[19] Hughes, V., *Phys. Rev.*, **105**, 170 (1957). This paper also discusses several macroscopic experiments which give considerably smaller limits for the charges of molecules.

[20] If the charge of the proton were $(1 + \epsilon) |Q_{e^-}|$ then, e.g., the decay $p^+ \rightarrow e^+ + \pi^0$ would be forbidden. However the stability of an arbitrarily large number of protons would not be guaranteed by this alone, unless ϵ is irrational. Formally, this follows from the fact that then a subgroup of the charge gauge transformations (1) forms a dense subgroup of the baryon gauge transformations, and this implies baryon conservation.

[21] Of course, if angular momentum were not conserved, there might be additional electromagnetic interactions which would produce $O^+ \rightarrow O^+$ γ-transitions. However, the effect of such new interactions will depend critically on the type of interaction assumed and so we do not discuss them here.

[22] Sunyar, A. W., private communication.

*MINIATURIZATION OF THE ELECTROMAGNETIC BLOOD FLOW METER AND ITS USE FOR THE RECORDING OF CIRCULATORY RESPONSES OF CONSCIOUS ANIMALS TO SENSORY STIMULI**

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Introduction.—The original electromagnetic flow meters[1–5] utilized large magnets. An artery (A in Fig. 1a) was inserted into the gap between the pole pieces of the magnet. As the blood traversed the magnetic field at right angles, an emf was induced in the blood stream. This emf served as the measure of the rate of blood flow. The flow signal was picked up by means of two electrodes E_1 and E_2 touching the outer wall of the artery at the end points of a diameter perpendicular to the magnetic field, as shown in Figure 1*a*. The use of a constant magnetic field necessitated the use of nonpolarizable electrodes. The size of the magnet and the complication of using nonpolarizable electrodes restricted the application of this method to exteriorized arteries of anesthetized animals. The introduction of the alterating magnetic field[3, 6] simplified the design of the amplifying system and made the use of ordinary metal electrodes possible. This paved the way for the development of a small flow meter which could be implanted into animals to study blood flow in the conscious state in chronic experiments.[7] Chronic implantations up to 4 weeks' duration have been thus obtained. But the implanted units of the original design whose iron and copper skeleton weighed 5.5 gm and whose weight when encased in a plastic body was somewhat over 10 gm were still too large in comparison with the artery diameter for successful permanent implantations (Fig. 2*b*). The present paper describes simple designs of flow meter implants which, for a given artery diameter, are greatly reduced in size as compared to units built according to the original pattern.[7] Reductions in weight by a factor of twenty and, in some instances, more have been achieved. Such flow meters can be easily constructed to accommodate arteries of diameters in the neighborhood of 1 mm. The same objective of design can, of course, be used also for larger blood vessels. A special design for arteries over 1 cm in diameter is described below. Figure 2 shows a comparison between the original "miniature" flow meter implant[7] for an artery diameter of

