INTERNATIONAL ATOMIC ENERGY AGENCY
UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION
INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
I.C.T.P., P.O. BOX 586, 34100 TRIESTE, ITALY, CABLE: CENTRATOM TRIESTE

H4-SMR 471/23

COLLEGE ON MEDICAL PHYSICS

10 - 28 SEPTEMBER 1990

INTRODUCTION TO BIOMAGNETISM

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INTRODUCTION TO BIOMAGNETISM

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Abstract

An introduction to the new research area known as Biomagnetism is made. Emphasis is given to the instrumental aspects and applications involving simple instrumentation.

Contents

1 Introduction 2

2 Detectors of Magnetic Fields 2
  2.1 Induction Coil 2
  2.2 Fluxgate Magnetometer 6
  2.3 SQUID 6

3 Noise Rejection 11

4 Applications 14
  4.1 Brain Studies 15
  4.2 Biosusceptometry 17
  4.3 Gastric Emptying 17
  4.4 Animal Studies 19

5 Acknowledgements 22

1 Introduction

Several good reviews on **Biomagnetism** have been published in the last 10 years dealing with various aspects of this new interdisciplinary research area. A good start can be made with references [22] [6], that deal with instrumental aspects. An excellent course was offered in Frascati and a book was published in 1983 [23]. This book is very comprehensive and can be used as a tutorial to get acquainted with the area. To be informed in the new developments and breakthroughs it is recommended to read the Proceedings of the International Conferences on Biomagnetism [8][3][4][2] held in recent years.

In these notes an attempt will be made to cover material with details that are not presented in those references. They may be used as introductory material by those who decide to pursue research in Biomagnetism.

What is Biomagnetism ? An unusual way to define something is defining what this thing is not. Biomagnetism is not magnetobiology. Well... What's magnetobiology ? Magnetobiology is a research field involved with the study of the effects of magnetic fields upon biological systems. These effects can span a wide range, from cellular and molecular effects to more complex effects such as changes in behaviour and performance. Biomagnetism on the contrary is concerned with the detection of magnetic fields emitted by biological systems. Figure 1 shows this situation.

Figure 2 depicts some areas or organs that can produce magnetic fields. Three categories of magnetic fields can be defined according to their production: 1-by ionic currents within the body, 2-by ferromagnetic contaminants or tracers and 3-by dia or paramagnetic constituents of the body.

The biomagnetic fields are very weak, ranging from 50 fT to 1 nT ($1Tesla = 1T = 10^4 gauss$), usually restricted to a frequency bandwidth below 1 KHz. Figure 3 shows the various signals already detected. The weakest signals are those from the brain, 10^{-9} times the earth's magnetic field.

2 Detectors of Magnetic Fields

In this section a brief survey will be made of the detectors that can be used to sense magnetic fields produced by biological systems.

2.1 Induction Coil

When asked to measure a magnetic field, probably the first method that comes to the mind of a physicist is one using an induction coil. By Faraday law it is known that a

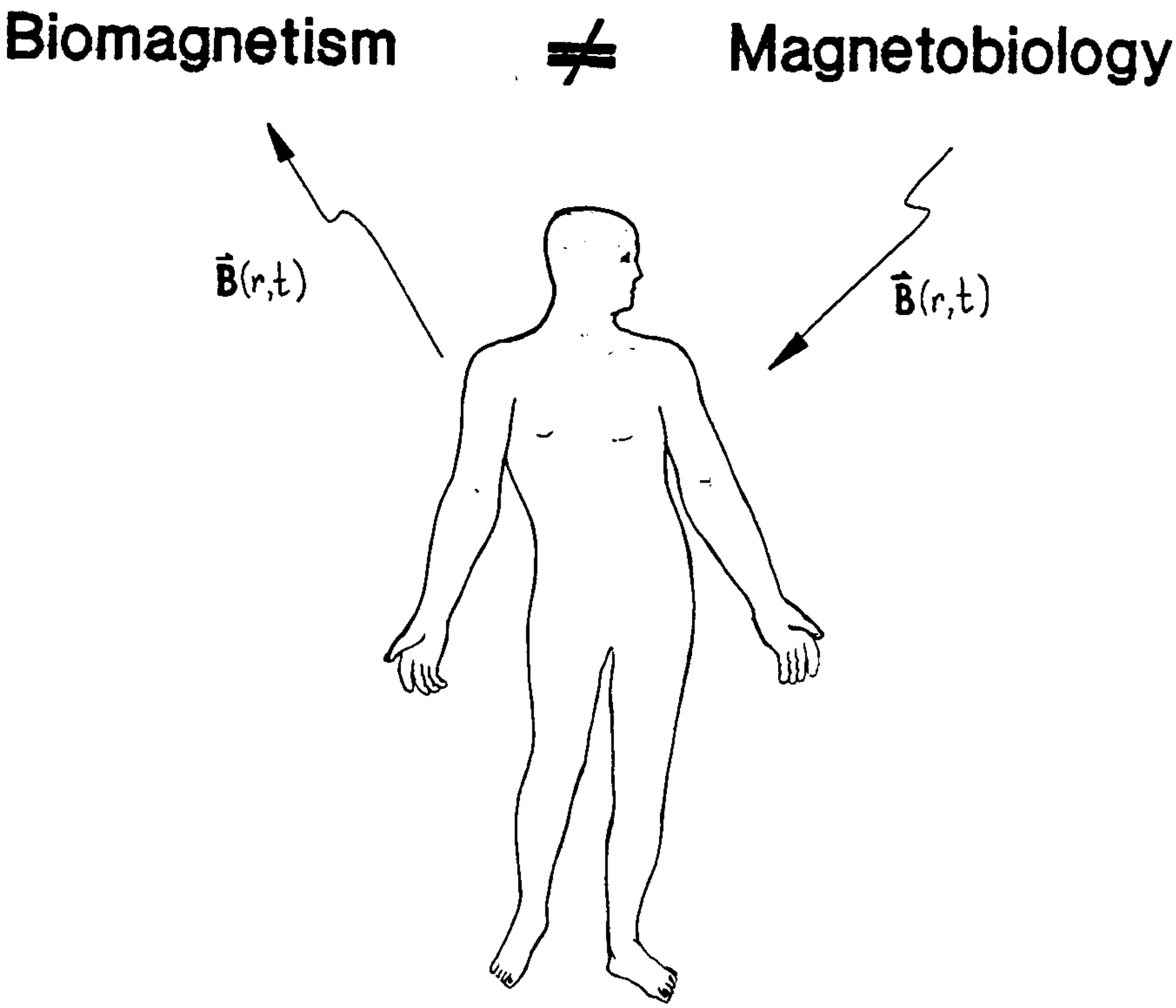

Figure 1: A pictorial definition of magnetobiology and biomagnetism.

