen so as to give in a homogeneous medium outside $S'$ the same potential and currents as the source current density $J_p$. Changing the sign of the double layer results in zero current density outside $S'$ and in the following expressions for the electric and magnetic potentials for bounded volume conductors:

$$V_s(r) = V_{\infty}(r) - \frac{1}{4\pi} \left| \nabla \cdot J_p \right| S' \, dS'$$

and

$$A_s(r) = A_{\infty}(r) - \frac{\mu_0}{4\pi} \left| J_p \right| S' \, \sigma S' \, dS'$$

The use of Eq. (3) to find the surface potential $V_s$ of bounded volume conductors is a nice undergraduate exercise.

For practical use, often extremely simple models have to be utilized. Consider as an example current sources in a homogeneous conducting sphere and take into account only the lowest order term of the multipole expansion. The problem is reduced to finding a current dipole in a sphere. The solution of the corresponding direct problem shows several representative features, which help in understanding the relative merits of bioelectric and biomagnetic measurements. Fig. 2 shows the contour lines of the electric surface potential and the radial component of the magnetic field.

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Fig. 2 — A) and B) The electric surface potentials $V_s$ and C) the component of the magnetic field perpendicular to the surface $B_r$ produced by current dipoles in an electrically homogeneous spherical volume conductor. The maximal values (normalized) are indicated by ± signs, the thick line is the half-maximum contour line and the broken lines indicate the zero value. The small spheres (a,b) show the current sources: a) a radial current dipole $P_z$ (for A) and b) a tangential current dipole $P_x$ (for B and C). Both dipoles are located at the $z$-axis with $a/R = 0.7$.

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Fig. 3 — Left, computer simulated magnetocardiograms (QRS-T morphology) in an anterolateral myocardial infarction (thick line) and the difference from the normal MCG (thin line). The measurement grid approximately covers the area of the chest of the subject. The computer program developed by D. Geselowitz and W.T. Miller (Pennsylvania State University) was used. (Siltanen P, Poutanen T, Katila T, Seppänen M, and Varpula T, Ref. 2)

Right an example of the measured traces of a patient with an anterolateral infarction.
The field was chosen instead of the magnetic potential, since it is closer to what is measured in practice. The following features which are valid exactly in our ideal case are also approximately valid for many real measurements:
- Both radial and tangential current sources contribute to the electric surface potential.
- The external magnetic field is caused solely by the tangential current sources.
- Current sources close to the surface create potentials at the surface which are higher by a factor of two than would be measured if we were dealing with an infinite volume conductor. Surface potentials caused by current sources close to the centre are magnified by a factor of three.
- In the radial component of the magnetic field, the second term of Eq. (4) is equal to zero. This can be generalized as follows: The component of the magnetic field perpendicular to the surface is least affected by volume currents, or in other words: concentric electric inhomogeneities to which the skull around the brain approximate often have no effect on the external magnetic field.
- Deep sources produce relatively weak magnetic fields. Thus it seems that biomagnetic measurements trace effectively the superficial current sources only.
- The distributions of the electric potential and of magnetic field reveal information on their sources, which with suitable simplifying assumptions can be used to localize the sources and to estimate their magnitudes. For superficial and tangential sources the surface potential and the radial component of the magnetic field seem to show similar contour lines and spatial resolution. The field patterns are oriented perpendicular to each other. The direct problem, i.e. to calculate the fields from the sources assumed, can be solved if the geometry is known. Very advanced computer models have been developed for this in cardiology. Computer programs are able to calculate the distribution of the surface ECG and MCG field components outside the human torso for standard torso geometry and bioelectric activation. The influence of abnormalities in the functioning of the heart can often be taken into account. Fig. 3 shows an example. It is the calculated map of the component of the MCG field perpendicular to the frontal plane for an (anterolateral) myocardial infarction. The figure also shows the calculated difference of the actual MCG from the normal MCG. The same program can be used to calculate the surface ECG as well.

