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Stratbucker, R. A.; Hyde, C. M.; and Wixon, S. E., "The Magnetocardiogram A New Approach to the Fields Surrounding the Heart" (1963). *Faculty Publications from the Department of Electrical and Computer Engineering*. 102.

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phase adjust potentiometers shown in Fig. 9. The excitation voltages are picked up across two turn windings (5 volts per turn at a field current of 1.5 amperes) on the appropriate field coil. This voltage is balanced to ground through 200 Ω resistors according to manufacturers' recommendations. The required excitation voltage at the carrier preamplifier should be 4.5 volts rms and should be stepped down by fixed attenuators not shown in Fig. 9. The local oscillator in the Sanborn Co. carrier preamplifiers may be deactivated simply by removing its plug-in coupling transformer. The carrier preamplifier contains a dc amplifier after demodulation and filtering which creates a single ended output voltage of ± 3 volts full scale across 1000 Ω . Channel gain is varied by means of a fixed step attenuator at the front end of the ac amplifier. The Sanborn power supply Mod 350-500AP contains a transistor dc amplifier with unity

voltage gain, a frequency response of 10 kc and a full scale output of ± 2.5 volts across 50 Ω . This offers an available current of ± 50 ma full scale which is fed directly to a mirror galvanometer (Mod 1650) in the recorder which is fluid damped to a factor of 0.64, has a bandwidth of 1900 cycles per second and a sensitivity of ± 10 cm deflection for ± 37 ma. An oscilloscope monitor is helpful. If e_θ and e_ϕ are placed on the horizontal and vertical plates of the oscilloscope one obtains a frontal projection of the movement of a hypothetical spot on the center of the pupil.

ACKNOWLEDGMENT

The author wishes to thank Dr. M. E. Langham of Wilmer Institute for ophthalmological counsel and guidance and Dr. C. F. Hazlewood and Mr. W. J. Sullivan for cooperating in the experiments.

The Magnetocardiogram—A New Approach to the Fields Surrounding the Heart*

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Summary—Experiments have been conducted which reveal the existence of a detectable magnetic field associated with cardiac electrical activity. The relationship between the magnetic record and the electrocardiogram has been explored and it is shown that under certain conditions of axis orientation the voltage induced into a toroidal sensing element around the heart has the form of the first time derivative of the electrocardiogram. A formula based on Maxwell's equations has been developed to relate these two phenomena.

INTRODUCTION

EARLY DEVELOPMENT of electrocardiography was based upon the concepts of static field theory. The fundamental nature of this dependence has continued to be recognized to the extent that the most recent contributions to this important branch of medicine deal almost exclusively with the concepts of electric potential and electric field intensity.

Time-varying electric fields associated with the conduction process in the heart (or any other irritable tissue) create the familiar time-varying potentials at points within and on the boundary of the medium surrounding the tissue. Maxwell's equations¹ predict the existence of a magnetic field associated with any time-varying electric field. The concept of a biologically produced magnetic field was suggested in 1958 by Valentinuzzi² in his classic treatise on magnetobiology. Apparently the suggestion was not subjected to experimental verification. Although considerable literature has accumulated on the influence of magnetic fields on biological systems, it appears that the first successful recording of the magnetic field associated with membrane electrical activity occurred in 1960 when Seipel and Morrow³ reported the detection of a magnetic field

* Received April 19, 1963; revised manuscript received August 20, 1963. The research reported in this paper was supported in part by the U. S. Public Health Service, Grant No. HE0133710.

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¹ S. Ramo and J. R. Whinnery, "Fields and Waves in Modern Radio," John Wiley and Sons, Inc., New York, N. Y., 2nd ed., pp. 177-206; 1953.

² M. Valentinuzzi, "Curso de Magnetobiología y Complementos de Magnetoquímica," School of Medicine, Montevideo, Uruguay. Published in English by Tech. Info. Center, Space and Info. Div., North Am. Aviation, Inc., Downey, Calif., p. 106; October, 1961.

