Part III

RESULTS OF BIOMAGNETIC RESEARCH

Although many reviewers of the modern biomagnetism usually classify information by the organs producing various MF, we believe that the information should be also classified by the MF generation mechanism. Having adopted this approach one arrives at the conclusion that the substantial part of the biomagnetic data is related to MF elicited by the alternating currents from the biological objects both spontaneous and evoked by various stimuli. Today, a branch of the biomagnetism is born which is supposed to study MF related to the direct or slowly alternating biomagnetic currents. There are also studied MF of the natural and artificial inclusions in the biosystem. This area of research is closely connected with studies of magnetic properties of the tissue.

Chapter 3

MAGNETIC FIELDS EVOKED BY ALTERNATING CURRENTS

The basic idea of this chapter is to present the main data on the modern biomagnetism. Though it is customary to begin with MCG we believe that description of MF of electrical fishes would be more appropriate for the start because MF evoked in the course of discharge of their electric organ appear to have the highest magnitude. The other important reason is that biological function of electromagnetic field has been proved experimentally only in case of MF of electrical fishes [43, 44].

The next in terms of the biomagnetic signal magnitude is the MF of the nerve elicited by its stimulation. According to our information this branch of modern biomagnetism emerged in the 1930's [27, 29].

The next area according to our classification — cardiomagnetism — has become a good theme for advertisement of the advantages of the noninvasive research of certain functions in man and animals. Surprisingly, the leading part in this area is played not by cardiologists but by representatives of other disciplines for whom introduction of the new method into a cardiologic clinic is a rather challenging task.

Magnetomyography, magnetooculography and magnetoretinography, outlined only in individual publications, merely indicate a possibility of detecting MF evoked in the course of functioning of striated muscles, eye ball or retina.

Finally, MEG dealing with MF evoked in the brain, as a rule in human brain, is the highest point of modern biomagnetism. This area of research is the theme of many publications and the field where the most sizable progress has been made.

The common objective of the many outlined branches of biomagnetism lies in the sphere of diagnosis and pursues estimation of the detectable MF intensity and localization of its sources. These studies are particularly important in dealing with pathological foci in the heart and brain.

This objective also prominently figures in the studies of MF evoked in the human brain especially by varying parameters of stimuli.

3.1. MAGNETIC FIELDS OF ELECTRIC ORGANS OF FISHES

Apart from the above mentioned research by D. Dawy we know of only one other publication by V. Protasov *et al* [43] dealing with detection of MF evoked by electric cattish discharge with IM.

It has been shown that the electric discharge from the fish in various behavioral situations evoked a detectable MF penetrating water, aquarium walls and the copper of IM receiving the MF with resolution of the order

of 10^{-12} T in the sound frequency range.

Since the above mentioned publication failed to specify the parameters of MF of the fish we reproduced the same experiments together with V. Protasov and A. Sukhanov.

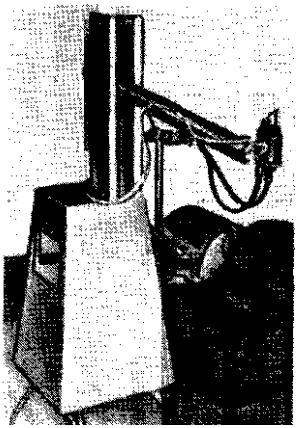

Fig 12. gradiometer with two OPM sensors

Electric cattish (*Malapterurus electricus*) was placed in a glass aquarium. Electrodes were positioned in the water on the remote opposite walls.

MF of the fish evoked by mechanical stimulation (a glass stick) was detected with a gradiometer using two OPM (Fig. 12) placed on the aquarium level at different distances from it. The electric and magnetic signals were recorded simultaneously with a magnetograph.

Interestly, we could detect MF of the fish only at a certain position of the object vs the OPM. Mechanical stimulation of the fish keeping its head to the sensor evoked a detectable MF (Fig. 13, *b*). If the fish turned its side to the sensor no MF was detected at the same distance from the aquarium (Fig. 13, *a, c*) although an electric signal of identical amplitude arouse during each mechanical stimulation.

The amplitude of the detectable magnetic signal from the fish was related to the distance between the sensor and aquarium with the catfish. Fig. 14 shows that the strongest signal (over 100 pT) is evoked at the I cm distance between the sensor and the front wall of the glass aquarium.

As the distance was increased to 22 and 49 cm the magnetic signal gradually attenuated. MF evoked by mechanical stimulation of the fish became undetectable at the distance of 90 cm. So, it may be seen that the magnetic component of electric signal from the fish can be detected with various magnetometers noninvasively in the air medium. We feel that the

magnetometric method may be employed in studies of the electromagnetic field of the fish also in its natural habitat with the view to explore biological functions of various EMF parameters.

The reported [66] MF evoked in the nonelectrical fishes (pike) by pain stimulus and its motion under a fluxgate sensor may be classified into MF evoked by direct currents. A very strong signal of 6 nT appears to be close to the threshold perception of artificial MF by certain biosystems [59]. Such a serious data of principal importance undoubtedly call for multiple comprehensive verification notwithstanding the fact that the function of the biological EMF in some fish species appears to be fully proved [40].

It should be also mentioned that the estimates presented in publication [67] speak of the MF of the order of 20 pT evoked by electric discharge in the 20 cm long electrical fish

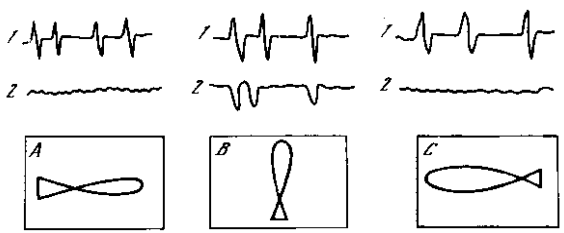

Fig. 13. Mechanically evoked electric (7) and magnetic (2) signal from the electrical catfish vs its position towards the magnetometer A, B, C— various positions of the fish

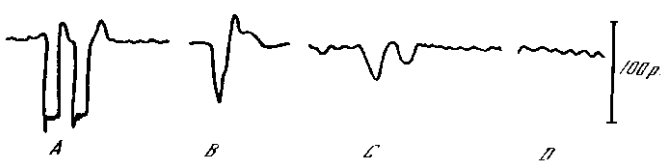

Fig. 14. Amplitude of magnetic signal evoked in the electrical cat-fish by mechanical stimulation vs the distance between magnetometer and aquarium A - I cm; B - 22 cm; C - 49 cm; D - 90 cm

of 314 cm^2 area, at the 10 cm distance. These estimates were found to be close to the results obtained by us.

Obviously enough, studies of the magnetic component of electric discharge of some fishes may help to resolve important problems of the electromagnetic ecology and some questions of modern magnetism. The studies of MF evoked by alternating currents are closely related to magnetobiology.

