and $y_n(r)$ are the eigenfunctions defined by equation (32) in close analogy with the usual Fourier-Bessel expansions.

5. *Concluding Remarks.*—As we have indicated in the Introduction, expansions of the type considered here should prove useful in the solution of many hydrodynamic and hydromagnetic problems. In particular, the classical problems of the stability of viscous flow between rotating cylinders[5] and in a curved channel,[6] which have never been solved when the spacing between the cylinders is comparable with their radii, can be treated by this method.

We wish to acknowledge with thanks Miss Donna Elbert's assistance in the numerical work. During the course of this work, one of us (W. H. R.) was in receipt of a postdoctoral fellowship from the National Science Foundation.

This research reported in this paper has in part been supported by the Geophysics Research Directorate of the Air Force Cambridge Research Center, Air Research and Development Command, under Contract AF 19(604)-2046 with the University of Chicago.

[1] Lord Rayleigh, *The Theory of Sound* (New York: Dover Publications, Inc., 1945), **1**, 278.

[2] S. Chandrasekhar, "On Characteristic Value Problems in High Order Differential Equations Which Arise in Studies on Hydrodynamic and Hydromagnetic Stability," *Am. Math. Monthly*, **61**, 32–45, 1954.

[3] S. Chandrasekhar, "The Stability of Viscous Flow between Rotating Cylinders," *Mathematika*, **1**, 5–13, 1954.

[4] G. N. Watson, *A Treatise on the Theory of Bessel Functions* (Cambridge: At the University Press, 1944).

[5] G. I. Taylor, "Stability of a Viscous Liquid Contained between Two Rotating Cylinders," *Phil. Trans. Roy. Soc. London, A*, **223**, 289–343, 1923.

[6] W. R. Dean, "Fluid Motion in a Curved Channel," *Proc. Roy. Soc. London, A*, **121**, 402–420, 1928; C.-S. Yih and W. M. Sangster, "Stability of Laminar Flow in Curved Channels," *Phil. Mag.*, ser. 8, **2**, 305–310, 1957.

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*ELECTROMAGNETIC DETERMINATION OF REGIONAL BLOOD FLOW IN UNANESTHETIZED ANIMALS**

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The interest in a method for continuous registration of blood flow in essentially normal conscious animals goes beyond the objective of studying flow as a circulatory parameter. By far the greatest utility of such a method would be in permitting the study of the activity of a great variety of organs by one single method. The rate of blood supply to an organ is an important parameter, revealing its rate of activity, which determines the required rate of supply of oxygen, hormones, and nutrient materials as well as the rate of removal of products of metabolism. The blood flow through an organ, when correlated with its state of activity, could be used to follow the variations in the activity of the organ. Thus it may become possible,

in studies aiming at initial detection of the effectiveness of various stimulating and inhibiting factors affecting various organs, to replace discontinuous and often cumbersome chemical tests of secretory or excretory functions of these organs, used as an index of their activity, by a continuous record of blood flow. The applicability of such studies to the solution of pharmacological and physiological problems as well as to investigations in experimental pathology is obvious.

An ideal method for the determination of regional blood flow in normal animals should have the following characteristics: it should measure flow through intact blood vessels; the blood vessel should be left in its normal place and not be exposed; the measuring device and procedure should be such that drugs (such as heparin or anesthetics) would not be needed, the animal being as nearly as possible in its normal state; the inserted instruments should be suitable for chronic implantation; the relation between blood flow and instrument reading should be linear and independent of variations in phyiscal factors like temperature, viscosity, velocity profile (laminar or turbulent flow), etc.; the response of the instrument to velocity changes should be instantaneous; and frequent calibrations of the instrument should not be necessary. It is believed that the method to be described below is the nearest approach so far to these desired ideal conditions.