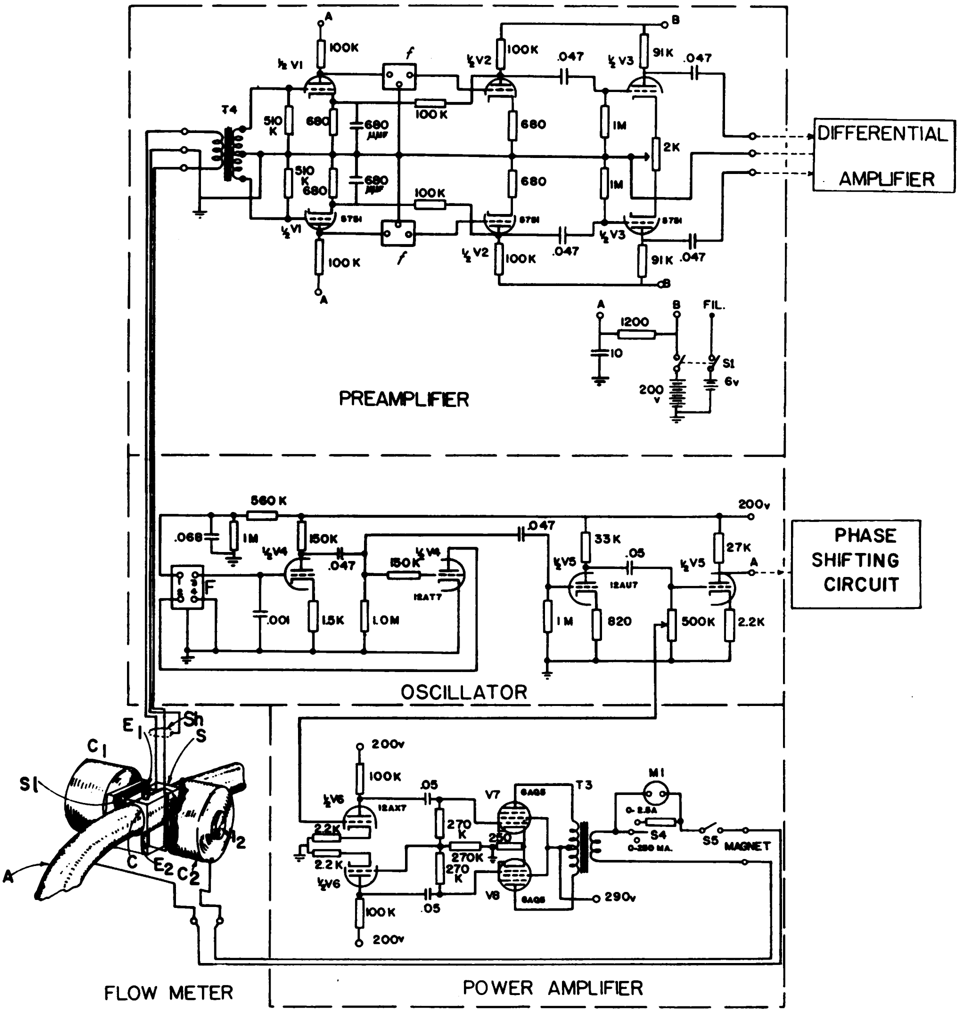

FIG. 1a.—Electromagnetic flow meter and associated electronic circuit, Part 1. The electronic components are represented by conventional symbols and their magnitudes are marked.

Flow meter section: I_2, magnet core; E_1, E_2, electrodes; C_1, C_2, magnet coils; S, sleeve; C, sleeve channel; Sl, slit; A, artery; Sh, grounded shield.

Power amplifier section: M_1, two-range ammeter; S_4, range switch; S_5, magnet switch; T_3, output transformer (Triad S55X).

Oscillator section: F, Tuning fork (Philamon Labs N. Y. type MJT400).

Preamplifier section: T_4, input transformer (triad geoformer g40) T.S; f, 400 cps LC filters (UTC type BMI 400).

2 mm (*b*) and the subminiature unit to be described below (*a*) weighing approximately 0.5 gm for an artery of 1.5 mm.

Illustrations of Blood Flow Changes Observed with Miniaturized Flow Meter Implants.—Figure 3*b*–*h* shows typical records of blood flow obtained with a transducer of the type shown in Figure 2*a* in a carotid artery of a conscious cat over a period of about 4 months. The base lines (indicated by arrows) were obtained by switching off the magnet. Figure 3*b* shows the contour of the blood flow during the cardiac cycle taken at high record speed. The following tracings, taken at lower

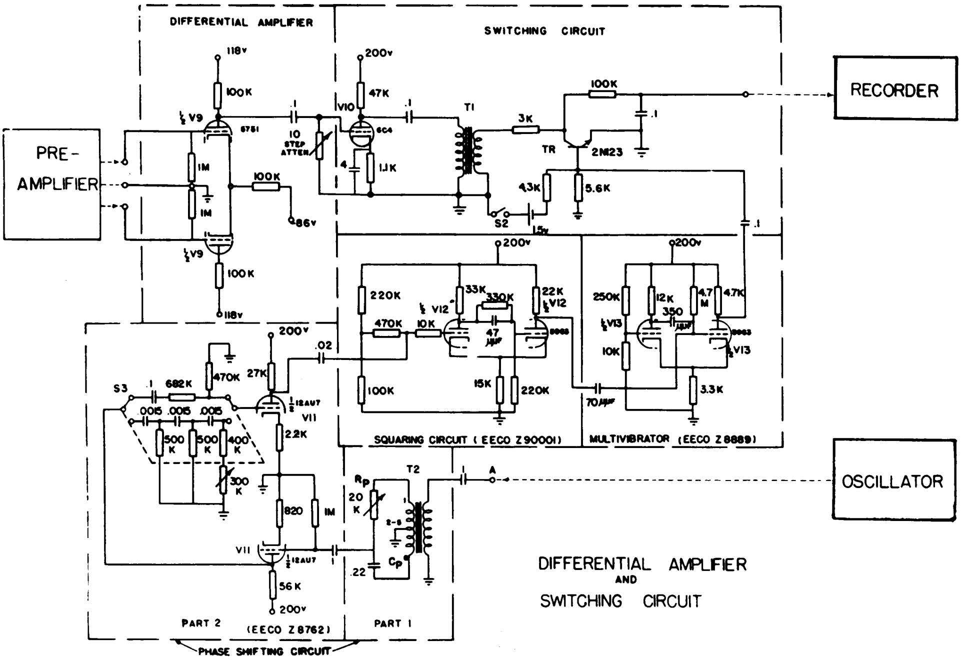

FIG. 1*b*.—Electronic circuit, Part 2.

