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Magnetoencephalography: Detection of the Brain's Electrical Activity with a Superconducting Magnetometer

Abstract. *Measurements of the brain's magnetic field, called magnetoencephalograms (MEG's), have been taken with a superconducting magnetometer in a heavily shielded room. This magnetometer has been adjusted to a much higher sensitivity than was previously attainable, and as a result MEG's can, for the first time, be taken directly, without noise averaging. MEG's are shown, simultaneously with the electroencephalogram (EEG), of the alpha rhythm of a normal subject and of the slow waves from an abnormal subject. The normal MEG shows the alpha rhythm, as does the EEG, when the subject's eyes are closed; however, this MEG also shows that higher detector sensitivity, by a factor of 3, would be necessary in order to clearly show the smaller brain events when the eyes are open. The abnormal MEG, including a measurement of the direct-current component, suggests that the MEG may yield some information which is new and different from that provided by the EEG.*

Masses of excitable tissue, such as the heart and other organs, generate ion currents within the body. These currents, which produce a weak magnetic field around the body, were first detected about a decade ago. The techniques of detection have now been improved, and a new range of high sensitivity has now been reached. I have been using this new sensitivity to look around the human head for magnetic fields which are produced by electrical activity of the brain. Earlier measurement of the brain's magnetic field, because of the equipment used, was far less sensitive than the new arrangement and required cumbersome noise-averaging. I now report the first results of measuring the brain's magnetic field at the new, high sensitivity. My recordings show that the brain's magnetic field can now be detected in a simple and direct way. Also, I suggest that some of this magnetic data may contain information different from that found in the electroencephalogram (EEG). Measurements of the brain's magnetic field are of interest because of the possibility of obtaining such new brain information, unavailable to the EEG.

There are at least three different ways in which measurements of the brain's magnetic field can reveal information which is either unavailable or very difficult to obtain with the EEG. The first way is the measurement of d-c (direct current) generated in the brain. Although the brain's d-c varies with the normal and abnormal states of the brain (*1*), it cannot reliably be measured with the EEG because of the steady polarizing voltages developed by the junction of the electrodes and the scalp; however, measurements of the magnetic field from d-c currents in the brain can be reliable since there is no surface contact. The second way is to show, for some special neural events, that zero current is flowing in the head even though there is a nonzero EEG of these events. There are some generator distributions (*2*) which produce zero current everywhere in the head but nonzero voltages on the scalp; unless electrodes can be placed inside the head, only magnetic measurements can reveal these special distributions because the magnetic field will everywhere be zero. The third way is to show, for some special neural events, that there is a nonzero current in the head even though there is a uniform voltage everywhere on the scalp (*3*). In this case there will be a zero EEG of these events but a nonzero magnetic field.

The first measurement of a magnetic field from living currents was of the magnetic field produced by currents from the human heart (*4*). The heart's field, at maximum, was found to be about 5×10^{-7} gauss. This was one-millionth of the earth's steady magnetic field which is about 0.5 gauss; it was also one-thousandth of the fluctuating background magnetic field in an urban environment, which is about 5×10^{-4} gauss, root mean square (r.m.s.), in a bandwidth of 0 to 40 hz. The problem was therefore how to measure the heart's weak magnetic field in the presence of the large background. This first effort used detectors consisting of two large coils on the chest which were connected in opposition to largely cancel the background fluctuations. Another scheme for detecting the heart's field was a single, compact coil situated in a magnetically shielded room to reduce the background (*5*). This system was used for the other, earlier brain measurement (*6*). The brain's magnetic field amplitude, due to alpha rhythm, was found to be about 1×10^{-9} gauss at a distance of 5 cm from the scalp, or hundreds of times weaker than the heart's field. Elaborate noise-averaging was required to extract the brain signal from the intrinsic noise of the detecting coil, which was some 30 times greater than the small signal from the brain.