3.2. MAGNETIC FIELDS EVOKED BY NERVE IMPULSE

It was already mentioned in the monograph that the idea of detecting MF of the nerve impulse was proposed in the course of morphologic studies [27, 29, 54] in the 1930's.

Three independent research groups, one in the USSR and two in the USA, detected, with the help of IM, MF evoked by electric stimulation from an isolated frog's nerve. However, change of the direction of the electrical impulse propagation along the nerve did not cause the signal polarity to change as well. It was, therefore, implied that this was the effect of rather the transverse than longitudinal currents. It was also suspected that the detected signal was the result of the nerve's capacitive coupling with IM.

The suspicion also fueled an extreme view of the absence of MF of an individual nerve fiber or a whole nerve because M. Khvedelidze *et al*. [58] was unable to experimentally detect MF of the nerve, muscle and the heart of the frog. Having analyzed the nerve's bioelectric activity the authors arrived at the conclusion that the absolute value of the nerve's total magnetic flux approaches zero. Proceeding from that it was believed more reasonable to study radiation from biological object in the ultraviolet, visible and infrared ranges of electromagnetic oscillations.

Nevertheless, relying on the modern technique of MF detection described in the corresponding part of this book D. Wikswo *et al*. [145] managed to perform as it is mentioned in the title of their publications the "first" measurement of MF of a nerve impulse meeting the polarity requirement. The measurements were taken from the isolated sciatic

nerve of the frog by applying electric stimulation to its distal or proximal end vs a relatively small toroid fixed on the nerve. Averaging of about 1000 responses in the range below I kHz produced signal-to-noise ratio up to 30-40. The main peak of magnetic signal reached 125 pT. Polarity changed depending on

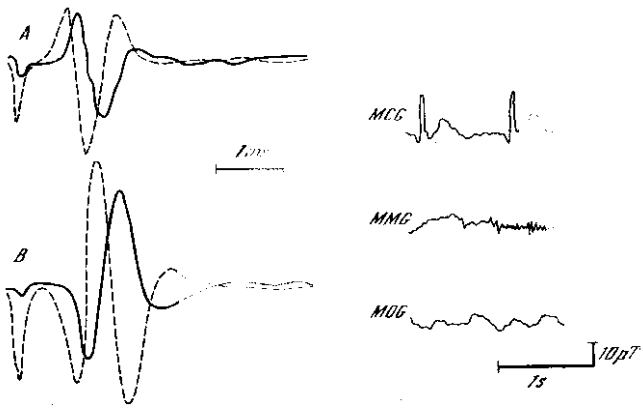

Fig. 15. Simultaneous registration of MF (solid lines) and electric potential (broken lines) elicited by proximal (a) and distal (b) electric stimulation of the isolated nerve of the frog (Wikswo et al., 1980)

Fig. 16. Recordings of magnetocardiogram (MCG), magnetomyogram (MMG) and magnetooculogram (MOG) of man with optical pumping magnetometer

application of electric stimulation either to the distal or proximal end of the nerve (Fig. 15).

Therefore, existence of MF evoked around the nerve by stimulation may be regarded as a proven fact although this problem is explored only by one research group. In 1984 it submitted its report on MF of the regenerating nerve- of monkeys to the Fifth World Conference on Biomagnetism [109]. This technique of noninvasive assessment of the reparation process in the nerve can be used in a clinic.

Apart from its practical dimension this branch of neuromagnetism is related also to theoretical problems of biomagnetism.

Since an isolated nerve of the frog has about 2000 fibers it would be interesting to explore MF of an isolated axon.

In 1982 D. Wikswo *et al*. reported at the Fourth International Workshop on Biomagnetism detection of MF from the medial axon of a 2 kg lobster. Averaging of 100 responses in the 0.1 Hz-5 kHz band produced the signal-to-noise ratio equal to 15 [110].

Another report was presented there by the same team on detection of MF of Purkinje fibers of dog's heart with signal-to-noise ratio equal to 10.

Clearly, the magnetometry techniques may be used to study excitation in isolated nerve and muscle structures, although studies of muscles and heart in complete organism are more valuable to the practical clinical work.

3.3. MAGNETIC FIELDS OF SKELETAL MUSCLES

The first report on detection of MF evoked by contraction of skeletal muscle in man with SQUID was published in 1972 by D. Cohen and E. Givler. Placing the pick-up coil on the forearm they detected MF with amplitude up to 20 pT and frequency peak of 40 Hz. The frequency peak of MMG taken from above the human wrist was 80 Hz [97].

M. Reite *et al*. detected alternating oscillations in MMG of the 2 pT magnitude. Relaxation of muscles caused these oscillations to disappear [134].

In our studies [30] we recorded MMG of the human shoulder muscle contraction with OPM placed I cm above the surface of the arm.

It may be seen from Fig. 16 that the human shoulder muscle contraction evokes an alternating MF with frequency around 30 Hz and amplitude over 10 pT. Apart from fast oscillations of MF we and other researchers observed slow deviations which may be attributed to MF evoked by direct currents.

Despite the relative simplicity of MMG recording and good perspectives of the noninvasive study of muscles no progress has been made in this area. We did not find a single publication on MMG of animals.

3.4. MAGNETIC FIELDS OF EYE

This area encompasses recordings of magnetooculogram (MOG) and magnetoretinogram (MRG) which were first made with SQUID by Finnish researchers, MOG by Karp *et al* [121] and MRG by Aittoniemi *et al* [78]. It can be supposed that only Finnish researchers concentrated on studies of MF of the eye not to mention the case of MOG recording with OPM by us (Fig. 16).

Moving his eyes the object evoked a magnetic signal of the order of 10 pT. The possible source of the signal is a dipole formed between retina and cornea with the magnitude of 100 mV. Therefore, it may be assumed that eye movements elicit artefacts in the process of detecting MEG of the forebrain. MOG shows a slow signal of the order of 5 pT while the eye adapts to darkness. A short flash on retina produced an MRG quite similar to an electroretinogram (ERG). The MRG arises simultaneously with the alpha-wave of the ERG 30 ms after the stimulus application and has the amplitude of 100 fT. This is one of the weakest signals detected by modern biomagnetism. Therefore, it is still a long way before the clinical use of MRG becomes real. This phenomenon has not yet been detected in animals.

The strongest magnetic signal from man is evoked in the heart. This subject will be discussed below.

3.5. MAGNETIC FIELDS OF HEART

Apart from the first experimental MCG recordings with induction sensors performed in the 1960's by Voronezh (USSR) medical experts MF of the heart has been studied since 1976 at the Institute of Higher Nervous Activity and Neurophysiology together with the Institute of Terrestrial Magnetism, Ionosphere and Radiowave Propagation of the USSR Academy of Sciences and Institute of Defectology of Academy of Pedagogical Sciences.