1. *Principle and Development of the Method.*—The principle of the method is based on the phenomenon of electromagnetic induction discovered by Faraday. Faraday demonstrated the generation of electromotive forces (emf's) in closed electric circuits traversed by a varying magnetic flux, as well as in solid conductors moving at right angles to a magnetic field (Faraday's unipolar inductor). Faraday could easily have demonstrated, by means available in his laboratory, the induction of an emf in a liquid traversing a magnetic field, by allowing mercury to flow through a pipe disposed at right angles to the magnetic field and by picking up the voltage induced in the moving liquid by means of two electrodes disposed at the ends of the pipe diameter perpendicular to the magnetic lines of force (Fig. 1*A*). Strangely enough, Faraday did not perform such an experiment but, instead, spent a considerable amount of time conducting experiments at the Waterloo Bridge in London, trying to demonstrate the induction of an electromotive force in the River Thames as its water moves across the magnetic field of the earth. Owing to difficulties caused by polarization of the electrodes, Faraday finally gave up these experiments. This negative result is mentioned by him in a Bakerian lecture.[1]

The qualitative idea of the possibility of inducing an emf in a moving fluid, which Faraday evidently conceived, is, owing to complications introduced by the velocity distribution in the flowing fluid, still considerably removed from the realization of the possibility of quantitative measurement of flow by electromagnetic induction. The importance of this factor was realized by Williams,[2] who, in fact, used electromagnetic induction for an indirect determination of the velocity distribution in pipes, using a special nonpolarizable system (copper electrodes in a copper sulfate solution). Although Williams' results imply the possibility of development of a flowmeter based on electromagnetic induction, there is no such suggestion made in his paper. That paper was not followed by further publications on this subject.

Unaware of the work of Williams and Faraday, Fabre proposed in a letter to the French Academy of Sciences[3] a qualitative biological use ("un hémodromograph sans palette") for electromagnetic induction. His note suggested the possibility of

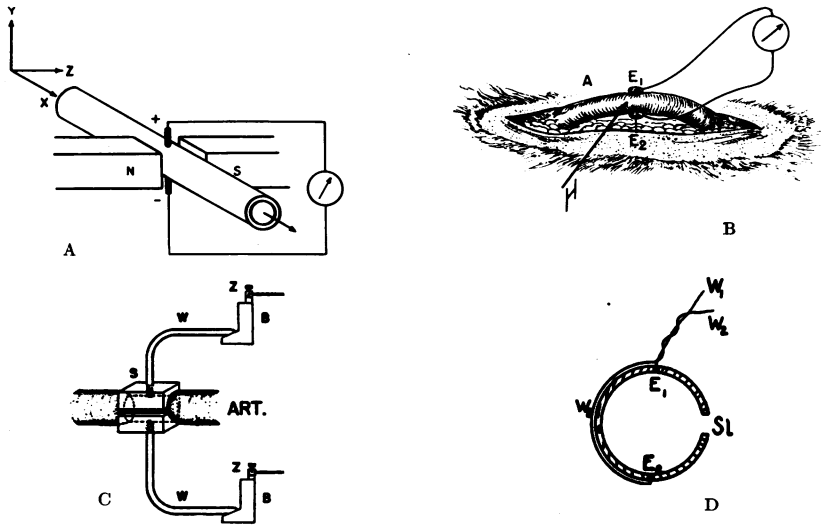

FIG. 1*A*.—Scheme of electromagnetic flowmeter. *N* and *S*, pole pieces of magnet; + and −, electrodes which pass through the pipe wall to make contact with the fluid.

FIG. 1*B*.—Scheme for determination of blood flow in intact artery. *H*, magnetic field vector; *A*, artery; E_1 and E_2, nonpolarizable electrodes touching the artery wall.

FIG. 1*C*.—Pickup sleeve *S* with artery and nonpolarizable electrodes. *W*, wicks soaked in agar-saline; *B*, porous clay boots filled with zinc sulfate; *Z*, amalgamated Zn electrodes.

FIG. 1*D*.—Pickup sleeve with metal electrodes. *Sl*, slit through which artery is slipped into the sleeve channel; E_1 and E_2, pickup electrodes contacting the artery; W_1 and W_2, electrode lead wires.

detecting variations in flow of blood through a pipe equipped with electrodes and tied between the two parts of a cut blood vessel. His discussion was qualitative, and no experimental evidence was presented. The instrumentation described by him could not have permitted measurement of the rate of flow, which evidently was not attempted. This note was not followed by further publications on this subject.