Differential amplifier section: 10-step attenuator changes amplification by a factor of 2 per step. Switching circuit: T_1, interstage transformer (Triad A42Z); S_2, switch; TR, switching transistor (Gen. Electr. 2N 123).

Recorder: SANBORN "Polyviso" model 67-1200 with model 67-300 dc amplifier.

Squaring ciacuit: plug-in unit EECO Z 90001.

Multivibrator: plug-inunit EECO Z 8889.

Phase shifting circuit: Part 1, T_2, transformer (Triad A4X); Rp, phase control rheostat with dial; Cp, capacitor.

Part 2, C_3, phase control switch (dpdt).

Variation of Rp permits a continuous change in the phase of the switching signal applied to TR over a range of approximately 150°; flipping of switch S_3 introduces an abrupt 90° shift in the phase of the switching signal applied to TR.

speeds, show changes in carotid blood flow in a conscious cat exposed to various sensory and emotional stimuli (see legends). The possibility of using this method for studies of effects of emotional stress on blood circulation through various organs is obvious. Of special interest is the possibility of taking simultaneous recordings from implants about arteries supplying different organs for studies of redistribution of blood flow in response to various physiological and psychological stimuli. Experiments of this kind are now in progress.

Miniaturization of the Flow Meter Design.—The possibility of designing symmetrical tuned a-c amplifiers (Figs. 1*a* and 1*b*) capable of yielding an adequately measureable output, with input signals of the order of 1 μV at a noise level not exceeding 0.2 μV, makes it practical to sacrifice field strength and efficiency of the magnet in favor of a greatly simplified design offering maximum ease of construction and a minimum of irritation in the animal's body by reduction in size of the implant. With an artery of 1.5 mm diameter, a magnetic field of 200 gauss will yield a flow signal of approximately 17 μV for a flow of 1 cc/sec. The design described below corresponds approximately to these specifications.

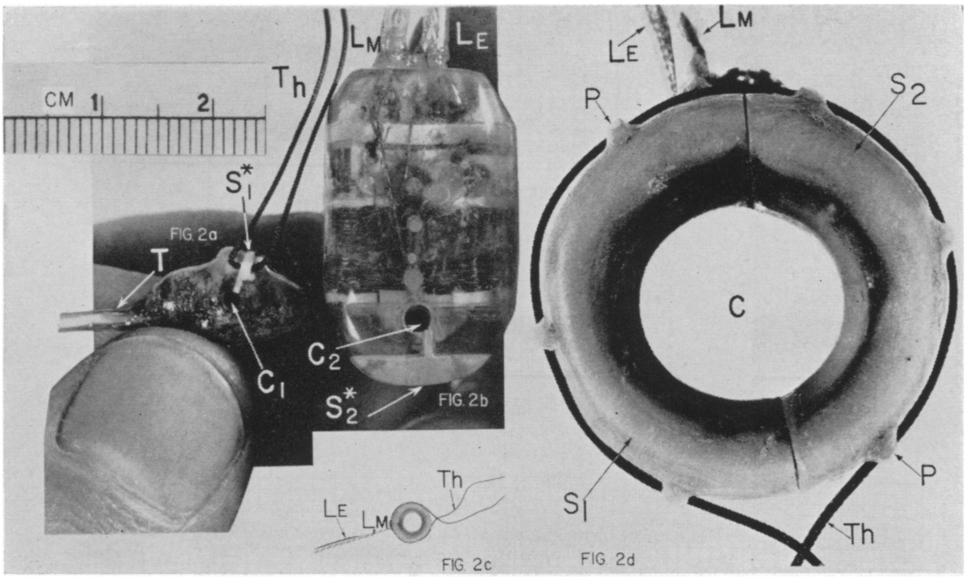

Fig. 2.—Comparison between different designs of implantable blood flow meters.