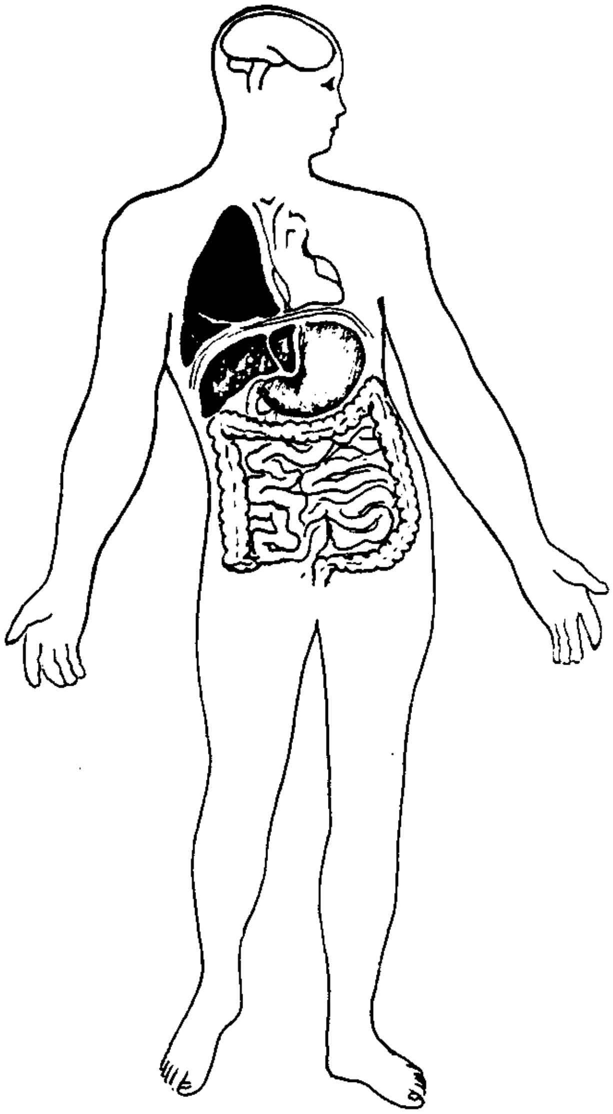

Figure 2: Typical magnetic fields produced by the human body. Different shades distinguish the categories cited above.

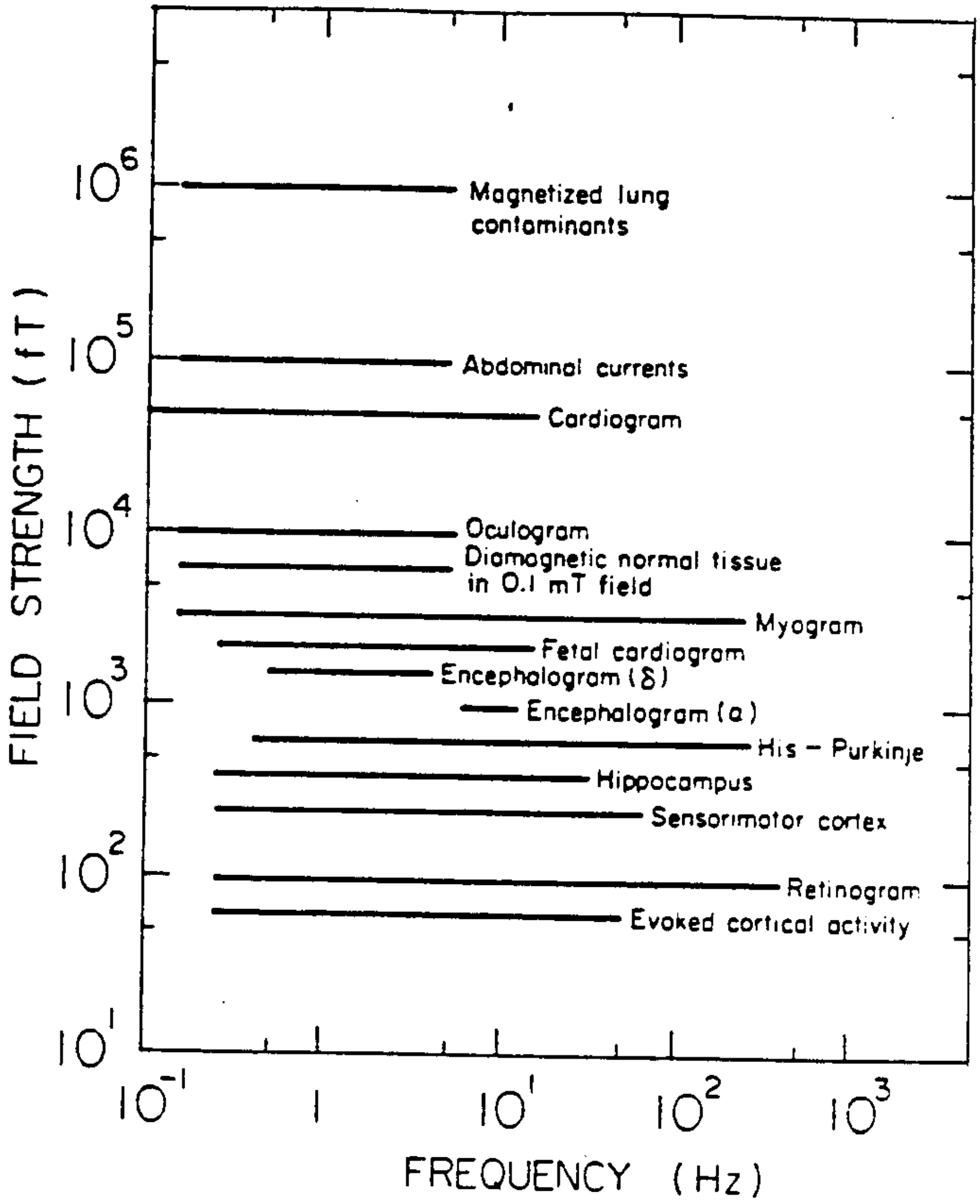

Figure 3: Typical biomagnetic signal intensity detected. The horizontal axis shows the frequency range of their Fourier components

magnetic flux change will produce an electromotive force according to: $\varepsilon = -\frac{d\phi}{dt}$ where $\phi = \int B.dA$ is the magnetic flux. In fact this was the first detector used in biomagnetism. Baule and MacFee [7] employed a set of two coils having $2\ 10^6$ turns to detect the signal from the human heart. A signal to noise ratio of 1 was obtained when measuring fields of 10 pT of intensity with a pair of coils with 10 cm diameter. Problems associated with this detector are the dependence on the frequency of the signal detected, of limited sensitivity and spatial resolution. It should be remembered that DC fields can not be detected by this method.

Even with these limitations there are some applications where a toroidal ferrite induction coil can be used with great sensitivity. If biological preparations with currents showing an axial symmetry need to be measured, a toroidal pick up coil, such as clamp AC ammeter, can be built to detect the current with the sensitivity of a SQUID. Wikswo et al [13][14] developed a series of magnetic sensors based on toroids. The sensors were coupled to a very low noise amplifier and fields of the order of pT could be detected from isolated axons and bundle of nerves.

2.2 Fluxgate Magnetometer

A way to avoid some of the problems associated with the induction coils, for example low response to low frequency fields and limited spatial resolution, is to use a fluxgate magnetometer. This device takes advantage of the magnetic saturation effect common to many magnetic materials. If a non saturated magnetic material is placed in a region where a magnetic field exists, the field lines tend to converge into the material owing to its high magnetic permeability. However if the material first is saturated the magnetic permeability $\mu \approx 0$ and almost no field lines from the neighborhood will enter the bar (see figure 4).If a sensing coil is mounted axially around a bar of such material, the coil could detect an emf associated with the flux change linked to the neighboring fields. In practice two coils are wound around a magnetic material, to driven by an alternating current that will alternately saturate the material, and the other sensing coil to detect the magnetic field as an emf. Figure 4 illustrates the typical configuration of a fluxgate magnetometer. The sensing coil should not detect the saturating field produced by the driven coil and two arrangements are shown (figure 4 B and C). With this device a sensitivity of 30 pT has been reported [16][5].

