STUDIES OF LIFE BEFORE BIRTH*

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Summary By surgical procedures, small physiological monitoring transmitters are placed within the body of fetal animals within the uterus of the mother. After a brief recovery period, various parameters are followed before, during, and after birth, the little animals being born with functioning transmitters already in place. The purpose of such studies is to determine normal values of various cardiovascular parameters in relatively undisturbed subjects and also to follow surgically-produced anatomical and physiological defects which mimic congenital embryologic abnormalities with the goal of learning to cope with these through fetal surgery. Transmission of fetal vectorcardiograms and intrauterine pressure will be described.

Telemetry in the biomedical sense allows one to study animal or human subjects with minimum disturbance to the normal patterns of activity, and also allows exploration of otherwise unobservable parts of the body. The tracking of freely moving animals is a familiar example where the procedures provide a clear advantage. Either in the laboratory or in a field situation, biological information can be superimposed on the radio signal by suitable modulation for physiological studies. A valid application of these methods is to the study of the fetus before and during birth by the use of transmitters that are surgically implanted, after which a rapid recovery by mother and offspring allows a relatively unaltered maturation and birth.[1] The present paper will describe the preparation of a multichannel voltage transmitter for implant applications, and its use in fetal studies. This work is being carried on with Benjamin Jackson, aided by George Piasecki and Marc Abel.

For the simultaneous transmission of several physiological variables, we often prefer to use a group of standard single channel transmitters functioning on different wavelengths, but for the transmission of the three voltages that describe the spatial vectorcardiogram of a fetus, we prefer to use a single multichannel transmitter powered by a single battery and radiating the signal from a single loop antenna. The circuit is given in Fig. 1, where it is seen that a subcarrier system is employed rather than using time-division multiplexing. In this transmitter a single channel of straight FM is employed in conjunction with two subcarrier channels. The voltage controlled oscillators are astable

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multivibrators rather than being sine wave oscillators. This has not caused problems with the number of channels indicated, though the center channel has its waveform made more symmetrical with the extra transistor so that excess second harmonic will not be produced to fall within the band of the upper channel. The three signals are added to frequency modulate the radio frequency oscillator shown at the right. The small square coil of the tuned circuit serves as the transmitting antenna.

Using standard small commercial components soldered together by hand, this circuit is approximately half the size of a human little finger. A convenient source of power is a #400 mercury cell battery which delivers a relatively constant voltage over its life. Since all presently known plastics apparently are somewhat permeable to body fluids.[2] the transmitter is coated with wax before use. To minimize disturbance to the wax and also reduce the possibility of tissue irritation, it is then coated with a medical grade of silicone rubber (Silastic #382, formerly RTV 502, with catalyst M which is stannous octoate). Though sterilization by soaking in Zephiran is relatively effective, for maximum security we use gas sterilization in ethylene oxide followed by a period for outgassing. The leads and electrodes are of stainless steel, the lead wires being coated with Teflon.

A number of receiving antennas prove effective. A small tuned loop is useful, as is a single strand loop with a circumference of 1.5 wavelengths. If the animal is to be in a metal cage, it is sufficient to insulate the metal shelf upon which she stands from the rest of the cage, and use the shelf and cage as the two input connections to the receiver; an impedance near 50 ohms will often be found. A random length of wire draped in the vicinity of the animal will usually serve as a sufficient and convenient receiving antenna.

The received signal is detected by a standard entertainment receiver (KLH stereo). By choosing a frequency of approximately 100 MHz an inexpensive FM receiver can be employed, and this is also an appropriate frequency range from other considerations.[2] The signal is taken directly across the discriminator, thus giving an unrestricted low frequency response (with respect to receiver characteristics) in all channels.

The detected signal is separated into three parts by filters, as is seen in the lower part of Fig. 1. We designed fourth order Butterworth filters for this purpose, in preference to Tchebyscheff filters. If the three telemetered signals are to be compared by forming loops of one plotted against another, then the time delay through each overall channel must be the same. To assure this, the otherwise superfluous extra filter is placed in the bottom receiver channel.

The transmitter is put in place by a surgical procedure involving an incision to expose the pregnant uterus, followed by an incision through the layers to the fetus. If the margin of this last incision is kept pulled upward, then the loss of amniotic fluid is minimal. In

Fig. 2 this can be seen while the transmitter and leads are being slid into an incision through the fur of a fetal dog (beagle). 4fter closure of the fetal incision, a separate FM pressure transmitter[2] operating on a different frequency can be dropped into the amnion before closure of the maternal incisions. These procedures need not interfere with the ability of the mother to again become pregnant.