³ J. H. Seipel and R. D. Morrow, "The magnetic field accompanying neuronal activity. A new method for the study of the nervous system," *J. Washington Acad. Sci.*, vol. 50, pp. 1-4; October, 1960.

accompanying impulse conduction in an isolated frog nerve.

Our initial work in magnetocardiography was concerned primarily with demonstrating that the magnetic field associated with cardiac activation was of sufficient magnitude to be recorded by standard electronic techniques. Statistical cross-correlation computer programs were developed to compare the information content of the electrocardiogram (ECG) and the simultaneously recorded magnetocardiogram (MCG).⁴

The discovery of observable and apparently significant data in the MCG signal stimulated further experimentation in this area. Subsequent animal experiments have been performed to obtain quantitative data. The results of these experiments are the subject of this communication.

EXPERIMENTAL METHOD

Following a sharp blow on the head, hearts were quickly isolated from heparinized 400–600 gram guinea pigs. A plastic cannula was tied into the aorta and the coronaries were perfused with a modified Tyrode solution according to the method of Booker.⁵ The perfusion apparatus contained an artificial lung mechanism through which 95 per cent O₂ and 5 per cent CO₂ was constantly bubbled. The temperature of the perfusate as it was delivered to the coronary arteries was 38°C and the pH was 7.4.

The heart was placed in the center of a double-walled plastic sphere which contained six silver-silver chloride electrodes protruding into the inside surface. These electrodes were so arranged that they formed three pairs of bipolar electrodes whose axes were mutually orthogonal and whose separations were 12 cm.

The volume conductor medium surrounding the heart was of the same composition as the perfusing fluid (resistivity of about one ohm meter) and was maintained at constant temperature by circulation of water at 38°C in the jacket between the two concentric spheres (see Fig. 1). Cardiac electrograms from the X, Y, and Z axes were recorded simultaneously using three identical pre-amplifier channels.

A toroidal solenoid containing 17,640 turns of No. 36 enameled wire wound on a Selectron⁶ core 6.5 cm OD × 4.5 cm ID × 1 cm was suspended in the center of the sphere with its major axis colinear with the bipolar electrode Z axis. The entire coil assembly was coated with Silastic⁷ rubber so that it was completely insulated from the volume conductor solution. (Insulation re-

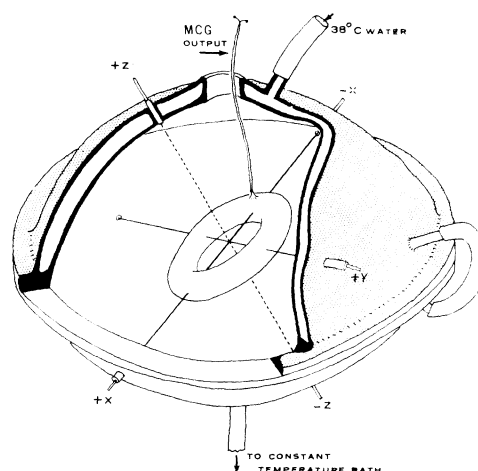


Fig. 1—Relative position of electrodes, toroid and lead axes.

sistance was greater than 1000 megohms.) The coil output was amplified by means of a high-gain ECG amplifier operated with a balanced input. The pass band of all amplifiers was from 0.1 to 2000 cps.

Fast sweep photographs of the ECG's and MCG's were taken on a Tektronix 565 dual-beam oscilloscope in such a manner that multiple low-intensity sweeps were superimposed upon the photograph. Superposition was accomplished by triggering on a consistent deflection of the ECG and delaying the start of the subsequent sweep by slightly less than one cardiac interval. This technique provided some degree of response averaging or integration which improved the apparent signal-to-noise ratio.

EXPERIMENTAL RESULTS

Our initial experiments indicated the presence of a detectable magnetic field in an air dielectric surrounding an exposed heart preparation. Such a result was expected when a time-varying electric field of the type recorded by Burr and Mauro⁸ existed in the air surrounding the heart. The low intensity of the field in air at distances which could be approached with our sensing element suggested the incorporation of the element within the spherical homogeneous volume conductor surrounding the heart.