(2*a*) Subminiature unit for an artery 1.5 mm in diameter. T, polyvinyl chloride tubing containing the leads; C_1, channel for insertion of the blood vessel; S^*_1, shutter closing the slit through which the blood vessel is inserted into the channel C_1; Th, thread which facilitates handling the shutter S^*_1.

(2*b*) The original design (ref. 7) for a 2-mm blood vessel. L_M, magnet leads; L_E, electrode leads; C_2, channel for blood vessel; S^*_2, shutter.

(2*c*) The coreless flow meter, shown in Figure 2*d* in proper proportion in relation to the units depicted in Figures 2*a* and 2*b*, is shown reduced in size to match the diameter of channel C_1. L_E, electrode leads; L_M, magnet leads; Th, thread.

(2*d*) Flow meter for a blood vessel of 1.5-cm. diameter (shown reduced $^1/_{10}$ in Fig. 2*c*) utilizing no iron core. The bent coreless coils are sealed in plastic material in the two sections S_1 and S_2 which can be separated; the section S_1 contains both electrodes; C is the channel for the blood vessel formed by uniting the sections S_1 and S_2; L_E, electrode leads; L_M, magnet leads; Th, thread which is tied to prevent the sections S_1 and S_2 from coming apart after insertion of the blood vessel; P, plastic protrusions with perforations through which the thread Th is passed.

The flow transducer skeleton, shown in Figure 4*a*, consists of 3 main parts, C_1, C_2, and S. C_1 and C_2 are coils generating the magnetic field. They are connected in series through the terminals W_2 and W_3 which are grounded through wire G. Each coil consists of 200 turns of AWG #36 teflon insulated copper wire wound on an iron core I.† The ends of the cores I_1 and I_2 are connected by a grounded wire J (only the upper connection is shown). A current of 200 mA (rms) is used for continuous operation yielding a magnetic field of approximately 200 gauss peak value. 400 mA may be used for short periods of time in intermittent operation.

S is the lucite "sleeve" into whose channel C the blood vessel is slipped through the slit S1 (the width of S1 should be between $^1/_4$ and $^1/_3$ of the artery diameter). The electrodes E_1 and E_2 (0.5 mm gold wires) which are filed flush with the wall of channel C, establish the contact with the vessel. The flow signal picked up by the electrodes is conveyed by the leads L_1 and L_2 to the amplifying and recording system. The lead L_2 runs through a thin, shallow groove (not shown in the figure) to the electrode E_2. It is desirable, in order to minimize the "transformer emf" (see below), that the plane passing through this groove and the center axis of the elec-