2.3 SQUID

The Superconducting QUantum Interference Device (SQUID) is a magnetometer based on the Josephson Effect. This effect was first proposed by Brian Josephson in 1962. He

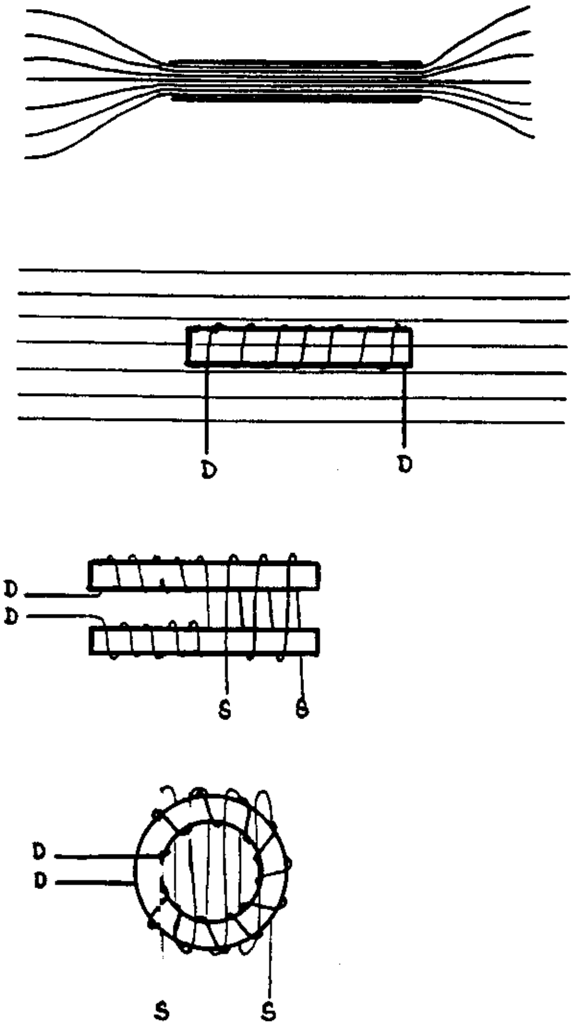

Figure 4: A non saturated bar of magnetic material is placed in a region of magnetic field. The field lines are denser inside the bar (A). If the material is saturated its magnetic permeability is approximately zero and the field lines from the vicinity do not go inside with the same density as before (B). A differential (C) and a toroidal fluxgate configuration (D)

proposed that if a superconductor material was interrupted by a thin resistive barrier a supercurrent will still exist. This was possible because of the tunneling of the supercurrent through the barrier. Two equations were deduced to describe this behavior. One describes the behavior of the current. If the current is kept below a critical value I_c, the material is superconductor and the current flowing through the barrier is related to the critical current as follows:

$$I = I_c \sin\theta \tag{1}$$

where θ is the difference in phase angle of the current across the barrier. If a current greater than I_c is forced through the barrier a voltage develops, expressed by:

$$V_j = \frac{h}{4\pi e}\frac{d\theta}{dt} \tag{2}$$

Figure 5 shows the behaviour of the current versus voltage and a possible way to make a Josephson junction to implement the idea of supercurrent tunneling. The resistive barrier can be made in different manners such as an oxide barrier, a thin mylar strip or a constriction in a superconductor material where the current will be greater than the critical current turning the material normal at this point.

The SQUID is composed of one or two junctions biased with a current $I \approx I_c$ by a bias circuit. The magnetic signal to be measured is also coupled to the circuit to drive it to the resistive region. Figure 6 shows how an RF-SQUID is built. The superconductor ring is biased by an RF probe and a current close to critical value is established in the ring. From the other side the current produced by the magnetic field to be detected is introduced in the ring. When the total current exceeds the critical value an absorption of energy can be detected through the readout (RF) probe. This signal is amplified by a lock in amplifier and fed back to the ring by means of a secondary coil to cause the system to operate as a null detector. This correction voltage can be calibrated in terms of the magnetic field applied.

This device can be view as a "black box" with a sensitivity of $\approx 10^{-30}$ joules/Hz, linearity $\approx 0.1ppm$ and transfer function of $\geq 10^7 V/A$. If the bias is provided by a DC current, another version of this device can be constructed known as a DC-SQUID. DC-SQUIDs are harder to make but have a better noise figure than the RF-SQUIDs. An additional compensation is that the electronics necessary are simpler than for the RF technique.

With the available materials these devices need to operate at liquid helium temperatures and a cryogenic facility needs to be set up around the equipment (see figure 7). Some SQUIDs have been built with the new high critical temperature superconducting materials. The results are promising and one High T_c DC-SQUID, operating at liquid

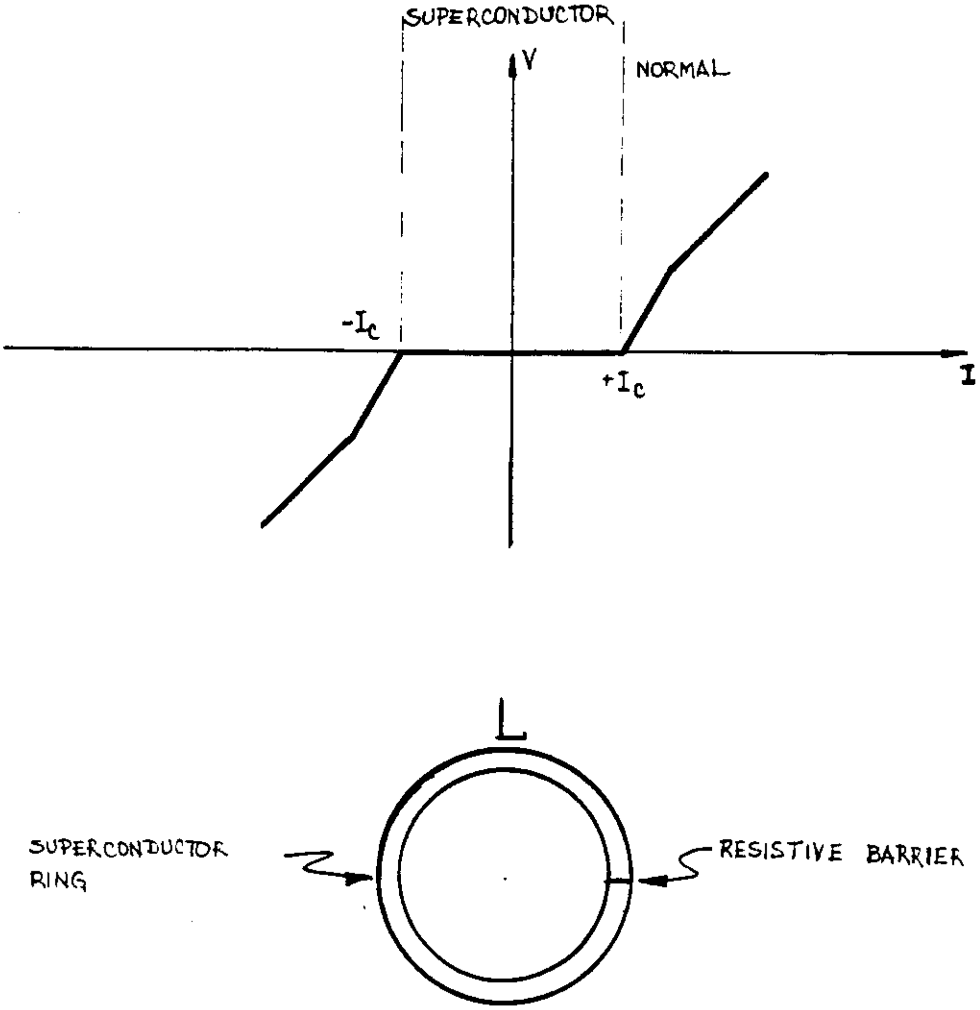

Figure 5: Curve characteristic of the current versus voltage in a Josephson barrier and Josephson junction to accomplish the effect.