Publications on MCG in the recent years emphasize the clinical analysis of MCG which speaks of the trend to depart from the purely experimental work towards introduction of MCG into the clinical practice

as an independent cardiac research method. Its wide clinical use is delayed by the absense of the correct electromagnetic model of the heart. Therefore, the clinical use of electro- and magnetocardiography is primarily empirical and relies mostly on correlation of morphological curves with the clinical and pathoanatomical data. Several teams studied a normal MCG in correlation with an ECG recorded with the Frank system of the regular 12-lead system.

As the cardiac muscle fibers are depolarized simultaneously the heart generates the strongest fluctuating field reaching a little less than 10^{-10}T in a healthy object. Some hearts with deviations from the norm can generate fields of even higher magnitude.

Results of the first experiments with MCG recording were published by Baule and McFee [83]. They registered a fluctuating MF above the chest and simultaneously recorded the potentials with an electrocardiograph. The maximal reading of the field in the *QRS* complex was approximately $5\text{-}10^{-12}$ T. Noise in the input signal to amplifier and imperfect background noise filtering prevented complete realization of the magnetocardiography's potential.

R. Stratbucker *et al* [142] used a toroid pick-up coil of 17,640 turns around an isolated heart of the guinea pig to detect MF. Recording of ECG in three channels and MCG was performed simultaneously. The experiments have detected MF of the heart and its relation to the electric function of the myocardium. There has been no subsequent verification of these experiments.

Experimental registration of MCG of the man in a shielded room was performed in the USSR by Yu. Safonov *et al* [46] and other authors. The object and pick-up coil were placed inside a shielded room with steel walls of 1.5 cm thickness which attenuated the background MF tenfold.

Since 1984 they have been using a SQUID-based biomagnetic system in the Institute of Higher Nervous Activity and Neurophysiology of the USSR Academy of Sciences to detect MF of the human heart and brain. The system consists of the cryogenic unit, two electronic units, a fiberglass cryostat and a platform manufactured exclusively from nonmagnetic

materials, capable of transporting the cryostat in three planes over the object (Fig. 17).

After signal filtration in the tracking comb filter and their narrow-band RC filter in the coupling amplifier channel it is recorded with TEAC magnitograph. The amplitude-frequency characteristic of the whole channel is practically linear in the 0.5 to 50 Hz range. The total noise of the system is 40 $fT/Hz^{1/2}$ allowing to operate with a signal less than 10^{-13} T.

The sensing element in the system is fitted with a second-derivative gradiometer balanced to the 10^{-5} level i.e. practically it is not sensitive to a homogeneous field induced by a remote source allowing operation in an unshielded room.

The sensor was placed several centimeters clear of the body surface for MCG recording and several millimeters clear for MEG recording. Special matrix were for the MCG and MEG field mapping.

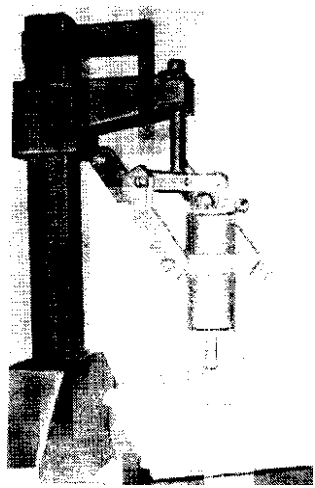

Fig 17. SQUID-based biomagnetic system. General view

Magnetometer calibration was performed with an artifical MF. Magnetic noise was assessed prior to each experiment. After the recording the signal was output to the plotter for visual study or processed in the Labtam minicomputer.

It was earlier mentioned that the 36-lead system was adopted by the first workshop on biomagnetism to standartize the MCG research. The system v- essentially a grid of six equidistant vertical and horizontal lines. The right and left margins of the chest are limited by direct Vines connecting the mid-points of clavicles and costal arches I he top margin is limited by the line connecting mid-points of claveles. The bottom margin is limited by the

line connecting the mid-points of costal arches and leaving the xiphoid process between quadrants D3 and D4 (Fig. 18).

Using the described system most researchers measure the MF component perpendicular to the torso.

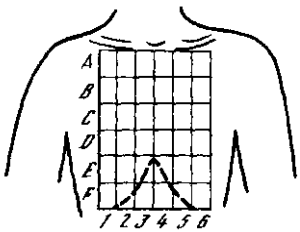

Fig 18. Human chest MCG recording grid

Being universal this system of precardial mapping fully meets the requirement of maximal simulation of the clinical diagnosis because it can register the bulk of the important cardiological indicators such as rhythm, position of the heart, variants of the norm, functional state of the conductive system and the contractile myocardium pathologies.

Practically all publications on magnetocardiography dealing with wave amplitudes of MCG of the normal adult subject point out to substantial fluctuations of cardiac MF intensity. Extreme wave amplitudes of MCG in pT are as follows:

P: from -4 to +7, *Q*: from -7 to +98, *R*: from -300 to +110 *S*: from 0 to +50, *T*: from -32 to +28, *U*: from 0 to +15. "-" stands for a negative, and "+" for a positive wave.

It may be seen that wave amplitude variability is higher in MCG than in ECG in a healthy adult subject. At the same time frequency ranges in the MCG and ECG detection are similar. In our work on identification of the magnetocardiographic norm we did not detect any variation in the MCG information value in the 0.1-40 Hz range. For other tasks such as detection of the *S-T* segment shift in the MCG the advantage of magnetocardiography is evident because magnetometer can detect signals in the 0 to I kHz range.

One of the publications correlates spectra of MCG and ECG of man [79]. The authors detected signals in the MCG spectrum below 4 Hz which could not be seen in the ECG spectrum. Dosed physical load caused the spectra to expand both in the MCG and the ECG up to 25 Hz.

A current dipole located in a volumetric conductor provides a simple description of sources generating the field pictures.

According to this model of a source the isomagnetic field lines corresponding to its zero level must be perpendicular to the current lines on the isopotential map.

Each map is related to a certain point of time in the cardiac cycle. Simplicity of details on maps facilitates correlation of experimental and simulated electric potentials and intensity of magnetic fields. It has been noted that maps using data obtained from the back have features more resembling dipole maps than those obtained from the breast bone side [85]. This may be well attributed to the fact that the back is more remote from sources of MF of the heart than the thoracic wall.

Another alternative method of representing electromagnetic function of the heart was developed by a team of Brazilian researchers [143]. It involves plotting in the x and y axes amplitudes of the magnetic and electric signals to reflect the amplitude and phase correlation of the both processes in a complete cycle. The output may be called electromagnetocardiogram (EMCG). It can be registered with a regular magnetometer, electrocardio-graph and storage oscillograph. Since ECG and MCG are highly sensitive to radial and tangential currents of the heart, correspondingly, their simultaneous recording will contain the most comprehensive information on the heart function.