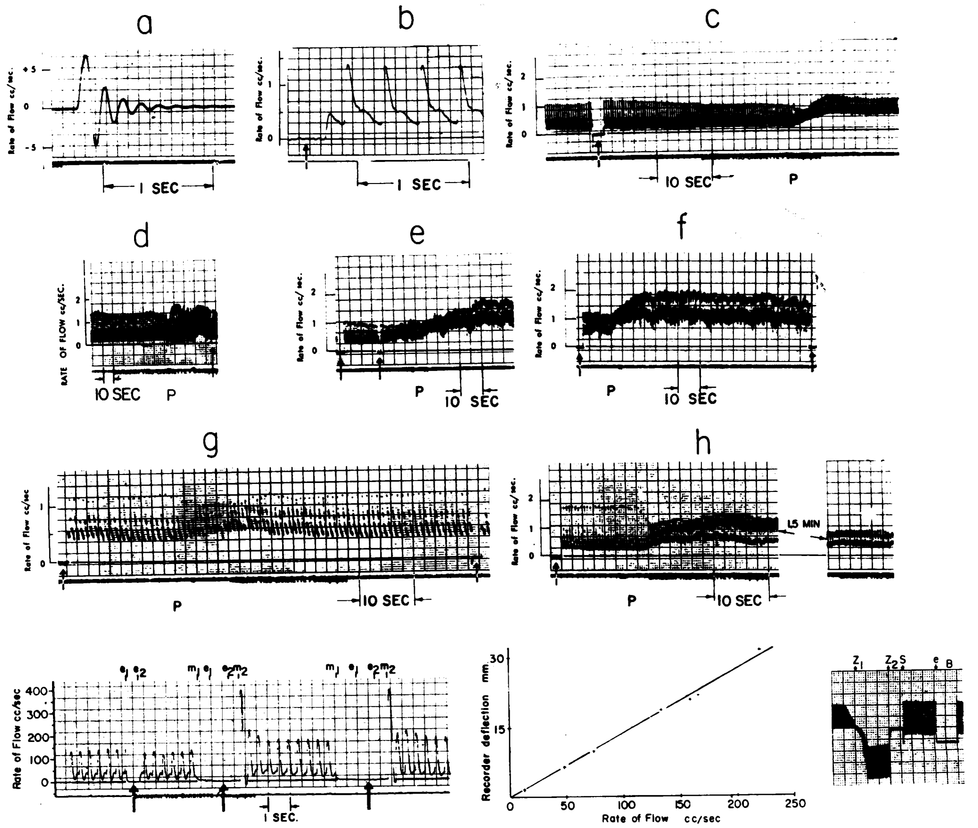

FIG. 3.—Examples of flow records.

(3*a*) Illustration of the ability of the flow meter to record rapidly varying flow in magnitude as well as in direction. This record depicts a damped oscillation of a liquid column in a conduit.

The following records *c–h* show changes in the rate of blood flow through the right carotid artery of a conscious cat in response to various sensory stimuli. The freedom of motion of the cat is limited only by the lead wires 10 ft in length. The arrows indicate base-lines ascertained by switching off the magnet; the continuous base-lines have been drawn in accordance with these sample base-lines. The records shown have been taken over a period of approx. 4 months following the implantation.

(3*b*) Normal variation of blood flow throughout the cardiac cycle.

(3*c*) Exposure of cat to ammonia fumes at point P.

(3*d*) Sleeping cat is awakened at P by a tactile stimulus.

(3*e*) Increase in systolic as well as diastolic blood flow in response to the odor of catnip presented at P.

(3*f*) Response to presentation of food at P and subsequently increased blood flow during the process of eating. It is noteworthy that immediately following P, the relative increase in diastolic flow is much greater than the relative increase in systolic flow.

(3*g*) Transient drop in systolic flow coupled with an increase in diastolic flow immediately following a startling light stimulus (a photographic flash exposure close to the cat's eyes at P).

(3*h*) Fright reaction induced by exposure of the cat to a dog at P. There is a sharp drop in systolic blood flow coupled with a rise in diastolic blood flow and an increase in heart rate. The last brief record section, taken two minutes after the fright stimulus, shows a persistent notable reduction in systolic blood flow.

(3*i*) Blood flow in the descending thoracic aorta of an anesthetized dog (27 kg) obtained with a flow meter of the design shown in Figures 2*d* and 4*c*. The arrows indicate base-lines obtained by switching the magnet current off (at e_1) and on (at e_2). The record also shows the close agreement between the base-lines thus obtained and the determination of the base-line by clamping the artery off (at m_1) and releasing it (at m_2). The compression interval between m_1 and m_2 is approximately 2 sec. The first systolic blood flow pulse (reinforced by retouching) following the occlusion of the artery is about three times as large as the preceding normal ones and is followed by blood flow notably above the normal level.

(3*j*) Calibration graph showing instrument reading as a function of flow rate for a flow meter of the type shown in Figures 2*d* and 4*c*.

(3*k*) Illustration of the method of adjusting the switching phase (see text).