Signals such as these can be recorded and displayed in a number of ways. If the voltage representing the momentary state of the heart is considered as a dipole, then the motion of this dipole in space as the cycle of a heart beat progresses can be considered as a loop having projections on three perpendicular planes. These loops can be displayed on an oscilloscope by combining pairs of the three independently transmitted electrode signals. By using rapid switching in the oscilloscope, it is possible to simultaneously display all three loops for a single beat of the heart, thus allowing one to follow beat-to-beat changes. Such a display is shown in Fig. 3 for a fetal lamb three days before birth.

In Fig. 3 the individual loops are interrupted at a rate of 1000 per second, so that the relative rate of progression in different parts of the cycle can be inferred. By modulation of the oscilloscope intensity input, each dot is also formed into an arrow with the point facing in the direction in which the loop is traced out. This last can be extremely important in some cases to prevent confusion. If only heart rate is required, then it is convenient to record any one channel on a penwriter to give a familiar electrocardiogram.

We have worked with a number of sheep and dogs. Though the latter are smaller, they seem less subject to disturbance by such procedures. Readings generally stabilize after a day, and the mothers appear unaware of the monitoring process; other observations are made over closed circuit television to minimize disturbance by the presence of the investigator. We see sudden changes in fetal heart rate associated with unexpected disturbances sensed by the mother. There can be relatively rapid amplitude changes about the time of birth and slower axis changes after birth. These last are consistent with a picture in which the right ventricle of the fetal heart is functioning about as vigorously as the left. Restricting flow in a major vessel is seen to produce axis changes.

The potentials associated with the beating of the heart of the fetus are seen, not those of the mother. It is known that the surface of a fetus is not a conductor through which electrical potentials can spread uniformly to the abdomen of the mother, but rather that all currents flow from a few spots. J Thus there is not a good expectation for being able to obtain a fetal vectorcardiogram by any system external to the mother. Telemetry not only provides relatively normal indications of the parameters being studied, but here yields signals that would be otherwise difficult to obtain at all. The same applies to other parameters such as pressure, flow, and blood gases whose telemetry we are presently considering.

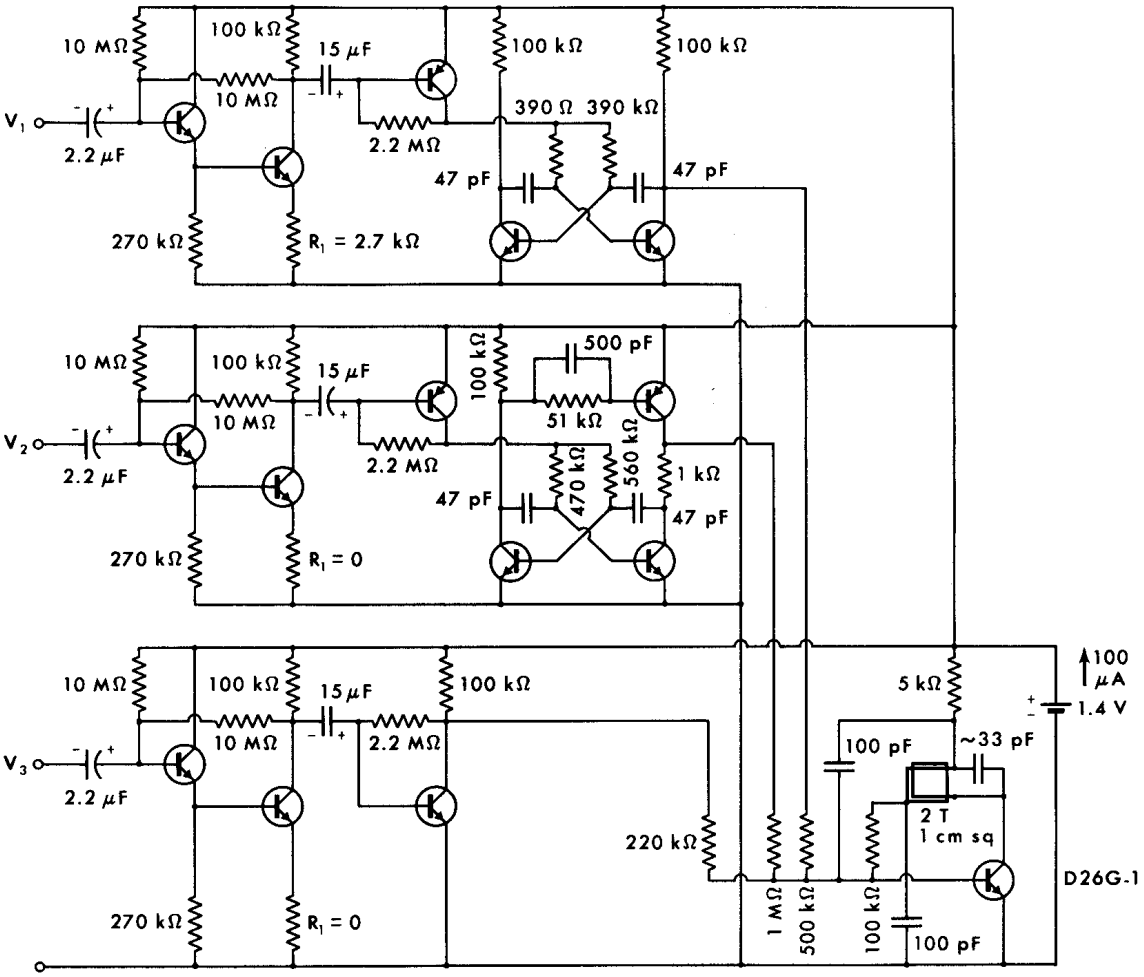
These matters have been discussed in a recent book[2] along with the generalities of equipment and procedures, and the interested reader is referred there for further details and references.