Recently, a more heavily shielded room was constructed at the Massachusetts Institute of Technology and a newly developed superconducting quantum interference device (SQUID) magnetometer was installed in the room. First measurements with this system (*7*) showed the heart's magnetic field with more clarity and sensitivity than was previously possible. The intrinsic magnetometer noise, which limited the sensitivity, was 1×10^{-9} gauss (r.m.s., per root cycle) during those first measurements; the frequency response was from d-c up to 500 hz. This ability to measure d-c, not possible with the previous coil detectors, was used in the next experiment with this system, which consisted of searching for d-c currents during heart injury (*8*). Simultaneously with these and other exploratory experiments, an effort was made to reduce the magnetometer noise (*9*). By redesigning several internal components, and by thinning the noise-producing silver

layers of the Dewar system, the noise has now been lowered to somewhat less than 4×10^{-10} gauss (r.m.s., per root cycle) which is the new noise level I have used in the work reported here.

A recording of one component of the magnetic field vector as a function of time, at the head, is called a magnetoencephalogram (MEG). MEG's were taken of four normal and one abnormal subject. The normal subjects were chosen, by examining their EEG's, to have large alpha rhythm and good photic blocking (ratio of eyes closed/open) of the alpha rhythm. This was the rationale in choosing such subjects: since their alpha rhythm currents were relatively large, were of constant frequency at about 10 hz, and could be stopped by opening the eyes, they would produce magnetic fields around the head which would be relatively large and identified through frequency and also sequences of eyes open–eyes closed. Stated otherwise, it would be possible to find and "tune in" on their alpha currents. The abnormal subject was chosen to have large EEG events which were associated with neurological abnormality and which could be made to appear and disappear during the recording of MEG's. In this way it would be possible to see whether the MEG showed abnormalities of brain function, at least in this single case, that were different from any shown by the EEG. Figure 1 shows the experimental arrangement for taking the MEG's. The detector is situated in liquid helium contained by a double Dewar flask, of which the outer jacket contains liquid nitrogen; this is a standard cryogenic technique. The Dewars are large so they need filling only infrequently, perhaps every 3 days.

Figure 2 shows the MEG of one of the four normal subjects and also of the abnormal subject, along with their EEG's. The MEG's shown here, as well as the other MEG's we have recorded, are not due to any artifact; they are due only to the same class of currents in the head as those which produce the EEG. This was confirmed by auxiliary experiments performed to check on any possible artifact. For example, one simple experiment consisted of recording the MEG of the alpha rhythm with and without the EEG electrodes on the scalp; as was expected, the presence of the EEG electrodes made no difference to the MEG.

In both cases (Fig. 2) the magnetometer, although located differently, was oriented to detect the magnetic field component that was normal to the scalp.

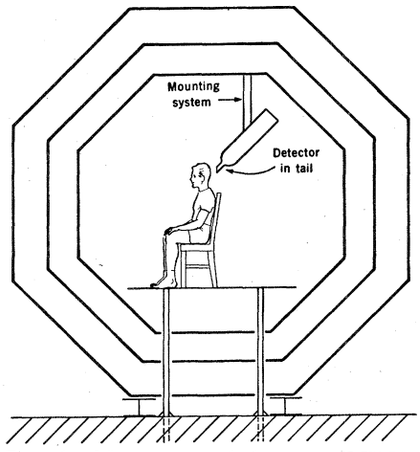

Fig. 1. Magnetoencephalogram (MEG) being taken in the shielded room. For the data presented here the subject's head almost touched the flat end of the Dewar tail and was about 2 cm from the enclosed detector. The detector output, which is proportional to the horizontal component of the magnetic field, goes to an external display station. The subject's clothing must be free of magnetic material, such as zipper fasteners or the nails of shoes.

The magnetometer location in Fig. 2A was chosen because it was found, for all four subjects, that the alpha MEG's were largest at the left and right occipital regions of the scalp; in Fig. 2A this is as high as 2.5×10^{-8} gauss, peak to peak. With the head away from the detector, the recording of Fig. 2A shows only the intrinsic detector noise; since the subsequent positions with eyes open are only a bit larger than this noise, a further reduction in detector noise would be necessary if the MEG is to reveal the smaller brain events when the eyes are open. A threefold reduction would yield MEG's as clear as the conventional EEG.