Measurement Techniques
The magnetometers used for measuring biomagnetic fields must be sufficiently sensitive yet able to reject the very much stronger "common mode" magnetic background noise. Although some conventional magnetometers, such as fluxgate or ordinary induction coil magnetometers, have been successfully used for measurements of biomagnetic fields they are generally not sensitive enough. Baule and McFee (1963) used in their pioneering work on magnetocardiograms two identical and parallel coils, two million turns each, wound oppositely on ferrite cores. Today parametric Superconducting Quantum Interference Device (SQUID) amplifiers are mainly used. A closed loop of superconducting wire transfers magnetic flux to the SQUID even in DC operation without contributing thermal noise.

Since external magnetic noise is such a serious limitation on studies of very weak magnetic fields, a magnetically shielded chamber provides an optimal solution. A shielded chamber large enough for human subjects with three layers of high-permeability ferromagnetic material and additional eddy-current shields has been successfully used by D. Cohen at M.I.T. (Boston) since 1971. The shape of the chamber approximates a sphere. A number of rectangular chambers have been constructed (e.g. recently at the Helsinki University of Technology and at the Physikalisch-Technische Bundesanstalt, West Berlin). Field noise as low as 3fT/√Hz has been measured with a SQUID magnetometer at about 10 Hz in the PTB-chamber. Such a level allows direct field recording of most biomagnetic signals. Nevertheless, differential flux transformers (gradiometers) are most often used instead of a single coil. One coil then acts as a reference and the other oppositely wound coil as the actual signal coil.

Most research groups do not have a magnetically shielded chamber available. One solution to the problem of magnetic noise is to perform the measurements outside the laboratories on a magnetically quiet measurement site. "Nonmagnetic" cottages situated in suburban areas are used by several groups. Then a first order gradiometric measurement can be used to obtain high quality data. However, a balance of the gradiometer at the 10 ppm level is necessary to compensate for long-range magnetic noise which is usually between 10^4 and 10^5 fT/√Hz at the frequencies of interest. Naturally, the measurement also contains a DC-background, since the Earth's steady magnetic field is some 10^5 times stronger than the weakest biomagnetic fields measured.

For clinical applications a remote measurement site is not feasible and measurements in a laboratory or in a hospital without a magnetically shielded chamber are even more problematic. The magnetic field at the main line frequency may easily reach a value of 10 nT and the low frequency noise several hundred nT peak to peak during 10 s. The usual answer to these constraints is a second order gradiometer (Fig. 4) very accurately balanced. With proper filter-
ternal magnetic noise. The unavoidable
liquid helium dewar in which the
2-hole Zimmerman-type RF-SQUID.

Results
The pioneering observation of Baule
and McFee started magnetoencephalo-
graphic measurements twenty years ago.
The electric activation sequences of the
normal heart and many abnormal cases
are reasonably well explored. Morpholo-
gical maps such as that in Fig. 3 can be
calculated using computer simulation
programs. It appears that the morpholo-
gies of the MCG and ECG waveforms
resemble each other. It is possible to
identify deflections which are associat-
ted with atrial and ventricular depolariz-
ations etc. The present signal-to-noise
ratio of the MCG measurements, about
40 dB, is of the same order of magnitude
as that of conventional ECG measure-
ments. However, the MCG so far has not
really been applied in clinical practice
although its diagnostic power appears
to be very similar to ECG, and the meth-

in Fig. 2 are used to localize the equiva-
lent current source. More accurate infor-
mation on the sources could naturally be
obtained from intracranial recordings
and from animal studies. However, not
all deflections show up in animals and
studies during neurosurgical operations

In studies of evoked electric poten-
tials, a suitable external stimulus is
repeated several times; the time aver-
aging improves the signal-to-noise ratio by
decreasing the level of the nonsynchro-
nous background activity. In Fig. 5 we
see examples of auditory evoked electric
potential and magnetic field recordings.
The stimuli are binaural tones at 1 kHz.
Both signals show prominent deflec-
tions at latencies about 100 ms and 200
ms after the stimuli and sustained
(SF/SF) contributions. The spatial distri-
butions of the amplitudes of different
sequences are mainly the technical difficulties
mentioned above.