In addition to markedly improving the signal-to-noise ratio, this arrangement made possible the determination of the vector dipole moment of the heart at any time during its cycle. The geometry of the volume conductor electrodes was so designed that the method described by Nelson⁹ could be used for calculation.

A typical slow-sweep recording of the MCG and the base-apex electrogram is shown in Fig. 2. The term "base-apex" refers to the orientation of the electrogram

⁴ S. Wixson, "A General Approach to the Fields Surrounding Conductile Tissue," M.S. thesis, University of Nebraska, Lincoln, Neb.; 1962.

⁵ W. M. Booker, "Comparison of the action of adrenaline and nor-adrenaline against cocaine on the isolated perfused guinea pig heart during normothermia and hypothermia," *Archives Internationales de Pharmacodynamie et de Therapie*, vol. 124, No. 1–2, pp. 1–10; 1960.

⁶ 3T5320T4, The Arnold Engineering Company, Morengo, Ill.

⁷ Dow-Corning No. RTV588.

⁸ H. S. Burr and A. Mauro, "Electrostatic field of the sciatic nerve of the frog," *Yale J. Bio. and Med.*, vol. 21, pp. 455–462; 1949.

⁹ C. V. Nelson, "Simple method for measuring heart vector of isolated animal hearts," *Science*, vol. 133, pp. 1831–1932; June, 1961.

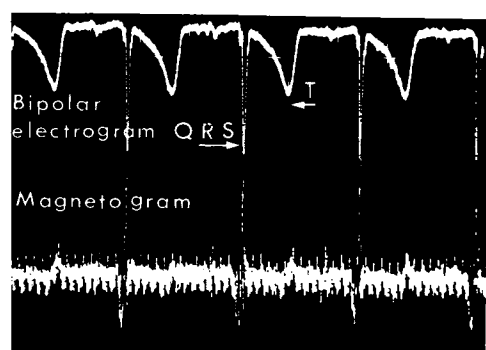


Fig. 2—Typical slow sweep recording of MCG and base-apex (Z axis) electrogram.

lead with respect to the anatomic axis of the heart. In all the figures the base-apex lead is the Z lead of Fig. 1. The polarity was established such that a mean depolarization vector from base to apex produced a downward deflection on the record.

The background noise on the MCG traces is that noise associated with an unshielded room containing considerable electronic equipment and motor powered laboratory apparatus. One can easily identify in Fig. 2 a large biphasic MCG complex associated with each QRS complex of the electrogram. In addition to the large MCG complexes there are smaller but temporally consistent complexes associated with each T wave.

Fig. 3 shows a fast sweep MCG-ECG composite of several successive but electronically superimposed complexes. The "average" MCG complex in this figure was derived by drawing a line central to the bundle of traces outlining the complexes. This response averaging results is a clear indication of the relationship between the MCG and the X-, Y-, and Z-axis electrogram traces when they are superimposed as in Fig. 4. Although not used in following calculations, the simultaneous X- and Y-axis ECG complexes are included in Fig. 4 for completeness.

Examination of the Z-axis MCG trace in Fig. 4 reveals an initial broad upward deflection, the peak of which corresponds to the maximum negative slope of the Z-axis electrogram. Similarly the sharper downward peak of the Z-axis MCG is coordinate with the maximum of the steeper positive slope of the electrogram. The construction of the average negative and positive slope of the Z-axis QRS complex of Fig. 4 makes possible a quantitative comparison of the MCG magnitude with the slope magnitude of the associated electrogram. The results of the theoretically determined and the recorded values for the particular MCG complex in Fig. 4 are shown in Table I.