It was indicated that according to magnetocardiographic maps some objects demonstrated coincidence of *R* and *T* wave inversion lines, while in other objects they formed an angle [85].

Making a preliminary comparison of MCG and ECG (Frank lead system) it should be noted that [116] three-phase complex in MCG is met more often than in ECG; *P* wave reaches its maximal magnitude near atria and its amplitude falls quickly as the sensor is moved in any direction; MCG contains more *S*-*T* shifts than ECG; *T* waves show the tendency to reverse polarity vs the *QRS* complex more often in MCG than in ECG and there often occur two-phase *T* waves.

High resolution cardiomagnetism is essentially a complex of techniques allowing researchers to concentrate on the study of:

1. Functioning of the cardiac conductive system (His— Purkinje fibers system).

2. Pathological delay of ventricular depolarization (late potentials).

Farrell *et al*. [143] detected variations of MF of the heart with SQUID related to the His' bundle activation and fading out at the onset of ventricular depolarization. In order to take advantage of the low instrumental noise the object in nonmagnetic clothes lied on a wooden coach and received no food or drink for two hours because stomach activity causes a noticeable increase of the general noise. The wooden coach could be carefully moved along wooden rails fixed to the floor. Design of the SQUID mount allowed to move the pick-up coil to the chest at ±l cm precision. The target of measurement was the vertical component of MF in points of a horizontal plane. Measurements were taken in 49 points i.e. in every cell of the grid centered around the xiphisternum.

The obtained results were plotted on detailed maps and analyzed. The authors indicated that although technically complex magnetic detection used in the studies of the cardiac conductive system has the following two advantages: 1) ability to make recording in the frequency range expandable to direct current, 2) higher degree of localization of sources for the mapping in the study of the cardiac conductive system.

Noninvasive clinical detection of cardiac late potentials is particularly desirable for it may be used as a valuable indicator of the risk of sudden death. Patients suffering from ventricular arrhythmia or myocardial ischemia showed delayed ventricle activation as it was detected in recordings from lead to epicardium or with the help of a catheter. This specific disturbance of the activation may be a cause of dangerous ventricular tachoarrhythmia.

Erne *et al* [85] used high resolution magnetocardiography to perform the first detection and analysis of *S-T* segment of patients in a shielded room. Electric and magnetic signals were recorded simultaneously.

The above technique exemplifies an improvement alternative of the MCG method although some problems may be encountered depending on specific features of the source of magnetic cardiac signal. The list of these problems involves pathological changes in the heart of an adult object, detection of magnetic signal of the fetus or newborn babies and studies of MCG of animals. The latter area of research may provide theoretical grounds

for study of MCG of man and serve practical purposes of veterinary science.

MCG of the human fetus was first recorded [120] in 1974. The SQUID gradiometer pick-up coil was positioned over the heart of the fetus without any contact with the mother. Magnetic signal was picked up in a low magnetic noise environment without shielding.

MCG of the fetus is an important additional evidence of the state of fetus development in mother's body and a means of monitoring its functional state. The matter is that the electric signal elicited by mother's heart strongly interferes with the fetal electric cardiac signal and sometimes makes identification of the latter impossible. At the same time rapid attenuation of magnetic signal with the distance to the pick-up coil assures detection of only the strongest nearby source i.e. the fetus heart in our case.

It was also noted that [118] magnetic signal of the fetus is detectable in the period between the 26th and 30th weeks when the electric signal from the heart of the fetus sharply attenuates for unknown reasons and the amplitude of magnetic signal remains steady.

Magnetic signal of six-day-old newborn boys was recorded in the University of Helsinki [120]. A SQUID gradiometer was used in an unshielded room to detect MF component perpendicular to chest. The morphological differences in MCGs of the newborn and adults were found to be quite substantial. Incidentally, the difference in amplitude between MCGs of the newborn and adults was much stronger than between the neonatal and adult ECGs.

The Finnish researchers also studied MCG variability in healthy objects and established criteria of the normal state. They pinpointed several anterior chest leads assuring highest data content of the magnetocardiographic signal [122].

Our laboratory and the Institute of Terrestrial Magnetism, Ionosphere and Radiowave Propagation of the USSR Academy of Sciences used OPM to perform simultaneous MCG and ECG recording from the three standard leads. ECG from the second standard lead was found to have the highest degree of resemblance with MCG. Visual analysis clearly shows that time characteristics of magnetic and electric signals, especially in ventricular

complex, are identical i.e. waves on MCG and ECG occur simultaneously. This coincidence is absolutely natural because MF detected by magnetometer is evoked by the identical cause i.e. motion of charges in the living organism reflected on ECG. All that explains similarity of MCG and ECG forms. It was also indicated that at certain orientation of pick-up coils the voltage elicited in the toroid sensor had the form identical to the first derivative of ECG in time.

However, these methods of cardiac electromagnetic function detection have substantial difference. Phase and amplitude variations of *T* and *R* waves of ECG and MCG are different. For example, relationship of *T* and *R* wave amplitudes was 20% on MCG and 41% on ECG (II). Perhaps, the difference should be attributed to the difference in the physical principle of ECG and MCG registration.

Based on the published sources, analysis of MCGs and comparison with ECG of normal patients substantiates the following conclusions:

1. Externally MCG is similar to ECG (same waves) and at least is as informative as the latter.

2. For each wave and complex on MCG there was obtained information on: a) maximal intensity field, b) wave amplitude, c) wave form and polarity.

3. Loss of weight by object was found to affect MCG (MCG appeared to be more sensitive to such factor than ECG). Variation in position of object affected MCG information as well.

MCG analysis was performed on 25 cardiac patients in USA, 41 in Finland and 140 in France.

There were studied MCGs of cardiac patients suffering from myocardial infarction, angina pectoris, infringement of intravascular conduction and ventricular hypertrophy. The research indicated that: 1) there were deviations on MCG of every object, 2) in case of anterior myocardial infarction MCG shows changes in septum function, intramural conduction disorder or *T* wave anomaly untraceable on ECG, 3) under posterior myocardial infarction ECG offers more information that MCG, 4) MCG contains more information essential for determining early hypertrophy and related disorder of intracardiac conduction under myocardial infarction,

5) MCG can show *S-T* segment shift caused by injury currents which could not be detected on ECG because of the electrodes polarization and the galvanic spin-effect [122].

There are a few more potential advantages of MCG over electrocardiography: magnetometers are safer since they do not touch the body of the patient and yield data rapidly. Most importantly, according to experts MCG supplies some additional data on the cardiac function (both normal and sick). It involves the following:

1. MF of the heart is less susceptible to distortions than electric signals sensed by electrocardiograph. Better localization of MP is noted. This advantage assures better focusing of the pick-up coil on the selected area.

2. Reproducibility and recurrence of MCG waves shows that they are not random but rather reflect fluctuation of difference of the heart's potentials during the systole and diastole.