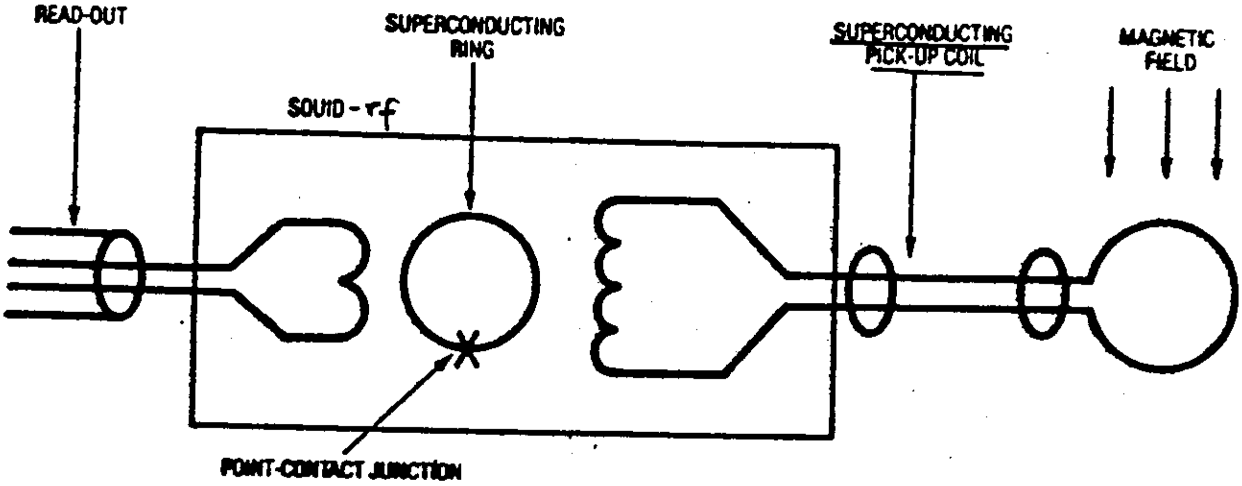

Figure 6: Schematic diagram of an RF SQUID. The magnetic circuit at the right, composed of the detection coil and the input coil, is known as the flux transformer.

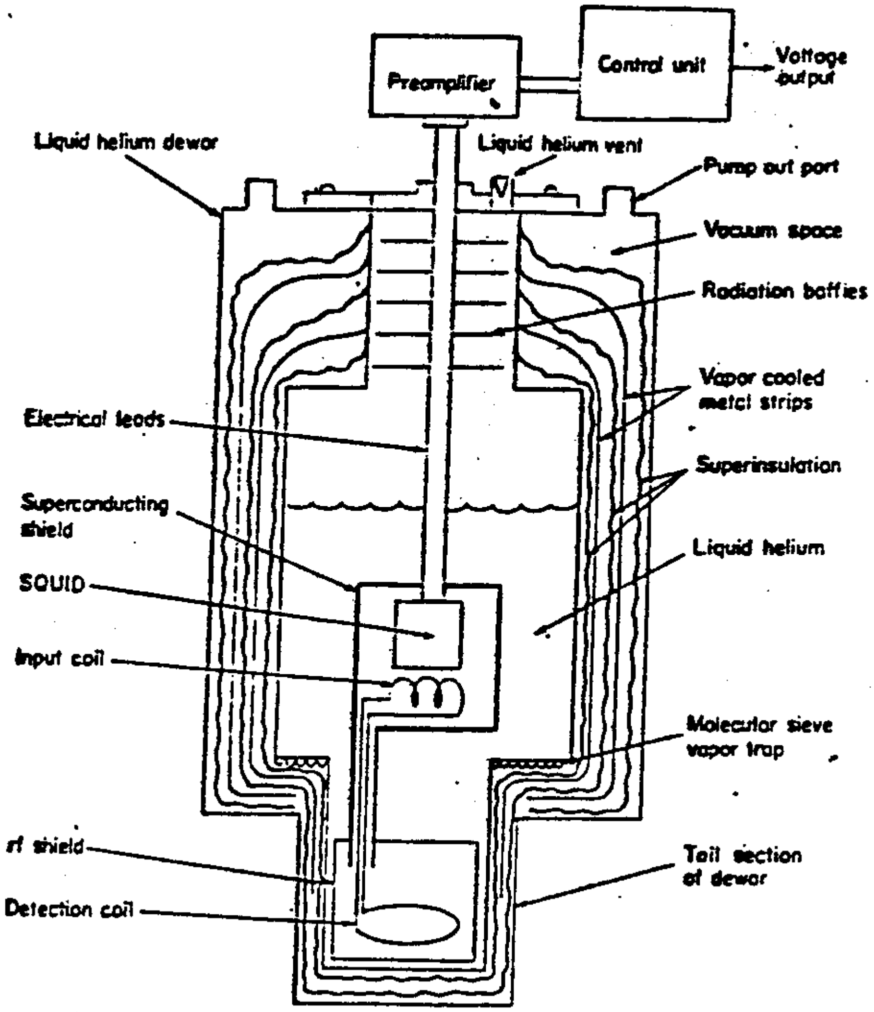

Figure 7: Schematic drawing of a SQUID based magnetometer.

nitrogen temperature, has been reported to have the same sensitivity as the first RF-SQUIDs produced [18].

3 Noise Rejection

Figure 8 shows that typical magnetic noise in an urban environment is several orders of magnitude higher than the signals of interest. These conditions impose conflicting demands: On one side the magnetic field detector must have a highest possible sensitivity capable of detecting 100 fT, and on the other side the detector must reject the ambient noise to avoid being overwhelmed.

Two possible means may be imagined to avoid this conflict: One is to shield the region where the magnetic measurements are to be accomplished and the other is to make a differential measurement. The first solution was used in early measurements with single channel systems. Magnetic Shielded Rooms (MSR) made with aluminum and several layers of high permeability materials such as $Mumetal^{TM}$ were built. They provided a very good noise attenuation, even at low frequencies. However the high cost