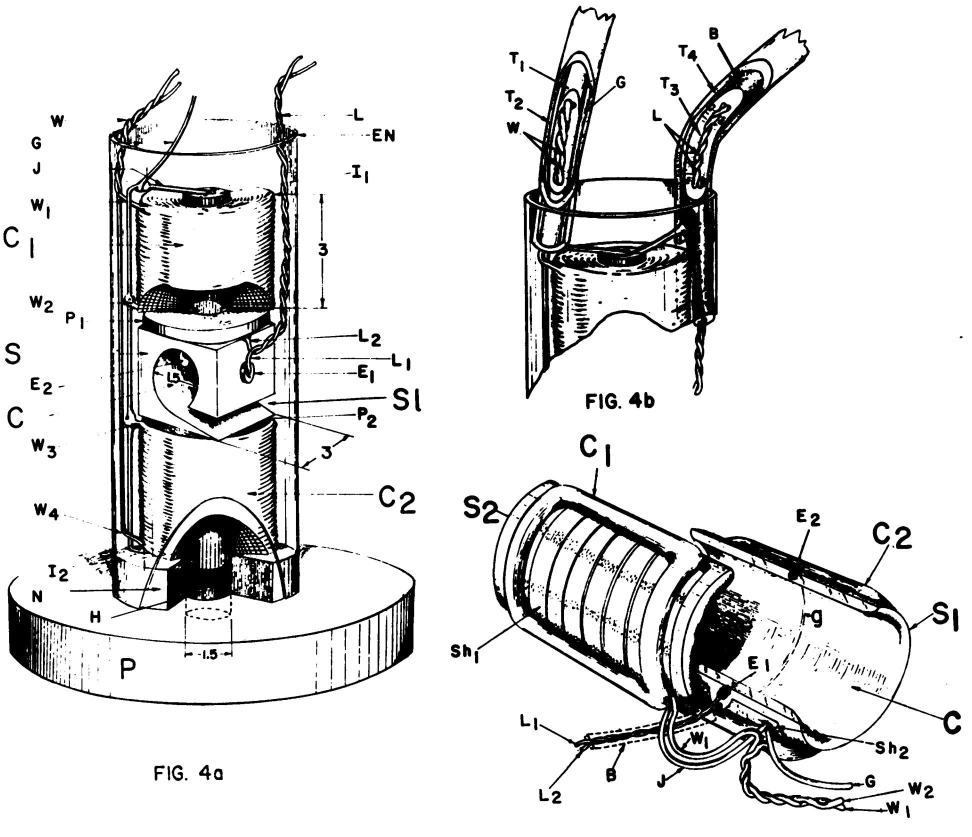

FIG. 4a

FIG. 4b

FIG. 4c

Fig. 4.—Flow meter designs in which the volume occupied by the magnet is greatly reduced as compared to the volume occupied by the artery.

(4*a*) Subminiature flow meter for a 1.5 mm artery. (The dimensions are given in the diagram in mm.) The unit is shown with accessories used for its fabrication. C_1 and C_2, magnet coils; S, sleeve; P, pedestal; N, pedestal neck; H, hole; I_1, I_2, iron cores of coils C_1, C_2; E_1, E_2, electrodes; Sl, slot; P_1, P_2, lucite mounting plates; L_1, L_2, electrode leads; W_1, W_2, W_3, W_4, coil terminal wires; J, wire joining the cores I_1 and I_2; G, ground lead; W, magnet leads; L, electrode leads; EN, cellulose envelope serving as a mold in the process of casting.

(4*b*) Shielding and insulation of the leads. The symbols for the wires have the same meaning as in Figure 4*a*. T_1, T_2, T_3, and T_4, polyvinyl chloride tubing. B, grounded wire braid shielding the electrode leads.

(4*c*) Coreless flow meter, especially suitable for large arteries. S_1, S_2, two sections which, when united, present the aspect shown in Figure 2*d* (after coating the coils with plastic material and insulating the wires with polyvinyl chloride tubing). The section S_1 contains the electrodes E_1 and E_2. C_2, magnet coils; C, channel for artery; g, groove for electrode lead L_2 (on the convex side of section S_1); Sh_1, Sh_2, silver shields [the "ribs" of Sh_1 (see text) can be seen framed by coil C_1]; L_1, L_2, electrode leads; W_1, W_2, magnet coil leads; G, ground lead; J, grounded wire joining the shields Sh_1 and Sh_2; B, grounded wire braid shielding the electrode leads L_1 and L_2. The insulation of the leads and their attachment to the flow meter body are as described in the text in connection with Figure 4*b*.

trodes be as nearly as possible parallel to the magnetic field lines. It is also important for the electrode axis to be as nearly as possible perpendicular to the axis of channel C to minimize pick-up due to possible axial currents passing through channel C.

P_1 and P_2 are lucite centering plates cemented to the sleeve S. Protrusions of the cores I_1 and I_2 fit snugly into central holes provided in these plates. The axes of the cores are thus aligned so as to pass through the electrode axis intersecting it at right angles. The coils and sleeve are assembled as shown in Figure 4*a* with the bottom protrusion of Core I_2 inserted into the hole H in the neck N of the pedestal P. The channel C and slit S1 are filled with Wood's metal prior to mounting the assembly on the pedestal. A cylindrical envelope EN of cellulose adhesive tape is wrapped around the neck N of the pedestal surrounding the assembly, as shown in Figure 4*a*. The nonadhesive surface of the tape is turned inward. The assembly is now ready to be cast in a nonirritant plastic material. "Teets denture material" (TDM) has been used successfully for this purpose. The polymerizing liquid is poured into the mold shown in Figure 4*a* which is placed into a vacuum desiccator. Evacuation for about 2 minutes removes air from small crevices so that on reestablishment of atmospheric pressure, the monomer is forced into the interspaces between the coil wires and other crevices. After completion of the polymerization, within about a half hour, the casting may be hardened by curing for about a half hour at 100°C.