The above publications have had no effect on the development of the electromagnetic flowmeter. The method was developed independently by investigators who have been unaware of the close approaches of the preceding authors. In 1936 it was demonstrated[4] that electromagnetic induction could be used for quantitative determination of fluid flow in pipes, and the anticipated linear relation between the volumetric rate of flow and induced voltage was demonstrated. Furthermore, it was shown that flow of blood through arteries could be recorded without injuring the artery wall, merely by applying nonpolarizable electrodes to the outside of the walls of the artery at the ends of its diameter perpendicular to the magnetic field (*H*) (Fig. 1*B*). At the same time, the instantaneous response of the apparatus to rapidly pulsating flow was demonstrated, and the average rate of flow of blood through a dog's carotid artery was determined. The instrumentation used in this communication was very simple, consisting of a d'Arsonval galvanometer for average-flow measurement and a string galvanometer for recording of instantaneous flow. In the subsequent communications[5–7] the use of a chopper amplifier was described, and a sleeve was introduced for convenient application of nonpolarizable electrodes (Fig. 1*C*).

Shortly after Kolin's 1936 publication,[4] an independent paper by Wetterer appeared,[8] describing the same method in a form very similar to that presented by Kolin. Experimental evidence in the form of calibration curves and blood-flow records was presented. The use of a d.c. amplifier was described in a subsequent paper.[9]

The initial version of the method, as described by Kolin[4, 5, 7] and Katz and Kolin,[6] utilizes a constant magnetic field, so that a d.c. emf is induced with unidirectional flow. This necessitates the use of nonpolarizable electrodes and of a suitable system of d.c. amplification. The nonpolarizable electrodes are quite cumbersome in use,[10] and d.c. amplifiers are, as a rule, less stable than a.c. amplifiers. The next logical step thus consisted of replacing the constant magnetic field by an alternating one.[11] In this case, an a.c. emf is induced in the case of unidirectional flow, so that nonpolarizable electrodes become unnecessary, ordinary metal electrodes touching the artery wall being quite adequate (Fig. 1*D*). An a.c. amplifier can be used to detect the signal induced due to flow of blood. It is, however, necessary to use a special compensator,[12] in order to adjust for a zero reading at zero flow. Such zero adjustment requires temporary occlusion of the blood vessel by special occlusion clamps or pneumatic devices.[11, 13, 14]

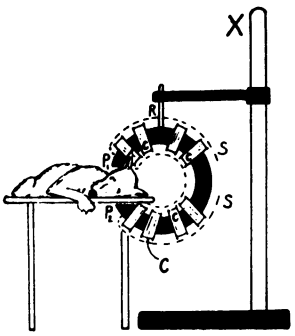

FIG. 2.—External magnet used in conjunction with imbedded sleeve of type shown in Fig. 1*D*. P_1 and P_2, magnet pole pieces; *C*, magnet coils; *S*, grounded shield. (From A. Kolin, *Rev. Sci. Instr.*, **23**, 235, 1952.)

In the initial experiments[4–11] the blood vessel, usually an artery, had to remain exposed during the measurement of blood flow. Thus anesthesia had to be maintained. A step toward elimination of anesthesia was taken by implanting the lucite sleeves containing the pickup electrodes into the animal, leaving the blood vessel in its normal place.[13, 14] In addition, a way was found to establish a zero base line without occluding the blood vessel to stop the blood flow.[15] This was accomplished by means of pickup sleeves with four electrodes. After the implantation of the pickup unit, the animal was placed in the gap of a large electromagnet (Fig. 2), and the flow was recorded as in previous modifications of the method.[14, 16]

The drawback of the above modification of the method lies in the necessity of maintaining the animal immobile in the magnetic field to avoid unbalancing the zero adjustment. The possibility of such a disturbance is avoided in the modification presented in this paper. This is achieved by a rigid coupling between the magnet, the electrodes, and the blood vessel. This coupling is accomplished by using a miniature magnet unit (Figs. 3*A* [front view] and 3*B* [side view]) with a pickup sleeve (*S*) fixed in its gap. This entire unit is implanted into the animal, the blood vessel under study being inserted into the pickup sleeve channel through the slit *Sl* (Fig. 3*C*).