REFERENCES

1. R. S. Mackay, G. J. Piasecki, and B. T. Jackson, “Fetal Vectorcardiography”, in Proc. 8th Int’l. Conf. on Med. and Biol. Engineering, IEEE, New York, p. 31-10; 1969.

2. R. S. Mackay, “Bio-Medical Telemetry : Sensing and Transmitting Biological Information From Animals and Man”, John Wiley and Sons, Inc., New York, Second Edition, 1970.

3. A. R. Kahn and S. Koller, “Effects of the Fetal-Maternal Interface on the Fetal Electrocardiogram”, in Engineering in Med. and Biol., Proc. 19th Annual Conf., IEEE, New York, p. 136; 1966.



Transistors: NPN, D26E-5; PNP, D30A-3; except final

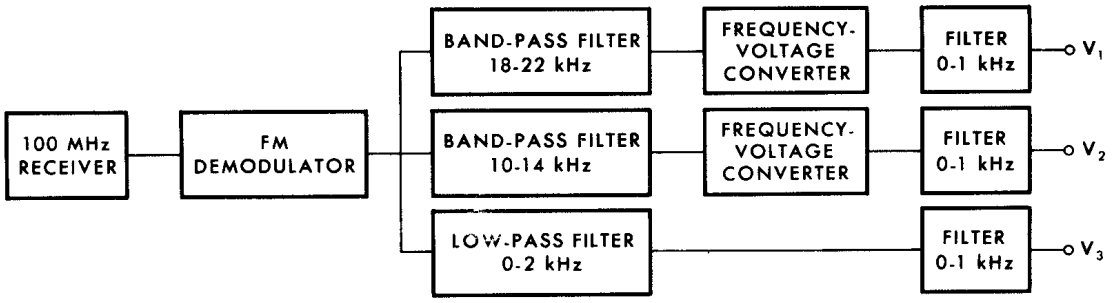


Fig. 1. Three channel voltage transmitting system with similar time delays through each channel.

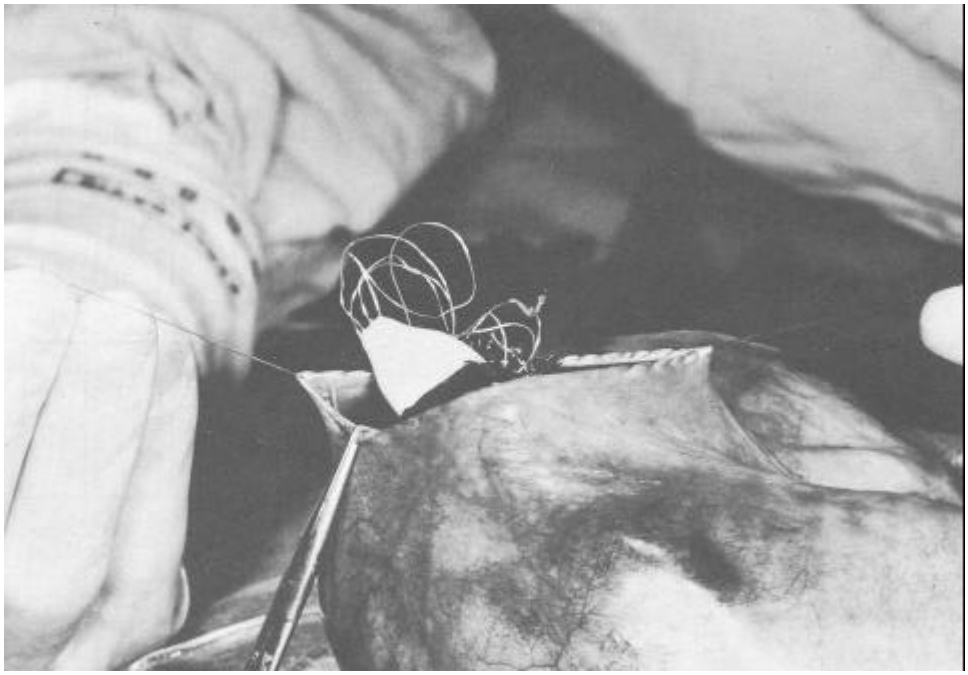


Fig. 2. **Transmitter being slid under skin of a dog fetus, the four electrodes having already been attached in suitable positions. The uterus has been raised through an incision in the maternal abdomen before exposing the fetus by another incision.**