The final step consists of insulating the lead wires by insertion into polyvinyl chloride tubing. It is most important to secure a watertight seal of this tubing to the plastic body of the flow transducer. The ends of the tubing are submerged into the polymerizing liquid which is poured into the mold over the upper coil C_1 so as to cover the protrusion of the core I_1. The tube ends are pre-soaked in the monomer for about one hour before submersion in TDM. This secures a leak-proof bond.

The arrangement of wires and insulators is shown in Figure 4*b*. The symbols have the same meaning as in Figure 4*a*. T_1, T_2, T_3, and T_4 are thin polyvinyl chloride tubes.‡ B is a thin wire braid which shields the electrode leads L. It is grounded by connection (not shown in the figure) to the ground lead G. The terminals of the wires W, L, and G are attached to small plugs. A gold plated-wire connected to ground wire G is permitted to emerge from the interior of the transducer to the surface for the purpose of grounding the animal.

The shape of the slit is seen in its initial stage in Figure 4*a*. The final shape is determined by the teflon shutter S_1^* shown in Figure 2*a*. After the flow meter is removed from the mold, some plastic material is filed away to expose the Wood's metal. The latter is removed from C and S1 by melting. The lower portion of the prefabricated shutter S_1^* is then inserted into S1 and the shutter is completely covered with TDM paste. After hardening of the paste, a sliding bed, fitting exactly the contour of the shutter, is obtained in which the shutter slides freely in and out. The thread Th facilitates its handling.

The flow meter is completed by depositing TDM paste at the lower end of the assembly to insulate the tip of the iron core I_2. After the plastic material has become hard, the unit is filed to the desired shape and polished and the sharp edges at the ends of the channel C are rounded. It is recommended to coat the outer flow meter surface and the adjacent polyvinyl tubing with a coat of a 10 per cent solution of polyvinyl chloride in cyclo-hexanone.

Coreless Flow Meter for Large Arteries.—A similar principle of design can be used for large transducers. The large flow in major blood vessels permits the reduction of the magnetic field to the order of magnitude of 10 gauss S.[§] In this case "miniaturization" consists in greatly reducing the volume of the magnet in comparison to the volume of the artery channel C. Figure 4*c* shows the skeleton of a flow meter, using no iron core, for an artery of 1.5 cm diameter. Figure 2*d* shows the end-on view of a flow meter of this type in correct proportion as compared to Figures 2*a* and *b*. The bent coils C_1 and C_2, using only 50 turns per coil, are cemented directly to the sleeve. Gauge #29 teflon insulated wire is used at 1 amp in continuous operation. A field of 20 gauss is obtained at the center of C. Figure 3*j* shows the linear calibration obtained with a unit of this type and Figure 3*i* shows normal flow tracings taken in the descending thoracic aorta of an anesthetized 27 kg dog. The baselines marked by arrows were secured by switching off the magnet. The two last baselines were taken so as to compare the effects of occluding the artery with switching off the magnet (see legend). Both base lines are seen to coincide as expected. The large increase in blood flow following an occlusion of the aorta for a little over 2 seconds is noteworthy.

To depict the reduction in space occupied by the magnet in this unit, as compared with the designs shown in Figures 2*a* and *b*, the aperture of the unit shown in Figure 2*d* has been reduced to 1.5 mm in diameter as shown in Figure 2*c*.

The Electronic Circuit.—The important step of ascertaining the base line corresponding to zero flow without interruption of flow is accomplished by special circuit design rather than through special adjustment of the flow meter sleeve previously described.[8] Phase sensitive rectification of the sinusoidal amplifier output is accomplished by a transistor switching circuit (Fig. 1*b*) which is triggered by rectangular voltage pulses controlled by a phase-shifting network. The latter is adjusted so that the transistor switch TR is open at the moment when the flow signal which is in phase with the magnetic field, is maximal. At this moment the "transformer emf" induced by the changing magnetic field in the loop formed by lead L_2 which runs from electrode E_2 toward electrode E_1 (Fig. 4*a*) is zero. Thus, this adjustment secures optimum rectification of the flow signal and rejection of the transformer emf which is in phase quadrature with respect to the flow signal. This method of rectification with phase discrimination yields an output which reverses direction with reversal of flow. This property is illustrated by the record of damped oscillations of alternating fluid flow in a conduit in Figure 3*a*. The rejection of the transformer emf is illustrated in Figure 3*i* where the base line does not change when the magnet is switched off after stopping the blood flow by clamping the artery.