3. MCG shows direction of the currents elicited by the heart. Form of MCG considerably depends on the pick-up coil position as to the patient's body. The vector pattern of MCG is regarded as its substantial advantage as well.

4. MCG also shows stationary effects such as continuous MF evoked by injury currents in ventricular aneurism. As a rule such fields affect ECG in its interval between the *QRS* complex and the onset of *T* wave i.e. *S-T* segment. Potentials elicited by these currents are so small in comparison with large and variable potentials on the skin surface that they cannot be detected with the electrocardiographic method. Generators of these weak potentials are located deep under the skin and their detection is difficult owing to strong local effects such as electrode's polarization and the contact difference of potentials between electrodes and the patient's body. At the same time scanning frequency of the standard ECG is about 0.1 Hz. Therefore, continuous potentials were usually measured directly from the heart surface in the dissected chest of experimental animals where magnitude of these potentials is considerably higher than on the skin surface.

The conducted experiments supplied extensive material showing relationship between *S-T* segment reflecting depolarization of the both

ventricles and the base line. Artificial squeezing of coronary artery causing myocardial infarction in experimental dogs showed *S-T* segment and base line shifts on MCG. The continuous MF level elicited by demarkation currents could be estimated by the base line position.

This phenomenon has opened up a new area of research involving correlation of MCGs of healthy subjects and cardiac patients. For example, 24 normal subjects and 31 patients suffering from various cardiac problems were examined with SQUID and their MCGs compared in the laboratory of heart diseases, Medical Faculty, Helsinki University. The so-called pre-cardial MCGs were similar to standard ECGs recorded from 12 leads and contained additional information. MCGs of patients suffering from different diseases were different. However, no unique conclusions could be drawn due to inadequate number of cases and measurements in different positions. The principal difference between ECGs (from 12 leads) and MCGs was found in different relative sensitivity of the two methods applied to various phases of elicited cardial EMF. For example, on MCG the magnitude of *S-T* segment shift (in relation to the *QRS* complex amplitude) was markedly higher. This could be attributed to the impact of "proximity effect" organic to magnetocar-diography. Therefore, some researchers maintain that it may prove a valuable clinical method of cardiac diseases diagnosis, particularly of those caused by initial distortions of myocardial repolarization.

5. It is important that MCG may be taken noninvasively and even at a distance of 7 cm to the body surface in some cases. Quality of detection is not affected by material between the pick-up coil and the MF source as long as it is nonmagnetic. This is attributed to the fact that MF remains continuous in transition from one medium into another (magnetic permeability of human body and air is roughly the same).Therefore, MCG does not depend on properties of material filling the space between human body and the sensor (and conditions on the transition border).

6. The principal difference between the two methods of diagnosis is represented in the fact that usually the fields detected in magnetocardiographic leads are described by circular currents in the periphery of cardiac muscle having low specific resistance. Anisotropy

of the cardiac muscle only serves to increase this effect. Besides, radial EMF in ventricles as well as radial and tangential EMF in the interventricular septum is not picked up by electrocardiographer but can be registered on MCG. The fact that radial EMF occurs more frequently in healthy subjects and tangential EMF is better reflected on MCG supported the assumption that MCG may be more sensitive than ECG to pathological variation in the excitation wave in the heart.

Presently, there are used two approaches to analysis of MCG. One approach involves direct comparison [95] of ECG and MCG of a patient suffering from certain malfunction of cardiac activity and their subsequent correlation with MCGs of healthy subjects. Researchers believe that relying on visual analysis they could identify specific regularities or anomalies in curves which might provide a key to conducting a more detailed analysis [105, 108,137].

The other approach involves simulation of electric "generators" (current dipoles) of the heart on the basis of MCG characteristics by analogy with generations "producing" surface potentials detected with ECG. For instance, computer simulation was used to estimate parameters of current dipoles of the heart by the normal (towards the patient's chest) component of MF. It was found that the emergence of the normal component of the field was the function of equivalent generator or current dipole "located" inside the heart while the impact of other currents elicited in human body can be neglected. All that makes solution of the task much easier and reduces the problem to a similar task of estimating generators (charge dipoles) for the case of surface potentials registration (ECG).

We started our research from magnetic mapping of certain rooms in the Institute's building. Conditions in the conference room on the fifth floor after the work hours when all facilities and lift were switched off were found best for detection of weak signals. Therefore, all experiments were conducted in the evenings.

The sensor mount and furniture for objects were fitted with nonmagnetic wheels in order to change the sensor's target area and to move the instrument closer to the object.

The objects were tested in the sitting and supine positions.

Simultaneously with MCG there was recorded ECG from three standard leads with ELCAR cardiograph. Sensors were placed at least 7 cm clear of the object.

A grid consisting of 30 quadrants, with the side of each ^easunng 5 cm, was superimposed on the chest to measure MF of the heart in different parts of the chest and to relate magnetic signals to their detection points (Fig. 19). The grid

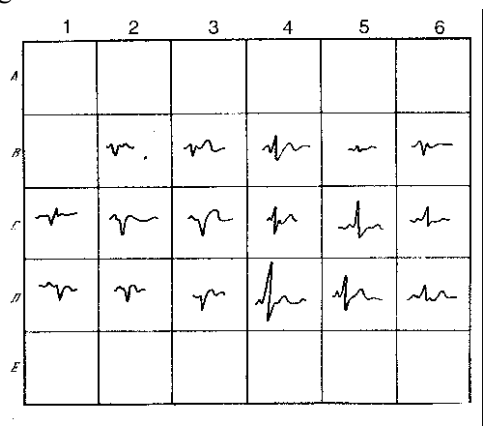

Fig 19. Magnitudes of MCG waves correlated to measuring grid quadrants from the chest

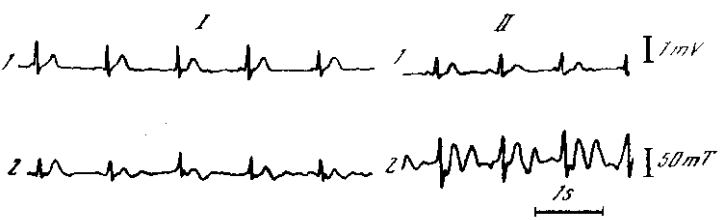

Fig. 20. **Simultaneously recorded ECGs (*1*) and MCGs (*2*) of two objects (*I, II*)**

was superimposed to match its median line to the center of xiphoid bone and the top margin to clavicles. The pick-up coil of gradiometer was positioned over the chest above the lead so that the sensor's bottom matched the center of the lead quadrant.

It was shown experimentally that MCG may be registered at a distance of up to 10 cm to the chest. The distance required for detection of magnetic signal from the heart depended on the location of the lead. Drawing of magnetocardiographic maps indicated that MF of the heart could not be detected over all sections of the chest. This could be attributed to: 1) local nature of magnetic signals (the most likely reason) and 2) inadequate resolution of the sensor meaning that the greater the distance to the anatomic location of the heart in the chest, i.e. to the source of activity, the weaker the signal detectable on the noise level.