The high amplification of the magnetic pickup circuit made this assembly quite sensitive to mechanical disturbances. We were interested in determining whether systolic contraction of the heart caused any mechanical transients which distorted the MCG signal. Such determinations were made simply by perfusing the

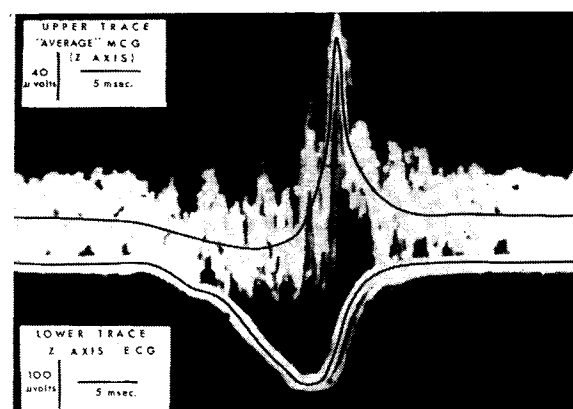


Fig. 3—Electronically superimposed MCG-ECG composite record.

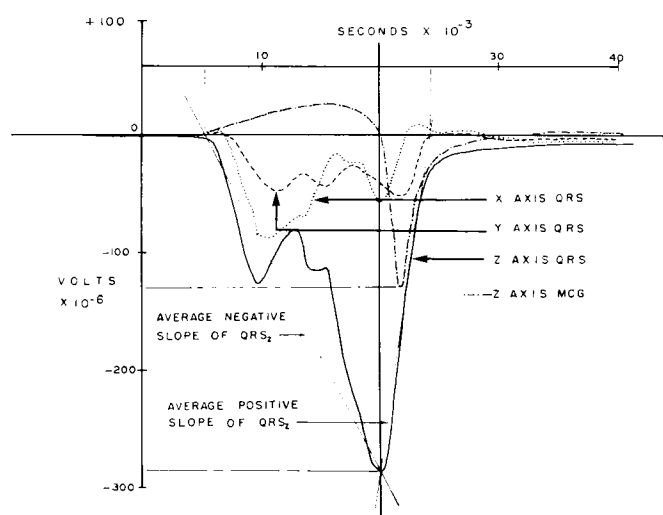


Fig. 4—Composite tracing of MCG and triaxial electrograms. (MCG polarity from Fig. 3 has been inverted for clarity.)

TABLE I

QRS slope	Maximum dipole moment	$\Delta M/\Delta T$	MCG voltage calculated from (5)	MCG voltage experimentally recorded
Downstroke of QRS_2	2.2×10^{-6} ampere-meters	0.15×10^{-3} ampere-meters per second	32×10^{-6} volts	45×10^{-6} volts
Upstroke of QRS_2	2.2×10^{-6} ampere-meters	0.5×10^{-3} ampere-meters per second	105×10^{-6} volts	125×10^{-6} volts

heart for a minute or two with a calcium-free Tyrode's solution. Short term perfusion with such a solution renders the heart motionless while maintaining relatively normal electrical activity.¹⁰ In all experiments in which this procedure was used, the magnitude and shape of the MCG were essentially unaltered during periods when the heart was not contracting.

¹⁰ G. R. Mines, "On functional analysis by the action of electrolytes," *J. Physiol.*, vol. 46, pp. 188-235; 1913.

DISCUSSION

Our attempt to quantitate the relationship between the electric and magnetic fields in the volume conductor surrounding the heart was based upon the geometry shown in Fig. 5. Implicit in all our considerations were the assumptions that the cardiac current generator could be replaced by a dipole current generator M and that the dipole distance which separated the current source and sink was small in comparison to the distance which separated the recording electrodes. For the size of tissue which was employed and the size of the volume conductor used, this assumption is justifiable in so far as the potential measurements at the boundary of the sphere are concerned.¹¹

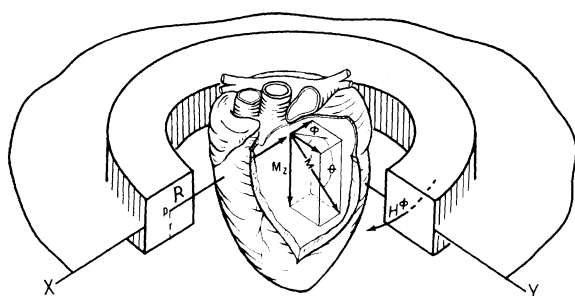


Fig. 5—Model used to derive (5).