The subject of Fig. 2B has psychomotor epilepsy and was being medicated with diphenylhydantoin and primidone. During voluntary hyperventilation the subject generally shows unusually large, slow (delta) waves at a frequency of 1 or 2 hz, without any seizure manifestations. EEG's from three different regions of the scalp are displayed with the MEG so that any differences between the MEG and EEG are seen more effectively; if there were differences between the MEG and the EEG from three widely different scalp regions, then there is a high probability that the MEG would be different from the EEG taken at any point on the scalp. The recording of Fig. 2B was taken some seconds after the start of hyperventilation and shows the beginning point of the large, delta waves. Also, on the three EEG's, theta waves at a frequency of about 5 hz are seen mixed with the delta waves. These

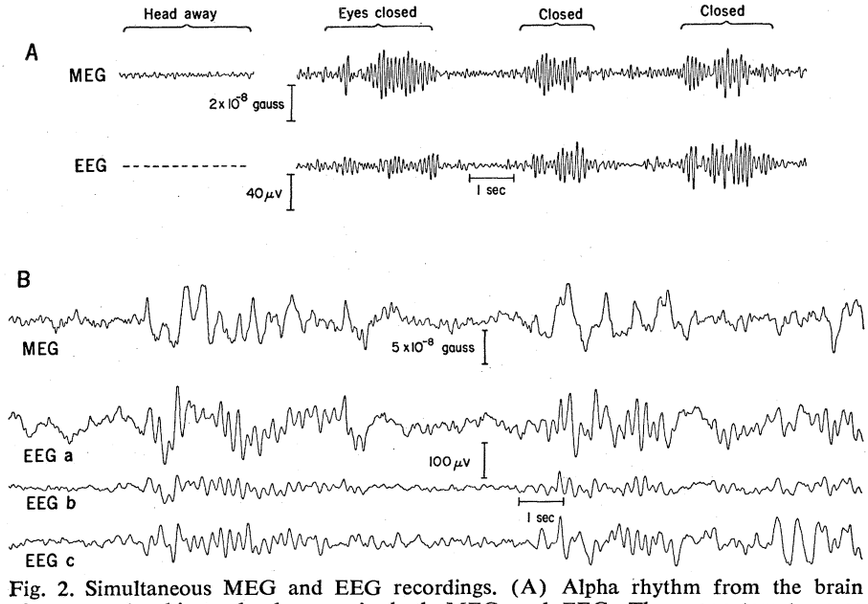

Fig. 2. Simultaneous MEG and EEG recordings. (A) Alpha rhythm from the brain of a normal subject, clearly seen in both MEG and EEG. The magnetometer was located at the left occipital region, as were the bipolar set of EEG leads. The bandwidth on both channels was 4 to 15 hz. (B) Large events, induced by hyperventilating, from the brain of an epileptic subject. The magnetometer was at the right temple. The three EEG bipolar leads all have the vertex in common, and the other lead at these locations about 3 cm above the ear line: (a) at the right temple, (b) above the right ear, and (c) above the inion. The bandwidth was matched on all four channels to be 0.4 to 15 hz. One difference between the MEG and EEG is that the 5-hz waves, present in all three EEG's, is largely missing from the MEG.

theta waves are largely absent from the MEG of Fig. 2B; they were also absent from MEG's (not shown here) taken at several other points around the head during the same sitting. At this time, without extensive EEG and MEG data taken from this subject, one can only speculate on the reason for this absence. Perhaps these theta waves are an example of the case, mentioned earlier, where there is an EEG voltage but no currents. On the other hand, there may be nonzero theta currents, but they would be symmetrically distributed to give a canceled, zero external magnetic field. Such symmetrical currents can be produced, for example, by one or more dipole generators near the surface, each oriented with its axis perpendicular to the surface; in general, magnetic detection of the zero magnetic field from symmetrical currents does not yield new internal information since the symmetry can be found from exact EEG measurements. Whatever the reason for the absence of the theta waves from the MEG, Fig. 2B suggests that the MEG can be substantially different from the EEG.

During the sitting in which Fig. 2B was recorded, a preliminary search was made for d-c in the brain before and during hyperventilation. There is some basis (*1*) for believing that d-c changes may accompany the delta waves, at about the same level, yielding an external d-c field of about 5×10^{-8} gauss. The technique for the d-c search (*8*) consisted of looking for baseline shifts of the MEG while moving the subject's head up to and away from the detector; the lower bandwidth limit of the MEG had been set at d-c. No d-c magnetic field was detected to within the sensitivity of this measurement, which was somewhat less than 2×10^{-8} gauss. It is too early to interpret the apparent absence of d-c fields in this case.