Maximal magnitude of MCG waves and consequently the best signal-to-noise ratio were obtained from leads in quadrants D4, D5, C4 and C5, approximately corresponding to the third Nebb's lead used in cardiography.

The results of research have indicated that MCGs and ECGs are similar in the generation of the main waves (Fig. 20). The *QRST* complex related to conduction in ventricles and corresponding to ECG system is represented on MCGs best. The maximal amplitude of *R*-wave (maximal wave on ECG) measured around 60 pT on MCG. It varied in different leads from the one object and in the same leads from different objects. The OPM sensor resolution assured fairly well detection and recording of MCG without signal averaging. Besides, the sensor produced MCGs from some leads with ECG level resolution showing precardial wave *P*.

Fig. 20 shows ECG (2nd standard lead) and MCG recorded from quadrants C4 (1st object) and D4 (2nd object) on two objects. It may be seen that despite considerable similarity between ECG and MCG additional waves may appear on MCG. For example, MCG of the second object showed a clearly seen additional wave after the *QRS* complex resembling the T wave of the object in terms of time and amplitude characteristics. Its amplitude ranged from 30 to 50 pT. Occurrence of additional waves on MCGs of two out of three examined objects showed no regularity in each experiment

on the given object. However, a wave detected in the course of a particular experiment remained during its entire length. Varying occurrence of additional waves on MCGs from one experiment to another is not the evidence of noise impact or external impact in any case. It may be seen from the same figure that they always occurred in a particular sequence and had clearly reproducible characteristics of time and amplitude. Their occurrence only on MCGs substantiates an assumption that they contain additional information on the heart function untraceable on electrocardiographic characteristics which may have various manifestations in objects or in one object depending on his state.

Comparison of MCGs of one object obtained in the course of different series of experiments showed considerable variability in amplitudes and sometimes even in wave phases in one and the same quadrant. These variations may be attributed to: 1) external MF impact; 2) fluctuation of the instrument's sensitivity from one experiment to another depending on the background; 3) different functional state of the object; 4) minor shifts of the grid and the object's position, regarded as the least possible cause.

Recording of MCGs of patients was performed jointly with S. Feidman, D.Sc. (Med.) and doctor A. Yarov in a sanatorium near Moscow using the above method and OPM. MCGs were recorded from 10 patients suffering from cardial ischemia aged from 52 to 76 years old and 6 practically healthy subjects aged from 30 to 50. All subjects were males. All patients treated in the sanatorium suffered from cardial ischemia and were placed there after clinical examination.

Judging by the case history, clinical manifestations of the disease as well as data of laboratory and instrumental research, the patient were classified into two groups: I - five cases of stable stenocardia of tension with infrequent seizures and athe-rosclerotic cardiosclerosis, 2 - five cases of stable stenocardia of tension and rest with frequent seizures, postinfarction and atherosclerotic cardiosclerosis and aorta atherosclerosis. The patients did not suffer from congestive heart failure. In all cases more than two years passed since the acute period of myocardial infarction. MCGs were used only for analysis of the ventricular complex.

Analysis of ECGs from the first group revealed no substantial pathology in two patients having normal electric axis of the heart. The remaining three cases (two with normal electric axis of the heart and one with horizontal) featured increased *QRS* complex amplitude and its expansion to 0.13 s in the left chest leads accompanied by certain diminishing of *S-T* segment and *T* wave. MCGs of patients with normal ECG showed recess of *S* wave in all leads and particularly in the top leads — up to -64 pT in B4, as well as increment of *R* wave amplitude in the bottom left leads up to +70 pT in E4.

Analysis of MCGs of other patients of the same group showed expansion of the complex to 0.13 s like in ECGs. One patient with normal electric axis of the heart showed gradual amplitude increment of *P* wave towards the bottom left leads up to +76 pT in E4 as well as *S* wave recess in the top leads up to -32 pT in A6. Another patient with the normal electric axis of the heart showed, apart from considerable increment of *P* wave in all leads, particularly in the bottom left - up to+108 pT in E4 and *S* wave recess in the top leads, also *Q* wave recess in the bottom left leads up to I/5th of the *R* wave amplitude in E5. The patient with the horizontal electric axis of the heart had the ventricular complex of the *R*s type from all the top left leads. In other leads the *R* and *S* wave amplitude increased.

ECG examination of patients from the second group revealed cicatricial myocardium changes on the anterior-lateral wall of the left ventricle in two cases. The *Q* wave was expanded to 0.04 s and recessed more than by I/4th of the *R* wave amplitude in AVL and V5-6 leads. Of these two one had a normal and another a horizontal electric axis of the heart.

One more patient who had had posterior myocardial infarction according to his case history showed no cicatricial changes of ECG recorded from standard leads as well from orthogonal and Nebb's leads. The patient had a normal electric axis of the heart. All patients of the second group had ECG evidence of myocardial hypertrophy of the left ventricle.

The patients with cicatricial stage of the posterior lateral myocardial infarction had different MCG maps although both showed horizonal electric axis of the heart. MCG of the patient with undiagnosed cicatricial stage of

the posterior myocardial infarction showed *Q* wave not only in the bottom left, which is quite normal, but also in all right, with the exception of A row, leads with maximal depth up to 1/5 th of *R* wave amplitude in D3 and C2. The *R* wave amplitude was increased in central leads to +82 pT in D4.

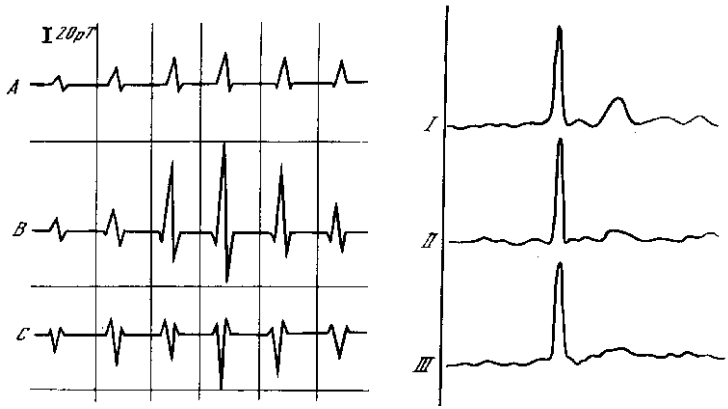

Fig. 21. Averaged readings of the QRS complex on MCGs of normal subjects (A) and patients with hypertrophy of the left ventricle (B) and myocardial infarction (C)
Fig. 22. MCG of man recorded at normal external magnetic field of the Earth (II - $0.49 \cdot 10^{-4}$T); at artificially increased external magnetic field (I - $1.1 \cdot 10^{-4}$T); at attenuated external MF (III - 0) (Peters *et al*., 1980)

In order to interpret the obtained data we introduced the notion of magnetic axis of the heart by analogy with electric axis as an equivalent of all magnetic vectors in the heart emerging during the myocardium depolarization. In contrast to other studies we revealed certain differences in MCG maps of normal subjects with normal and horizontal electric axis of the heart. Magnetic axis in subjects with normal electric axis of the heart was directed from the top left to the right corner of chest, and from the top right to bottom left corner in subjects with horizontal electric axis of the heart making in both cases the right angle with electric axis of the heart. This explains why

MCGs of patients with cicatricial stage of the anterolateral myocardial infarction showed *Q* waves in the bottom right leads in contrast to ECGs where they appeared from the left chest leads. Absense of similar deviations on MCGs from the first group points out to specificity of these deviations for the pathology in question.