$$V = N \frac{d\Phi}{dt} = \frac{\mu_0 \mu_r N}{\pi} \left(\frac{r}{R} \right)^2 \frac{dM}{dt} \sin \theta.$$

The toroid used in these experiments is smaller than the volume conductor since the available toroidal cores had a radius of revolution of approximately 2.5 cm. Hartmann *et al.*¹² have shown that, for the rabbit heart, electrode distances approximating two heart diameters from the surface of the heart provide sufficient separation such that the equivalent cardiac generator is symmetrically represented at the electrodes. Their records, however, seem to indicate that a two diameter limit is conservative and that distances as small as $\frac{3}{4}$ diameter do not cause appreciable error. The findings of Craib¹³ also support this argument. It would seem then that if the pickup core had a radius of revolution greater than $1\frac{1}{4}$ heart diameters, the point source character of the cardiac generator in relation to the ECG electrode would also apply to the magnetic pickup core. Guinea pigs of the size used have heart diameters of about 1.5 cm which means that the radius of revolution of the toroid should be greater than 2 cm. With a radius of revolution of 2.5 cm, the insulated toroidal core assembly which was used can be assumed to introduce

negligible proximity distortion in both the ECG and MCG recordings.

The only volume conductor currents which are effective in inducing a voltage into the sensing coil are those currents which encircle the core. The total effective current is found by integrating the current tubes penetrating the plane of the toroid between the limits of the radius of revolution and the essentially infinite boundary of the volume conductor. See Fig. 5. The time rate of change of the total effective current is directly related to the voltage induced into the turns of the coil. One would expect, therefore, that the form as well as the magnitude of the MCG would bear a direct relationship to the first time derivative of the cardiac dipole moment. The magnitude of the dipole moment is related analytically⁹ to the boundary potentials recorded at great distances on a homogeneous volume conductor surrounding a heart. Since the electrode distances used in these experiments, 6 cm, can be considered great in relation to the dipole dimensions, it is possible to derive an expression relating the MCG with the ECG.

Consideration of Maxwell's equations allows the development of this relationship in the following way. The component of magnetic field intensity of interest in Fig. 5 is H_ϕ . The development of an expression for H_ϕ at a point p a distance R from a dipole current source is given by Stratton.¹⁴ Using the symbol, M , for the dipole moment the equation becomes

$$H_\phi = \frac{\sin \theta}{4\pi R^2} M. \quad (1)$$

To simplify calculations we assume that the dimension r of the toroid is small compared to the radius of revolution, R . Then the flux density will be essentially uniform throughout the cross section of the core and the total flux Φ in the core is the product of the flux density and the cross-sectional area, where

$$B_\phi = \mu H_\phi \quad (2)$$

and

$$\Phi = B_\phi A = \frac{\mu r^2}{\pi R^2} M \sin \theta. \quad (3)$$

Noting that μ is the product of the permeability of free space μ_0 and the relative permeability μ_r of the core material, the equation becomes

$$\Phi = \frac{\mu_0 \mu_r}{\pi} \left(\frac{r}{R} \right)^2 M \sin \theta. \quad (4)$$

The voltage induced into N turns wound on this core is given by

$$V = N \frac{d\Phi}{dt} = \frac{\mu_0 \mu_r N}{\pi} \left(\frac{r}{R} \right)^2 \frac{dM}{dt} \sin \theta. \quad (5)$$

¹¹ P. Rijlant, "Discussion," *Ann. N. Y. Acad. Sci.*, Pt. IV, vol. 65, p. 1062; 1957.

¹² I. Hartmann, R. Veyrat, O. Wyss, and P. Duchosal, "Vectorcardiography as studied on the isolated mammalian heart suspended in a homogeneous volume conductor," *Cardiologia*, vol. 27, No. 3, pp. 129-134; 1955.