Rectification of flow signals by means of a somewhat more complex gating circuit using exclusively vacuum tubes has been described previously in connection with flow meters actuated by square wave current pulses.[9] The present circuit, utilizing a transistor switch, accomplishes the same purpose more simply with sinusoidal currents energizing the magnet. The first suggestion of use of a gating circuit with an electromagnetic flow meter appears to have been made by James.[10]

The various sections of the electronic circuit shown in Figures 1a and 1*b* interact as follows. The power amplifier shown in Figure 1*a* supplies the 400 cps current to the magnet. It derives its input signal from the oscillator section which also supplies the synchronizing signal to the switching circuit. The flow signal is derived from the electrodes E_1 and E_2 of the flow meter and is conveyed to the input of the preamplifier whose input is connected to the differential amplifier of Figure 1*b*. The output signal of the latter passes through the switching circuit controlled by the transistor switch TR. The rectified output of this circuit reaches the pen recorder (SANBORN "Polyviso" Model 67-1200).

The remainder of the circuit shown in Figure 1*b* serves the important purpose of delivering properly synchronized voltage pulses to the transistor switch TR to insure that the flow signal is sampled at the moment when the transformer emf is zero. The switching pulses, lasting about $^1/_{20}$ of a cycle, are derived from the multivibrator which is triggered by pulses derived from the squaring circuit. The phase of the output of the squaring circuit is controlled by the signal fed into it from the phase-shifting circuit which, in turn, receives its input signal from the oscillator section (Fig. 1*a*). The phase-shifting circuit consists of two sections. The first one permits a continuous variation in phase over a range of about 150° by control of the rheostat Rp which is in series with the capacitor Cp. The second part permits the introduction of an abrupt 90° jump in phase in the signal delivered to the squaring circuit through flipping the d.p.d.t. switch S_3. The continuous and discontinuous phase shifts are used as follows in adjustment of the instrument for rejection of the transformer emf. We make use of the fact that the arterial blood flow is pulsating. Thus, when we adjust the resistor Rp so as to reduce the pulsations in our signal to zero, we know that we are sampling our flow meter output at the most inappropriate moment, namely, when the pulsating flow signal is zero and the transformer emf is at its maximum. Flipping the switch S_3 shifts the switching phase through 90° and thus reverses the situation. The switch TR transmits now the flow signal to the recorder at the maximum point of the signal at which time the transformer emf is zero. This procedure of adjustment is illustrated in Figure 4*k*. As the resistor Rp of the phase shifting circuit (Part I, Fig. 1*b*) is varied, a point Z_1 is reached at which the recorded upward pulses, caused by pulsating blood flow, vanish. When this point is passed, the recorded pulses are directed downward due to reversal of the switching phase of the transistor TR(Fig. 1*b*). The point Z_1 determines the dial setting of Rp for elimination of the flow signal. When Rp is left at the setting corresponding to Z_1, a line Z_2 is recorded whose height above the baseline B measures the transformer emf. At S the switch S_3 of Fig. 1*b* is flipped and the transistor switch TR is phased to sample the flow signal and reject the transformer emf. The blood flow record between points S and e is thus obtained. At e the magnet is turned off and the baseline B is obtained. At the end of the section B, the magnet is turned on again.

The flow meter design and circuitry described herein extend the applicability of the electromagnetic flow meter to blood vessels down to the size of 1 mm in diameter and possibly to smaller ones, making it possible to tackle problems on localized regional blood flow in conscious animals which could not be attempted heretofore because of the large bulk of the implant.

Summary.—A high gain low noise amplifying system coupled with a properly synchronized switching circuit makes it possible to minimize the bulk of the magnet of an electromagnetic flow meter. Designs are described permitting blood flow measurements in arteries ranging from about 1 mm to over 15 mm in diameter. The magnet is energized with 400 cps ac. The base-line is established by switching off the magnet. Illustrations of blood flow changes in a conscious, freely moving animal in response to sensory stimuli are given.

* This work has been supported by a grant from the Office of Naval Research.

† Nonlaminated round iron rods can be used for magnets of the small size shown here. For artery diameters above 2 mm, laminated cores of grain-oriented silicon steel are recommended.

‡ Tubing of greatly reduced diameter can be easily obtained from available tubing by stretching and heating it in an oven to approximately 120°C. for about a half hour.

§ For instance, for an aorta of 2 cm diameter and an average linear fluid velocity of 50 cm/sec, a field of 10 gauss will yield a flow signal of 10 μV.

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[3] *Ibid.*, 122, 797 (1938).

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