Certain difference of MCG maps of two patients with posterior lateral myocardial infarction and horizontal electric axis of the heart is probably related to the pronounced ischemia of anterolateral wall of the left ventricle of one patient. Both patients had *Q* wave more deep than normal in the bottom left leads. In contrast to MCG maps of patients with cicatricial stage of the posterior lateral myocardial infarction *Q* wave appeared only in the extreme bottom left leads in row E which, perhaps, may be attributed to the left deviation in these patients of electric and accordingly of magnetic axis of the heart and the size of infarction.

Three patients from the first group showed ECG evidence of the left ventricle hypertrophy. Emergence on MCGs of these patients of *R* waves higher than in normal subjects primarily in the bottom left leads (Fig. 20) and deeper *S* waves in the top leads as well as absence of verified data from this group of patients on other pathologies allow to consider these deviations on MCGs as specific to the left ventricle hypertrophy. ECGs of two patients showed no pathological deviations. The study of MCGs revealed deviations similar to those of other patients of the first group although not so pronounced. It speaks, probably, of the early stage of the myocardial hypertrophy of the left ventricle in these patients.

So, like ECG, MCG may be used to diagnose myocardial hypertrophy of the left ventricle as well as to better identify and topologically localize cicatricial myocardium changes. Being a noninvasive examination method magnetocardiography requires no special preliminary treatment of patient and is more efficient than electrocardiography.

The results of our experience in recording MCGs from patients suffering from cardiac problems confirmed the published data that there is a stable relationship between electric and magnetic vectors of the human heart, and that there is a method featuring better localization and higher

sensitivity to manifestations of cardiac pathology than ECG.

These experiments were in a way unique because they were performed with OPM and not with other type magnetometers. Similar results based on the use of the same instrument were recently published as well [56].

The Japanese cardiological study [113] of 30 normal subjects and 95 patients showed that MCG may provide information which cannot be obtained from standard ECGs. It noted increment of *R* wave at the left ventricle hypertrophy. *T* wave inversion occurred more frequently on ECG than on MCG.

Therefore, MCG can be used for better early detection of abnormal repolarization.

Higher sensitivity of *T* wave of MCG is pointed out by results of recording MCGs from man at different external MF. It may be seen from Fig. 22 that *T* wave on MCG increased in its amplitude with the external MF increment up to 1.1 10^{-4} T and attenuated almost to zero at external MF attenuation to 0. *R* wave amplitude on MCG did not vary in the course of the above manipulations.

Theoretic studies of MF of the heart are conducted primarily in physical laboratories [86, 87, 91, 98]. At the same time the above method has been used on the growing scale in clinical institutes as well [23].

MAGNETOCARDIOGRAM OF ANIMALS

In 1971 D. Cohen *et al* recorded MCG of a dog in a magnetically shielded room in the process of recording direct currents of MCG of prepared animals [100].

Direct currents elicited by damaged cardiac muscle are related to local myocardium damage caused by acute ischemia, in-farction and pericarditis. These diseases cause a necrotic spot to develop in the cardiac tissue which appears to be an electrically "silent" zone. Continuous difference of potentials between the normal and necrotic tissues elicits direct injury currents. This area is a dipole type generator. In its structure it is similar to a generator operating at regular proliferation of cardiac stimulation. However, in contrast to the latter it is not reflected on ECG because current intensity

variation over time is quite slow.

Researchers experimentally estimated contribution of the current generator dipole element and of volume currents into MCG by inserting a piece of cardboard between the breast bone and the heart of anesthesized

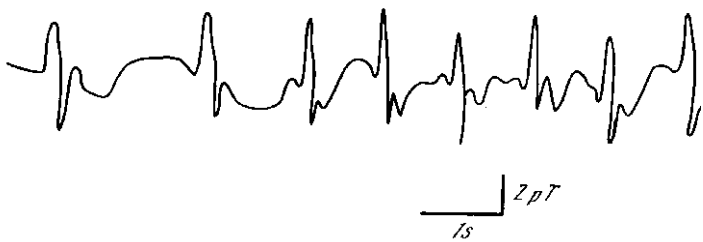

Fig 23 Magnetocardiogram of rabbit

dog and recording MCG and ECG simultaneously.

Albrecht *et al* in 1982 studied MCG of rabbit. They extracted the heart from the chest of the animal and rotated it in various directions [79].

Leifer *et al*. [85] studied in 1983 contribution of auricles repolarization and the His-Purkinje system activity into the vectormagnetocardiogram of dogs (*P—R* section).

Each animal in these experiments was anesthesized and subjected to tracheotomy in order to be able to place magnetometer directly above the pericardium. *R* wave of electrogram recorded from electrodes implanted into the right auricle was used to trigger the magnetic signal averaging facility. Following the verifying experiment medicamental preparations were administered intravenously to cause substantial expansion of the *P—R* interval and second degree atrioventricular block. The authors concluded that inclined section of *P—R* segments on MCG also reflected the early stage auricles repolarization.

One must recognize that MCGs of animals are studied highly inadequately. This may be attributed to remoteness of physical labs possessing magnetometers from vivariums where animals are kept. In any case dramatic progress in this field may be expected in the near future.

It should be also noted that we succeeded in recording MCG of rabbit with SQUID where *R* wave can be easily identified (Fig. 23). Similar MCGs were earlier obtained in the GDR.

In conclusion of the chapter it must be stressed that in the process of joining the biomagnetic research our team duplicates in a certain degree the studies performed by other groups. In the beginning we recorded MCGs as the strongest signals from man and animals and then proceeded to detection of MF of the brain which we regard our principal objective.

3.6. MAGNETIC FIELDS OF THE BRAIN

Researchers in the field of magnetography, like as in electrocardiography, proceeded from detection of MF of the heart to noninvasive sensing of MF of the brain. These activities were affected by the scientific and technological progress as well. While G. Berger registered EEG approximately 45 years after the first ECG recording, D. Cohen published his first report on MEG registration five years after the first report on MCG.