2. *Design of the Miniature Flowmeter Implant.*—Figure 3*C* shows a photograph of a magnet used for flow measurement in the carotid artery of a dog. The lucite sleeve *S* is inserted in the gap of the magnet. It was found most practical to use miniature magnets manufactured for erase heads and recording heads of magnetic

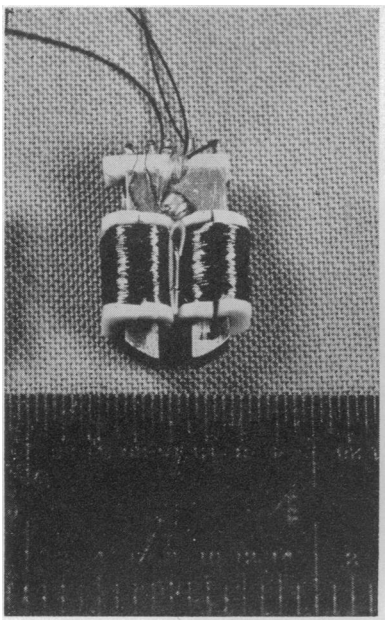

FIG. 3A.—Front view of magnet

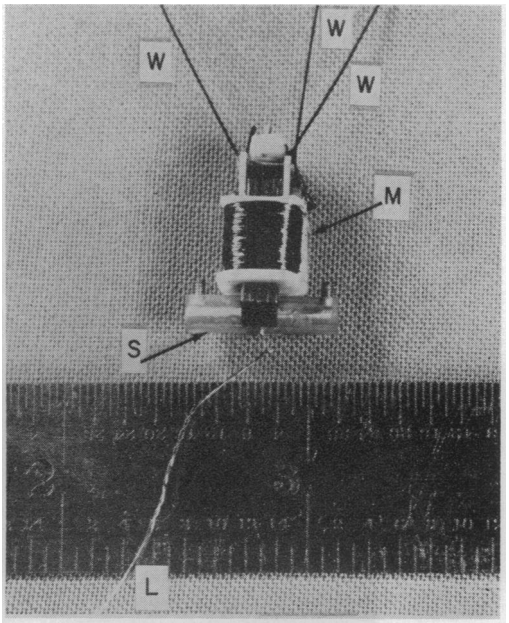

FIG. 3B.—Side view of magnet M and sleeve S. W, suspension wires; L, electrode lead wires (scale in inches).

tape recorders. The magnet shown is from a Brush Electronics Company magnetic-tape erase head, Model BK944. Its dimensions are indicated by the inch scale. Its weight was 5.5 gm. The coils had to be rewound on a nylon or teflon bobbin, since the commercially provided one dissolves in the monomer used in the polymerization process (see below). The total number of turns of both coils (#39 formvar insulated copper magnet wire) was 1,600, and the current used in continuous operation was 65 milliamperes, which resulted in a magnetic field of 800 oersteds in the gap. The electrodes were made of $^3/_4$-mm.-diameter brass rod. The tips of the brass electrodes, flush with the inner surface of the sleeve S, were gold-plated after the completion of the flowmeter unit. Figure 4 shows the sleeve S in the gap of the magnet M (greatly magnified). P_1 and P_2 are the magnet pole pieces, E_1 and E_2 are the electrodes, Sl is the slit, and W_1 and W_2 are the lead wires connecting the electrodes to the amplifier. W_1 has been shown for clarity inside the sleeve body, but actually it runs through a shallow groove in the lucite which is located between the sleeve and the pole piece P_1 coplanar with the line joining E_1 to E_2. The two wires W_1 and W_2 are twisted to minimize the emf induced in the input leads.

In order to secure adequate electrical insulation between the magnet wire, the electrode leads, and the animal, the combination of magnet and sleeve is cast into a block of plastic (methyl methacrylate). The limits of the plastic are indicated by dashed lines in Figure 4. The magnet lead wires and the electrode leads are insulated by separate flexible polyvinyl tubes ($^3/_{32}$-inch i.d.; $^1/_8$-inch o.d.) through which they run (T_1 and T_2). A ground wire connected to the laminated magnet core made of sheets of silicon steel ($^3/_8$ mm. thick) is imbedded in the same tubing as the magnet leads. The polyvinyl tubing is polymerized within the methyl meth-