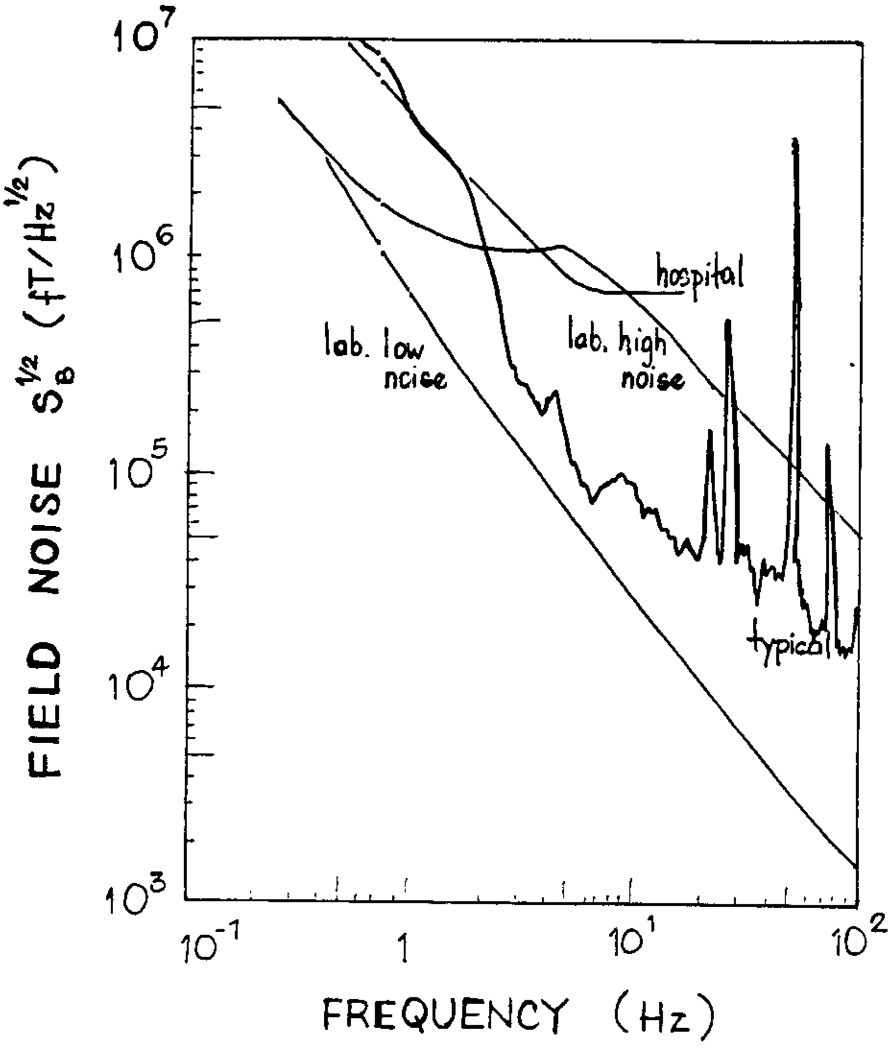

Figure 8: Typical magnetic ambient noise in an urban environment

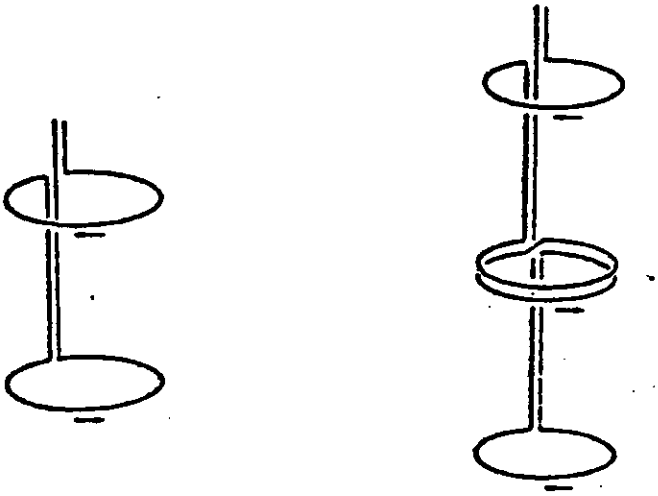

Figure 9: Typical coil configuration of a first order gradiometer and a second order gradiometer used to reject ambient noise

($\approx US\$ 400K$) of these MSR prevented most laboratories from obtaining one. Also, for single channel systems the investment is not justifiable, and an alternative approach, known as spatial discrimination was developed [1]. The basis of this method is that the ambient noise comes from relatively distant sources (fans, elevators, building structures, cars...), whereas the magnetic source of interest (parts of the human body for instance) comes from a near source. Figure 9 depicts a possible configuration of coils used in this approach. The lower coil will detect the signal of interest plus ambient noise and the upper coil will detect only the ambient noise, if they are connected in opposition a real time subtraction will be performed and the signal is retrieved. It should be understood that the signal itself has an intrinsic noise that will be detected if not suppressed by other means.

To understand the advantages and limitations of this approach we model each source as a magnetic dipole. The magnetic field is given by:

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi}[\frac{3(\mathbf{r}.\mathbf{m})r}{r^5} - \frac{\mathbf{m}}{r^3}] \tag{3}$$

The sensors so far discussed detect magnetic fluxes. The flux threaded in a coil is:

$$\phi = \int \mathbf{B}(\mathbf{r}) \cdot d\mathbf{A} \tag{4}$$

where dA is an area element and the integral is over all the coil. Inserting 3 in 4 the flux for the lower coil is given by:

$$\phi_l = \frac{\mu_0 m}{2R}[1 + (\frac{d}{R})^2]^{-3/2} \tag{5}$$

where d is the distance from the magnetic dipole to lower detection coil and R the coil radius.

The flux threaded through the upper coil is:

$$\phi_u = \frac{\mu_0 m}{2R}[1 + (\frac{d+b}{R})^2]^{-3/2} \tag{6}$$

where the base line b is the distance of separation between the two coils. Usually, the lower coil is referred as the signal coil and the upper as the noise rejection coil. The net flux detected is given by:

$$\phi_t = \phi_l - \phi_u \tag{7}$$

By a Taylor expansion, it can be seen from expressions 7, 5 and 6 that for distances $d \gg b$ the net flux goes to zero, and the noise rejection is accomplished. For distances $d \approx b$ the net flux will be proportional to the first derivative of the field. This device is known as an axial first order gradiometer, several other types of gradiometers can be made, axial of higher order that cancel other terms in the Taylor series. Figure 9.B shows a second order gradiometer that will cancel the noise up to first derivative, but will detect the second derivative of the signal. In designing a gradiometer attention must be paid to several factors such as the base line, self induction, symmetry, to catch the best sensitivity from the SQUID detector.

4 Applications

Owing to the high sensitivity of the present detectors, the use magnetic measurements to study biological phenomena is significantly increasing. It is very difficult in a limited space to cover all the interesting applications and some selection imposes. In the following sections some applications will be discussed based on their importance and/or on their feasibility.

4.1 Brain Studies

Neuroscience is one of the most important areas of study of biomagnetism. Spatial localisation of cortical sources is information that can be obtained from magnetic maps of the scalp. In this sense it is possible to produce a physiological imaging of the brain showing areas that are activated or are abnormal. This kind of information is of great importance for the understanding of the brain (Is it possible ? A brain knowing a brain ?) and to detect pathological states in neurology.

Until very recent the electroencephalogram (EEG) was the principal method to study the brain. Today other techniques like Computed Assisted Tomography (CAT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET-Scan) and magnetoencephalogram add to the weaponry to study the brain.

Information is processed in the brain through the conversion of chemical energy into electric current. Axons are connected to other axons by means of synapses and electric current flows inside an axon until it reaches a synapse to send the information on. In the biomagnetism jargon this current is called impressed current, and can be modelled as current dipole (soma) or a quadrupole (axon). There is another current in the conducting medium surrounding the dipole that obeys ohm's law and is called volume current. Viewed from this perspective the brain activity can be modelled by electric currents and the detection of where and how strong are those currents is information relevant to the neuroscientist. A way to locate and determine the intensity of a current is by measuring the magnetic field it produces.

The magnetic field produced by a current can be calculated by one of the following procedures:

$$\vec{B}(\vec{r}_2) = \nabla \times \vec{A}(\vec{r}_2) = \nabla \times [\int \frac{\vec{J}(\vec{r}_1)}{r_{12}} dV_1] \tag{8}$$

$$\vec{B}(\vec{r}_2) = I_1 \oint_1 \frac{\vec{dl}_1 \times (\hat{r}_2 - \hat{r}_1)}{\mid \vec{r}_2 - \vec{r}_1 \mid^2} = \int \frac{\vec{J}(\vec{r}_1) \times \hat{r}_{12}}{r_{12}^2} dV_1 \tag{9}$$

where the substitution $Id\vec{l} = \vec{J}dv$ was made in the latter equation (Biot-Savart law).

The concept of current dipole $\vec{Q}$ comes from the Biot Savart law if we imagine a small region that has a $\vec{J} \neq 0$. In this situation $\vec{r}_{12}$ is approximately constant and we end up with a volume integral of $\vec{J}$ that will have dimensions of current times distance. In a multipole expansion this will be the dipolar term $\vec{Q}$.