Electric and magnetic measurements
yield complementary information on the
cellular level, simultaneous
electric and magnetic measurements
provide information on the
potential and current distributions eg. of
the action potential of a nerve. J.P.
Wikswo et al. at Vanderbilt University
(Nashville) were able to measure the
magnetic field of isolated axons. The
magnetic field data provide more direct
means to study the currents than the
electric measurements. On the other
hand SQUID-measurements are more
limited due to the large size of present
magnetometers and their still relatively
low sensitivity.

Electroencephalographic (EEG) studies
of the human brain are widely used
both for basic brain research and for
clinical applications. In practice the elec-
tric potential distribution caused by a
 dipole source is not as sharp as in the
e xample of the homogeneous spherical
volume conductor of Fig. 2. The electric
inhomogeneities due to the liquor
spaces, skull and scalp smear consid-
ervably the potential distributions, while
the magnetic field is less affected.
Therefore, magnetoencephalographic
(MEG) measurements are suited for
localizing cortical electric activity. Again
there are limitations: the magnetic field
sees the tangential part of cortical
sources only and deep dipoles in a
homogeneous medium contribute very
little. A synchronous collective action of
numerous neurons is required to see the
signal above noise. The simultaneous
activity of several cortical areas com-
plicates the interpretation of sponta-
neous EEG and MEG. Nevertheless, suc-
cess in localizing epileptic activity eg.
has been obtained using magnetic
methods.

The most often used SQUID so far is
the 2-hole Zimmerman-type RF-SQUID.
The weak link in such a SQUID used to
be the screw point contact, but recently,
modifications to the design have resul-
ted in very reliable low noise amplifiers.
Field sensitivities around 10 fT/Hz have
been reported. The new DC SQUID de-
signs should allow field sensitivities still
better by about a factor of ten. To utilize
fully such sensitivities much attention
must be paid to the noises produced by
the liquid helium dewar in which the
gradimeter is immersed and to the ex-
ternal magnetic noise. The unavoidable
use of some, albeit simple, low tempera-
ture techniques complicates the measu-
rements in two ways. First, liquid helium
is rarely in routine use outside physics
laboratories and its handling requires
some extra training. Second, the liquid
helium dewars are large, unwieldy con-
tainers that cannot be tilted arbitrarily.

The electric and magnetic field
responses. The stimulus was a 1 kHz
sound, 800 ms in duration. a) Average of 87
electric responses. b) Average of 330
magnetic responses. c) The distribution of
the amplitudes of magnetic N 100 respon-
ses. The component of the magnetic field
perpendicular to the skull was measured.
Open circles indicate magnetic flux into the
skull (Hari R., Aittoniemi K., Järvinen M.-L.,
Katila T. and Varpula T., Exp. Brain Res. 40
are of course limited for other reasons. The magnetic measurement technique, often augmented with electric surface measurements has helped in localizing a number of source activities in the cortex, elicited by stimuli of different modalities. The studies made at New York University especially deserve to be mentioned. Although the evoked magnetic fields are only a few hundred femtotesla in amplitude, they were successfully measured without any magnetic shielding!

It would not be appropriate to list here all possible applications of biomagnetic measurements. Instead we shall finish by mentioning the studies of magnetic biosusceptibility or magnetization in vivo. The mechanical activity of the heart produces an induced signal in the external magnetic field. Excess iron in liver has been detected by a group at Case Western Reserve University using a similar technique. Several groups have studied the accumulation of magnetic contamination in the lungs of welders. The subjects were magnetized in an external magnetic field and the remanence magnetization was measured. Often these fields are so high that conventional flux-gate magnetometers can be used.

REFERENCES

EPS History
We apologise for the omission of a line in the President's article in May. To set the record straight, the sentence dealing with the early days of EPS should read:

"At the time of the inaugural conference in Florence in April 1969, following the establishment of the Society in Geneva in September 1968..."

Delegates of Associate Members
Following the recent ballot, the delegates to Council of the Associate Members are:

E. Feldtkeller, Siemens (4 years)
J.-C. Lehmann, CNRS (4 years)
R.W. Brander, British Telecom. (2 years)
J.A. Goedkoop, ECN (2 years)