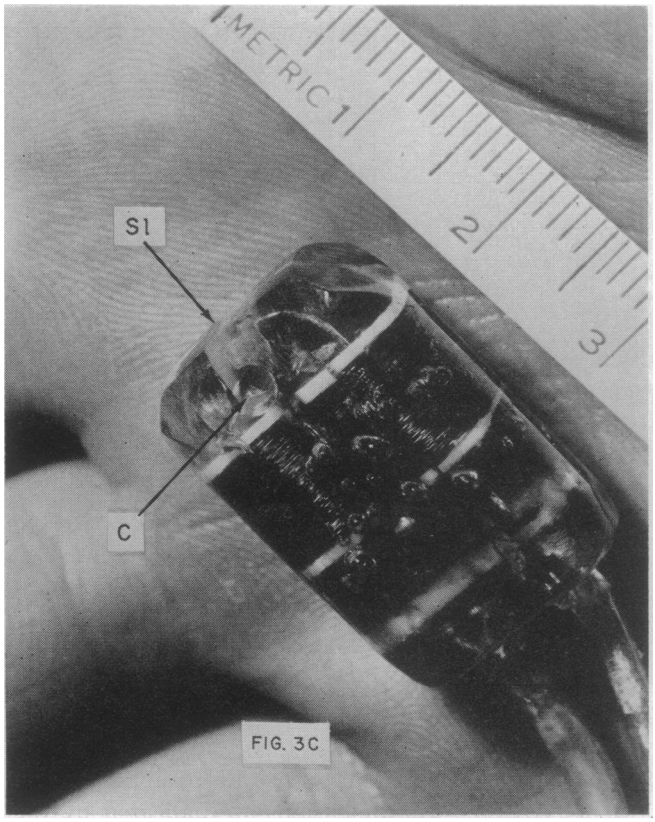

FIG. 3C.—View of flowmeter encapsulated in pastic. *Sl*, slit; *C*, artery channel.

acrylate plastic, so that a very secure watertight seal is achieved. The adequate moistureproof electrical insulation between the above-mentioned components of the system was the main experimental difficulty which had to be overcome. Miniature magnets, small enough to be inserted into the neck of a cat, were prepared by one of the authors (A. K.) in 1952 (unpublished), and successful tracings of blood flow in the cat's carotid artery have been obtained. But the flowmeter units were of limited value, owing to an inadequate seal between the polyethylene tubing which was used to insulate the leads and the insulating material encapsulating the magnet. The present method of insulation results in flowmeter units which remain in perfect condition even after prolonged implantation into an animal.

Figure 5 illustrates the casting procedure. The magnet M (seen in side view) is suspended with the gap (space behind P_1) facing downward in a glass vial V. The lucite sleeve S, with the pickup electrode E_1 showing at the bottom, is inserted in the gap. The polyvinyl tubing (T_1 and T_2) insulating the lead wires dips into the vial. The methyl methacrylate is then poured into the vial. The vial is now immersed for 6–8 hours in a constant-temperature bath kept at 120° F. One milligram of benzol peroxide is then added per cubic centimeter of monomer, to act as an accelerator for the polymerization process. The casting is accomplished by polymerizing several layers of the monomer successively. Upon completion of the polymeriza-

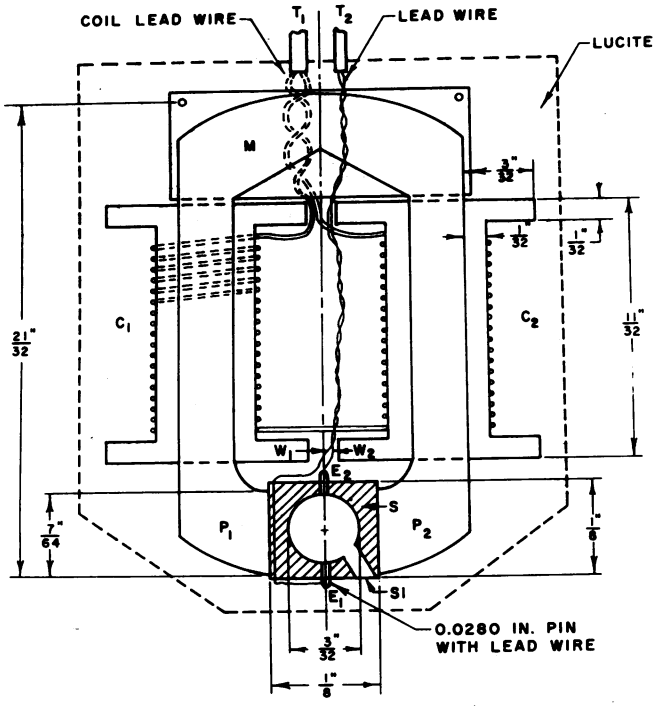

FIG. 4.—Front view of electromagnetic flowmeter. T_1 and T_2, insulating polyvinyl tubing; M, magnet core; C_1 and C_2, magnet coils; W_1 and W_2, electrode lead wires; E_1 and E_2, pickup electrodes; P_1 and P_2, pole pieces of magnet; S, pickup sleeve; Sl, slit.

tion process, the glass vial is broken and excess lucite (polymethyl methacrylate) is removed by abrasive action of a wet sanding-machine belt.