The magnetic field intensity of a current dipole at a distance r from $\vec{Q}$ making an angle

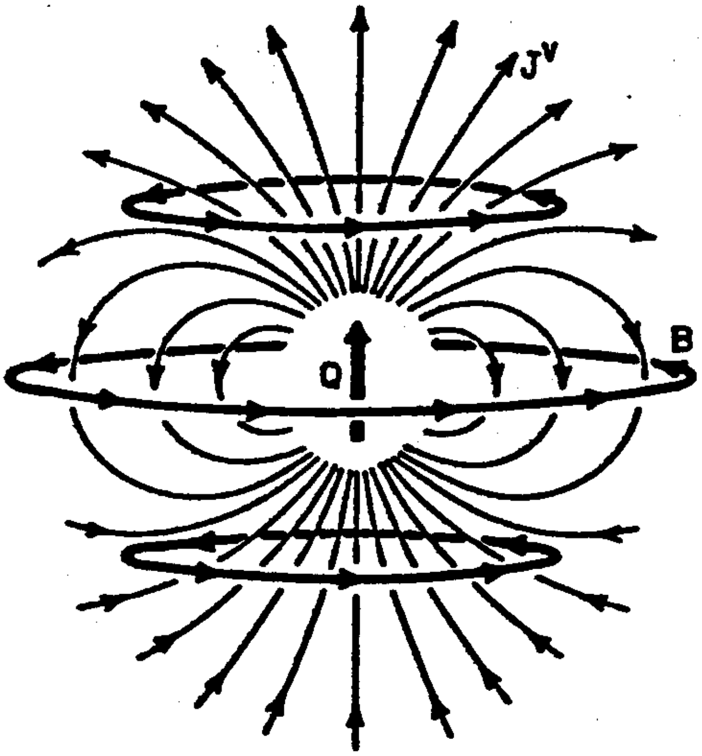

Figure 10: The magnetic field produced by a current dipole $\vec{Q}$ and the volume current associated.

Ψ with $\vec{Q}$ is given in the SI system as:

$$B = \frac{\mu_o Q sen\Psi}{4\pi r^2} \tag{10}$$

From Biot-Savart's law it can be deduced that the field lines of $\vec{B}$ will be circular in a plane perpendicular to $\vec{Q}$, also the distance dependence will be with r^{-3}.

The volume current gives no contribution to the magnetic field if the conductivity of the medium is homogeneous, they are ohmic (passive) currents produced by gradients of the potential Φ associated with the current dipole (active). If $J = \sigma\nabla \cdot \Phi$ is inserted in the expression for the magnetic field 9 the result will be zero.

If the current dipole is immersed in a semi-infinite conductor, oriented in the y direction, the normal component of the magnetic field to the surface can be expressed as:

$$B_z = \frac{\mu_o Q}{4\pi d^2}\frac{x}{(1+x^2+y^2)^{3/2}} \tag{11}$$

If the dipole is at a distance d below the surface of the hemispace and oriented in the y direction, and the x y coordinates are expressed in units of d the equation 11 will give the value of B_z for any point on the surface.

This expression is valid even if different conductivities, piece wise constant, are present between the source and the measuring plane. The flat brain approximation assumed in this expression is enough to treat relatively shallow sources. For deep sources a more realistic model needs to be used.

This non invasive method of source locating has been used with great success in localisation of epileptic sources and for basic studies in neuroscience such as visual evoked fields, tonotopic localisation and pain evoked fields (see the list of references).

4.2 Biosusceptometry

In patients with thalassemia or hemochromatosis an iron liver overload eventually develops that modifies the behavior of the liver tissue in a magnetic field. Normal diamagnetic liver tissue becomes paramagnetic, if the iron concentration is high. Iron is normally stored mainly in the liver, spleen and heart. Kupffer cells and hepatocyte in the liver normally store iron inside hemosiderin molecules as a paramagnetic complex. It is of clinical importance to develop a non invasive method to assess the iron content in the liver. In principle this can be accomplished by measuring the magnetic susceptibility.

The magnetic susceptibility χ of a sample is defined as the ratio of the magnetization produced in the sample M to the external applied field B. If a field is applied to a biological sample and the increase in the field can be measured the magnetisation will be determined and χ can be calculated. Once the susceptibility is determined a model can relate this quantity to the concentration of paramagnetic particles in the sample.

The magnetic susceptibility can be given by:

$$\chi = \mu_o \frac{M(\vec{r})}{B(\vec{r})} \tag{12}$$

where $\vec{M}(\vec{r}) and B(\vec{r})$ are the magnetisation and applied magnetic field.

The magnetisation will be the average density of all magnetic moments present in the sample. In this way it can be related to the individual moments as follows:

$$\vec{M} = N\langle\vec{m}\rangle \tag{13}$$

where N is the concentration and $\langle\vec{m}\rangle$ is the mean value over the microscopic dipoles.

Figure 11 shows a typical experimental arrangement for performing a susceptibility measurement in a subject's liver. The signal given by the SQUID can be calibrated with phantoms containing an iron salt similar to that found in the liver and this calibration factor is used to infer the amount of iron present in a patient.

4.3 Gastric Emptying

Magnetic measurements present an attractive method to study the dynamics of the gastro intestinal tract. Since magnetic tracers that are inert and harmless of different sizes can easily be produced, a variety of studies can be designed to assess the diverse functions of the stomach. Bennair et al. [24] and Di Lusio et al. [21] used different magnetic