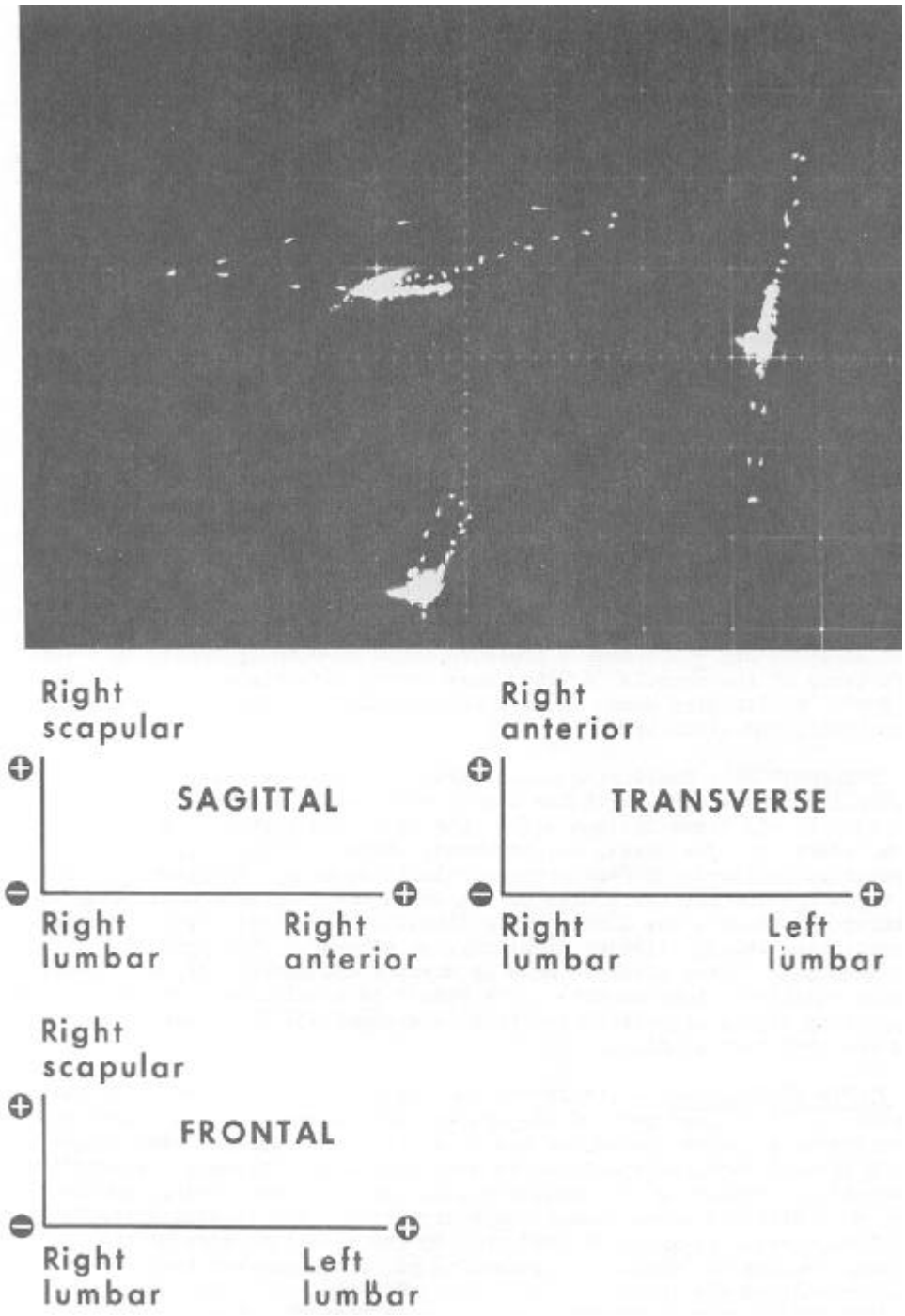


Fig. 3. **Display of the three vector loops from a single beat of the heart of a lamb in utero. The mother was eating hay at the time. Sensitivity is 0.02 mv/major division.**

The corresponding electrode positions and deflection directions are indicated below.