SPONTANEOUS MAGNETIC ACTIVITY OF NORMAL BRAIN

D. Cohen writes in his recollections [85] that the first steps in the field of biomagnetic research caused considerable scepticism on the part of the broad scientific public. It took a great deal of persistence to overcome numerous difficulties. The first magnetically shielded room was built approximately in 1967 in the F. Bitter National Magnetic Laboratory. The first report on MEG registration by averaging with induction sensor and use of EEG as a reference signal was published already in 1968. Four years later there was reported the feasibility of direct MEG registration with SQUID in a shielded room. Two years after that Finnish researchers [76] reported the possibility of direct MEG registration with SQUID gradiometer in a nonshielded room in a suburb (wooden house).

Both the US and Finnish teams used their colleagues (not more than five persons) as objects. The procedure involved placing SQUID over the back of the head of the objects and simultaneous standard recording of EEC

from the same area. The subjects were requested to open and close the eyes. Alpha-rhythm could be better identified in the last case.

Closing of eyes caused alpha-rhythm on EEG and MEG, though full identity of these two characteristics of brain activity was not observed. There was noted alpha-rhythm asymmetry of MCG recorded from the two hemispheres. Slow synaptic processes rather than neuron spikes are believed to be the sources of MEG and EEG. With the standard MEG recording procedure the 1 pT amplitude on MEG corresponded to 50 μV on EEG.

In our experiments we also used OPM to register MEG of man. Cylinder shaped magnetosensitive probe was 4 cm in diameter and 5 cm long. Base distance between sensors was 6 cm. Properly oriented sensors were fixed several millimeters clear of the scull surface of the object lying on a nonmagnetic bed. EEG was recorded from two leads with nonmagnetic silver plated electrodes filled with current conducting paste. One electrode was fixed 3 cm higher (inion) and the other - under the MEG sensor. The indifferent electrode was clipped to lobule of the ear. The band of MEG and EEG registration was 0.3-15 Hz. The noise level elicited by the operating gradiometric system at these frequencies was $5 \cdot 10^{-11}$ T on the average. After amplification MEG and EEG signals were simultaneously recorded on two channels of magnetograph and processed in a computer.

Experiments were staged in the evenings in the laboratory wing of the Institute of Higher Nervous Activity and Neuro-physiology of the USSR Academy of Sciences without shielding. MEGs and EEGs were recorded from 15 objects during 2 minutes with their eyes open and closed. Ten-second sections of EEG and MEG recordings were analyzed with quantization frequency 102.4 Hz. MEG and EEG spectra in some sections of the alpha-rhythm band were found to coincide considerably.

Maximal peak to peak amplitude of the alpha-rhythm in normal objects was from 2.5 to 3.5 pT. Alpha-rhythm is often characterized by substantial amplitude variability traceable in one or several objects.

Systems of MEG leads provided quite reproducible spatial and time characteristics of the alpha-rhythm studied at the four month interval. Reproducibility of the measurements was within the limits of individual variability organic to the alpha-rhythm.

Opening of eyes caused sizable attenuation of the alpha-rhythm in most of the objects. Depression was also observed when subject was engaged in a simple task. There was observed correlation of electric and magnetic alpha-rhythms when the subjects were awake. During the sleep the correlation was absent.

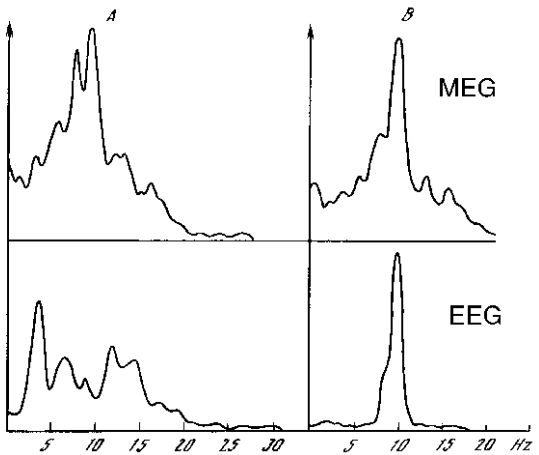

Fig. 24. Power spectra of magnetoencephalogram (MEG) and electro-encephalogram (EEC) recorded under the occipital area with eyes opened (A) and closed (B), x-coordinate shows frequency in Hz; y - magnitude of frequencies in relative units

Alpha-rhythm sources were localized with the method of relative covariance between MEG and the simultaneously recorded EEG. Extremes of opposite polarity on the left and right sides of the occipitoparietal area were detected pointing out to the presence of dipole source of current at the 4-6 cm depth at the center of the head coinciding with the location of calcarine fissure.

The researchers operated a four-channel magnetometer [11] to find the field flowing out of one hemisphere and entering the other and twice changing the alpha-rhythm direction during each period. It was shown that the alpha-rhythm fluctuations were not sinusoidal but rather pointed at peaks or slopes depending on the area of the MEG recording. It was also

noted that the waveform and frequency remain unchanged during one spindle of the alpha-rhythm oscillation [12,13].

Theta-rhythm was the common waveform on MEG recorded during the sleep. It was not detected during the state of awakeness. MEG showed no spindle-like function during the sleep.

Slow waves appeared in the course of hyperventilation either on MEG or only on EEG or sometimes on the both. Lack of correlation between MEG and EEG may be attributed to the limited

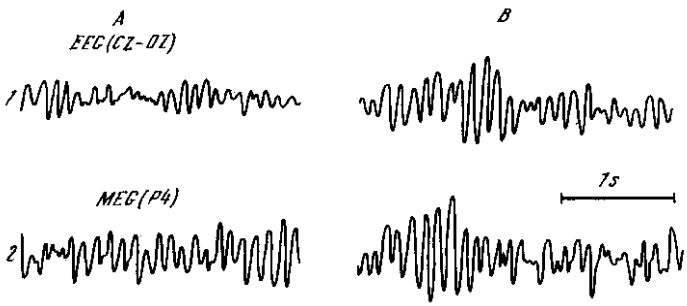

Fig. 25. Simultaneously recorded EEG (7) and MEG (2) under the occipital area of the same subject with eyes opened (A) and closed (B). Recording performed with a SQUID based biomagnetic system

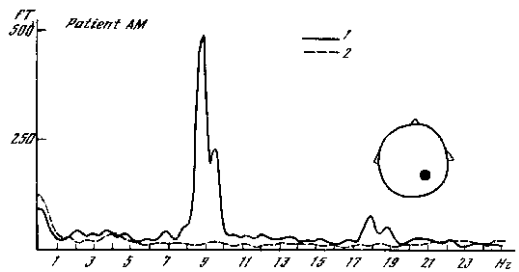

Fig. 26. Power spectra of MEG recorded above the occipital area (7) with subject's eyes opened and (2) noise of the biomagnetic system