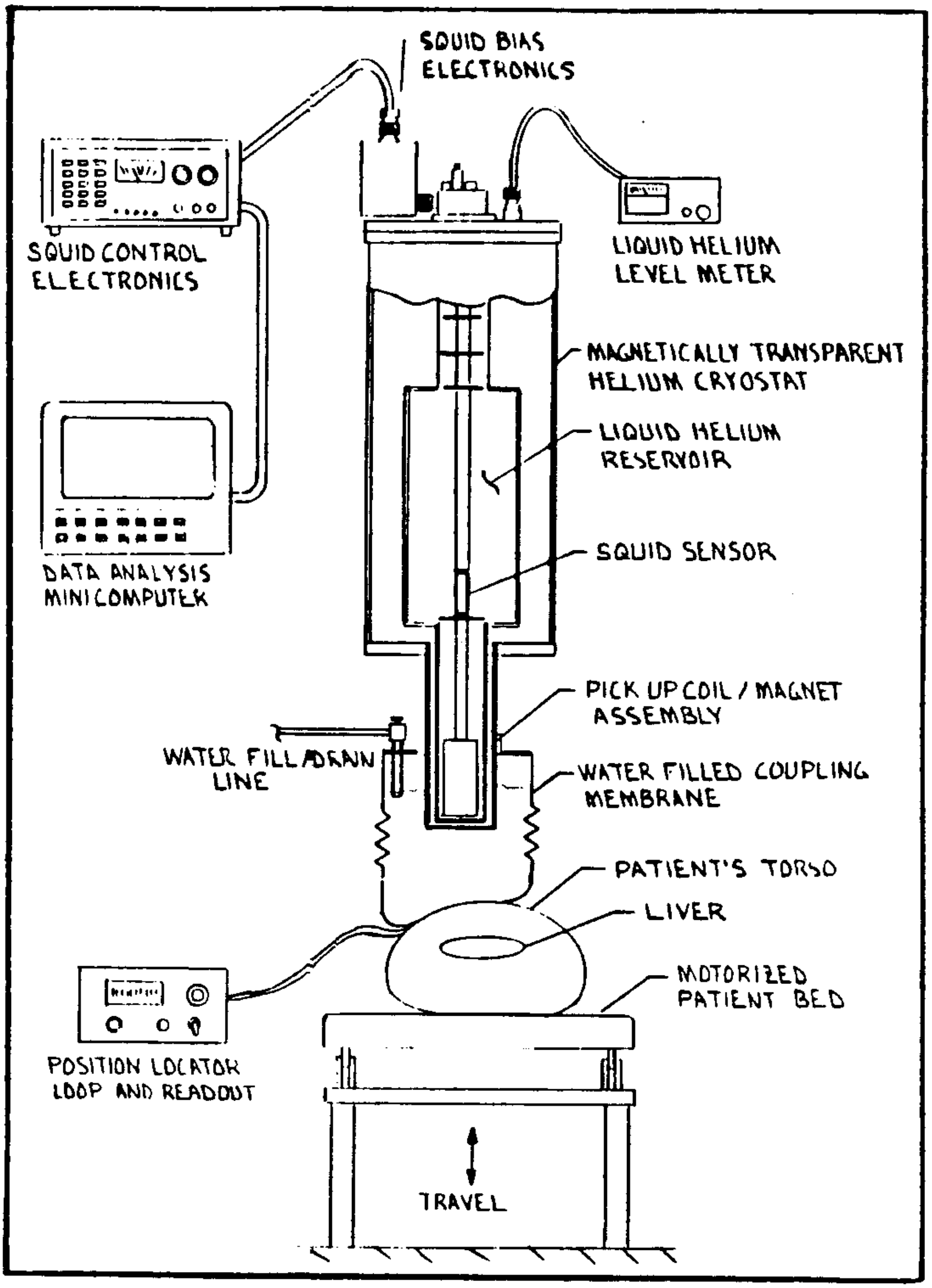

Figure 11: Typical experimental arrangement used to measure the iron concentration in the liver

measurements to study the gastric function. In the former a susceptometer consisting of one energizing and two detection coils were incorporated in a bed to measure a test meal with iron contents of about 20% [24], and in the latter a superconductor magnetometer based on a SQUID was used to follow the motion of a small steel sphere through the gastro intestinal tract [21]. The first method showed some drawbacks such as the necessity for high iron content in the test meal and some non localizability of the measurement. The second, despite being close to the ideal experimental situation in terms of patient disturbance, is expensive and rarely found in a hospital environment.

In this section the construction of an ac biosusceptometer, based on an axial first order gradiometer, to study the stomach emptying is discussed. Owing to its simple construction, high sensitivity and low cost, this instrument can be widely used in medical studies.

Figure 12 depicts the AC susceptometer. An astatic pair of coils, or a first order detecting gradiometer coupled to a pair of exciting coils, is mounted in a PVC plastic tube of 5.0 cm diameter.

The internal coils (2 and 3) wound with 55 turns AWG 30 copper wire, separated by 5.0 cm, are the exciting pair. The external coils (1 and 4) wound with 200 turns of AWG 35 wire, separated by 7.5 cm, are the sensing ones. These sense coils were connected in series with opposite polarity to cancel the detected voltage. However when one end of the susceptometer is approximated of a magnetic material a voltage is detected. This signal can be calibrated to give the mass of the magnetic material. A test meal containing a 10 % by weight manganese ferrite powder is ingested by the subject. Measurements were made over the stomach region at a 10 minute interval to assess the quantity of the test meal present.

Figure 13 shows the results obtained with the susceptometer and with radioactive measurements of the meal simultaneously labeled with the radioisotope technetium.

4.4 Animal Studies

Many studies with animals have been reported. Isolated axons from lobster were used for the detection of the action field associated with the membrane depolarisation wave [13]. Guinea pigs were raised in an ambient with magnetic dust to simulate deleterious conditions found in mines and to study the lung clearance of magnetic particles. Turtle brain has been used for *in vitro* studies of evoked fields and effects of conductivity boundaries [25]. Magnetic dipoles were implanted in rabbits head to further develop techniques of source localisation [12]. Recently the magnetic field associated with a small electric fish (*G. Carapó*) was studied by our group [17]. The magnetic measurements allowed

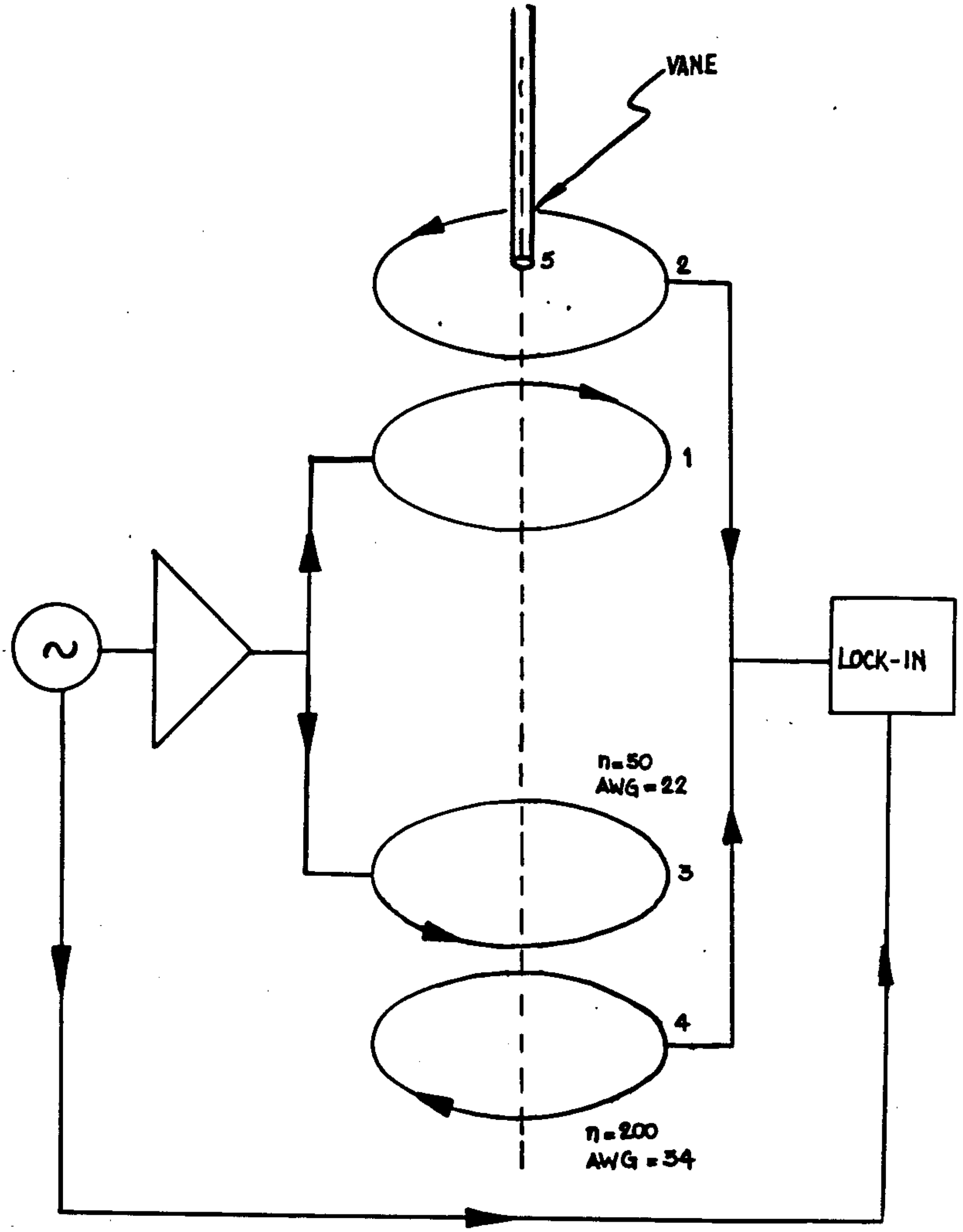

Figure 12: First order gradiometer (coils 1 e 4), exciting system (coils 2 e 3) and vane coil (coil 5). The ancillary instrumentation is also shown.