¹³ W. H. Craib, "A study of the electric field surrounding heart muscle," *Heart*, vol. 14, No. 1, pp. 71-102; 1927.

¹⁴ J. A. Stratton, "Electromagnetic Theory," McGraw-Hill Book Co., Inc., New York N. Y., p. 436; 1941.

The parameters in all of the experiments were:

$$\begin{aligned}\mu_r &= 730 \\ r/R &= 0.2 \\ N &= 1.8 \times 10^4 \text{ turns} \\ \theta &= \pi/2 \text{ radians.}\end{aligned}$$

In order to use (5) for the calculation of the values of the theoretical potentials, the average derivative $\Delta M/\Delta T$ was computed from Fig. 4. The degree of comparison between the observed and calculated values shown in Table I together with the time derivative character of the MCG complex is convincing evidence that the mathematical relationship shown by (5) is sound. The relationship of the MCG to the electrogram under the conditions of the geometry of Fig. 5 has been observed in fourteen consecutive experiments. The data from one experiment is shown in Table I and is typical of the results of all.

These findings suggest that the orientation of the ECG vector could be determined by experimentally

positioning the MCG pickup with respect to a pair of ECG electrodes until the MCG record is the time derivative of the signal detected by the ECG electrodes.

The derivative of the electrocardiogram contains easily visualized information which shows good correlation with cardiac pathology.¹⁵ Further refinements in recording with an improved signal-to-noise ratio may render possible the clinical use of the magnetocardiogram. Such a system would eliminate the necessity of electrical contact to the patient as required in electrocardiography.

ACKNOWLEDGMENT

The authors wish to thank Dr. F. Lowell Dunn of the Cardiovascular Research Laboratory, the University of Nebraska, for valuable assistance and for use of electronic equipment.

¹⁵ P. H. Langner and D. Geselowitz, "First derivative of the electrocardiogram," *Circulation Research*, vol. X, No. 2, pp. 220-226; 1962.

An Analysis of Desmedt's Titration Procedure*

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Summary—The "titration" procedure is reviewed together with its application to the auditory system of the cat. The relevant portion of the auditory system is described by a mathematical model, and calculations based on it show the merit of titration over the direct observation of a stimulus-response ratio. The model yields a good approximation to Desmedt's experimental titration data.

INTRODUCTION

THE METHOD of titration compares two stimuli by balancing their effects on a specified response. One stimulus may alter the response to another, and, if the response can be restored by changing the value of the first stimulus, it is possible to use the change as a measure of the second stimulus.

The constant-response procedure has been applied to a variety of psychophysical and physiological measurements. Frequently the two variables that are balanced represent different aspects of the same stimulus, as in the determination of the visual sensitivity-wavelength

curve.¹ More rarely, completely different stimuli are compared, as in the study of muscle-spindle bias by Eldred, Granit, and Merton.²

Desmedt³ used the constant-response titration technique in a recent study of an important feedback path in the brain of the cat. Electrophysiological acoustic responses were inhibited or augmented by electrical stimulation of the olivo-cochlear nerve fiber bundle. When changes in the electrical stimulation were titrated with changes in sound intensity to produce a constant response, it was found that the decibel sound intensity change was independent, within wide limits, of the initial sound intensity. The titration curve for sound intensity change vs electrical stimulation was approximately piecewise logarithmic. The present analysis explains these results in terms of a model, and thereby specifies sufficient conditions for similar observations elsewhere in the nervous system.

¹ R. Granit, "Receptors and Sensory Perception," Yale University Press, New Haven, Conn., pp. 113-114; 1955.

² E. Eldred, R. Granit, and P. A. Merton, "Supraspinal control of the muscle spindles and its significance," *J. Physiol.*, vol. 122, pp. 498-523; December, 1953.

³ J. E. Desmedt, "Auditory-evoked potentials from cochlea to cortex as influenced by activation of the efferent olivo-cochlear bundle," *J. Acoust. Soc. Am.*, vol. 34, pp. 1478-1496, pt. 2; September, 1962.

* Received August 2, 1963; revised manuscript received October 14, 1963.

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