I believe the high-sensitivity detection system used here shows promise both as a clinical and as a research tool for studying the brain.

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2. A simple, idealized example is a spherical shell consisting of two conducting hemispherical shells separated by a thin, circular band of insulator. A battery is placed inside with each terminal connected to a hemisphere, along with a resistor and switch across the terminals so that a current flows through the resistor when the switch is closed. A voltage measurement on the surface will give the voltage difference of the hemispheres without giving information on the current flow through the resistor; magnetic measurement will, however, show whether the switch is open or closed.
3. A simple, idealized example is a conducting sphere, say of salt water, with an internal ring concentric with the sphere consisting of a continuous distribution of generators closed on themselves so that a current flows in the ring. There will be no potential difference between any points on the surface but there will be an external magnetic field as a result of the ring current.
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9. The SQUID section of the magnetometer is based on the Josephson effect; the point-contact type of SQUID used in these experiments is described by J. E. Zimmerman, P. Thiene, J. T. Harding [*J. Appl. Phys.* **41**, 1572 (1970)]. It is believed by Zimmerman that the noise of this magnetometer can be reduced well below 1×10^{-10} gauss (r.m.s., per root cycle) before any hard, natural low-noise limit might be reached.
10. The Francis Bitter National Magnet Laboratory is supported by the NSF. D.C. is an established investigator of the American Heart Association. This research was supported by grants from American Cancer Society (10 152), the Massachusetts branch of the American Cancer Society (1355-C-1), the American Heart Association (69 555) and the Damon Runyon Memorial Fund for Cancer Research (DRG-106T). This research cuts across several disciplines and is a result of the effort and encouragement of many people. The author thanks these many people, including Mr. Ed Edelsack, Mr. Sandy Goldstein, Prof. John Hughes, Mr. Larry Rubin, Dr. Edward Wolpow, Prof. Lester Winsberg, Dr. Robert Young, Mr. Leonard Zablow, and Dr. James Zimmerman. Special thanks are due to Mr. Edward Givler for his patient engineering in reducing the detector noise.

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Behavior of B-Chromosomes in Xanthisma texanum DC.: A Nonrandom Phenomenon

Xanthisma texanum DC. (Compositae) is a diploid plant in which $n = 4_{II}$ with zero to four small supernumerary chromosomes (B-type). As in *Claytonia virginica* (Portulacaceae), the number varies within the individual but that variation is not random (*1*). Recent discussion of the phenomenon in *Claytonia*, a tetraploid, centered on genetic control of supernumerary chromosome distribution within individuals (*2*). Parnell argued that Lewis had not fully considered polyploidy as an explanation for the multiple genome phenomenon.

True roots lose B-chromosomes in embryogenesis, although rarely they may persist in low numbers in seedlings (*3*). Such behavior has been observed consistently in more than 75 plants. On the other hand, adventitious roots from cuttings may retain B-chromosomes in low numbers, even after 5 months of growth. In one plant $2n = 9$ was the most common number found in emergent adventitious roots and in some adventitious roots of the same plant after the roots had grown several decimeters. Clearly there is some controlled difference with respect to genome of true root tissue and stem tissue which has differentiated into root tissue.

Behavior of B-chromosomes in meiosis is consistent with time. Thirty-six buds taken from one plant over the space of 8 months were examined. Among 1,073 pollen mother cells, 1,019 had 5_{II}, eight had four $A_{II} + 2$ B_I, 15 had nondisjunction of the B_{II} at A1 or of the B chromatids at A2, three had 4_{II}, five had $4_{II} + 1B_I$, two had 6_{II} and the remaining were A-chromosome abnormalities. There were many micronuclei in adjacent tapetal tissue, which indicated loss of B-chromosomes. There was no correlation between time of flowering and percentage of abnormal behavior of B-chromosomes.

In a single floret of another plant 322 pollen mother cells had 5_{II}, two had precociously dividing B-chromosomes and two ontogenetically related cells had 4_{II} and 6_{II} each.

Because behavior of B-chromosomes is so consistent within single thecae and often among whole anthers and florets and even buds from the same plant, control of B-chromosomes in a diploid, such as *Xanthisma* with multiple genomes, is clearly indicated.

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