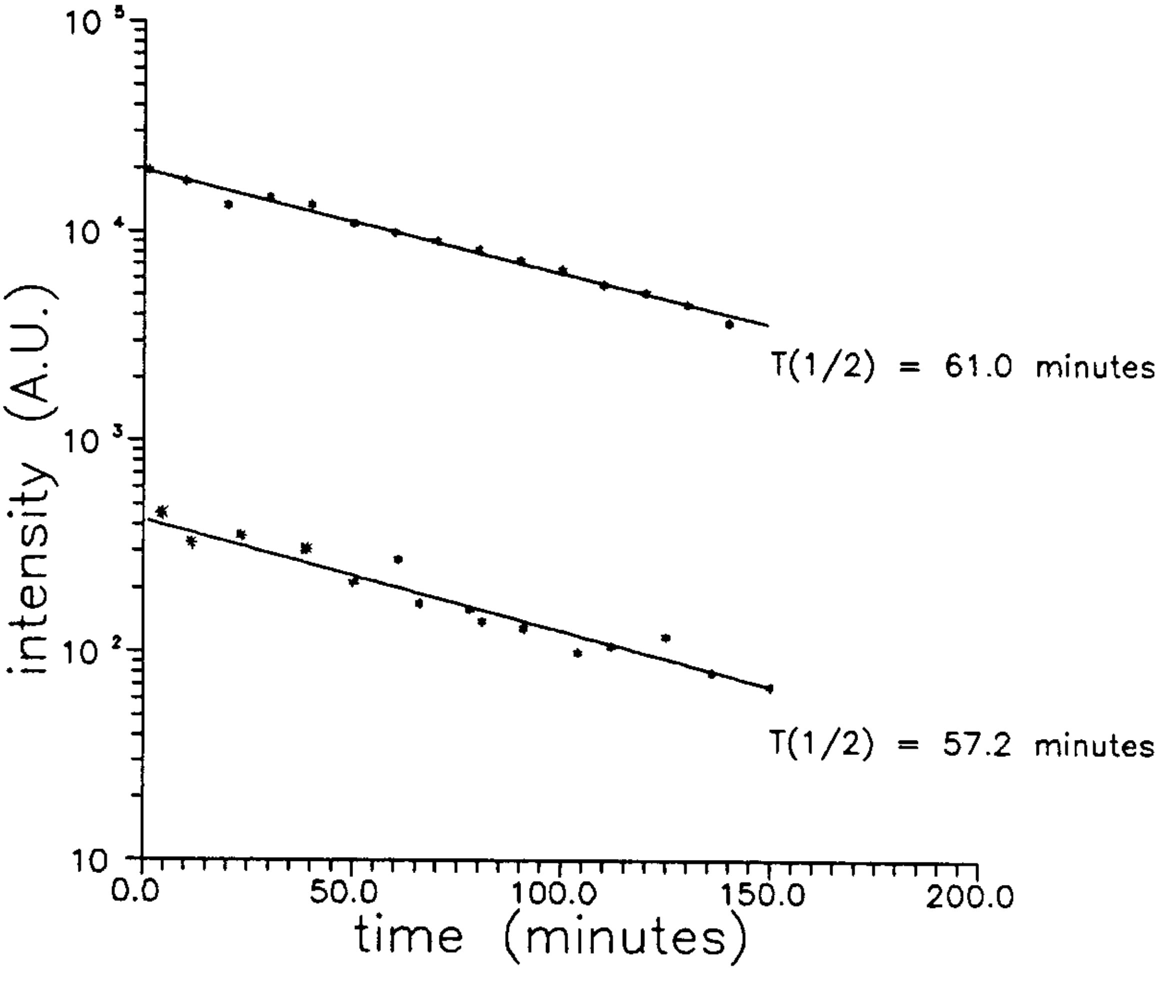

Figure 13: Comparison of the susceptometer signal intensity (curve A) and the signal from the gamma camera (curve B) as a function of time. Note the good agreement of the $T_{1/2}$ obtained from each method.

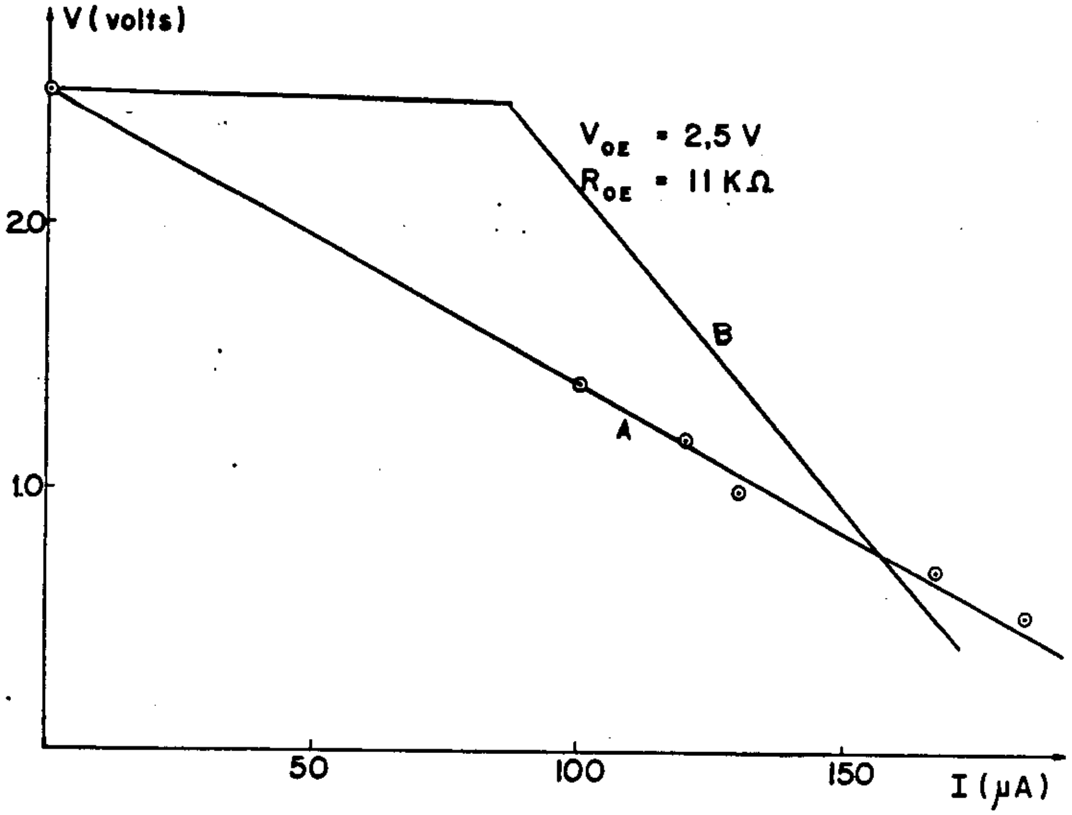

Figure 14: Voltage versus current curve for the electric organ of the fish *G. Carapo*. A depicts measurements in tap water and B in water containing anesthetics

the determination of the electric current and the internal resistance of the electric organ. These measurements are now being used to assay anesthetics. Preliminary results show that it is possible to detect a dose effect by measuring the electric current and potential. Figure 14 shows the characteristic voltage versus current curve for normal conditions and those modified with anesthetic.

5 Acknowledgements

The author is grateful to Prof. Sérgio Mascarenhas for the invitation to participate in this College, to my colleagues of the Physics Department at FFCLRP-USP and to Iraídes for the drawings. The financial support from the Brasilian Agencies: Conselho Nacional de Desenvolvimento Científico e Tecnológico and Fundação de Amparo a Pesquisa do Estado de São Paulo to the Biomagnetism project is also appreciated.

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