Prior to the polymerization, the cylindrical channel of the sleeve S (Figs. 4 and 5) is filled with a low-melting-point metal alloy (Cerrolow 136). This secures the alignment of the electrode pin (a $^3/_4$-mm. brass rod of which E_1 and E_2 are initially the ends) during the process of polymerization, during which the lucite sleeve, which supports the electrodes, may dissolve. After solidification of the plastic, the Cerrolow core is drilled out, and with it the portion of the brass rod which lies between E_1 and E_2. The surfaces of the electrodes E_1 and E_2 thus produced are flush with the inside wall of the sleeve. The last step consists in gold-plating the electrode tips electrolytically. After removal of all sharp edges and polishing, the flowmeter unit is ready for implantation. A more detailed description of the manufacturing process of the flowmeter units will be published elsewhere.

3. *Calibration and Response to Pulsating Flow.*—The emf (in volts) induced in a conducting liquid flowing through a pipe at right angles to a magnetic field is given by the expression

$$V = 10^{-8}\,\mu H d\bar{v}, \qquad (1)$$

where μ is the permeability, H is the magnetic field strength in oersteds, d is the

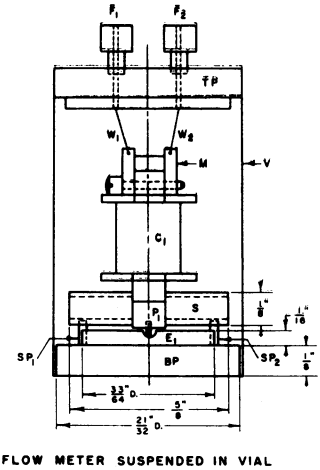

FIG. 5.—Magnet suspended in vial for encapsulation in plastic (side view). F_1 and F_2, clamps for fastening the suspension wires; W_1 and W_2, suspension wires; TP, top plate (aluminum); M, suspended magnet; C_1, one of the magnet coils; V, glass vial; P_1, one of the magnet pole pieces; S, pickup sleeve; E_1, protruding pickup electrode; BP, base plate (aluminum); SP_1 and SP_2, support pins.

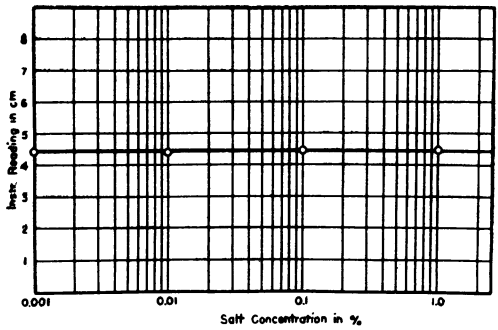

FIG. 6.—Independence of the flowmeter sensitivity of the electrical conductivity of the solution. A constant flow is maintained through an a.c. pipe flowmeter. The conductivity of the liquid is varied by varying the concentration of NaCl solution (*abscissa*). The instrument reading is measured by the ordinate. (From A. Kolin, *Rev. Sci. Instr.*, **16**, 109, 1945.)

diameter of the pipe in centimeters, and $\bar{v}$ is the average velocity of the liquid in centimeters per second.[4] This emf is independent of the electrical conductivity of the liquid (Fig. 6, reproduced from an earlier paper[16]) as well as of the velocity distribution, provided that the latter is axially symmetrical.[16] Contrary to intuitive expectation, the emf induced in the moving fluid for a given volume rate of flow is the same regardless of whether the fluid flows through a nonconducting pipe or through an artery whose electrical conductivity is nearly the same as that of the fluid. This is true regardless of the thickness of the artery wall.[14] This paradox is a consequence of the independence of the induced emf of the velocity distribution, as pointed out in an earlier paper.[14] It is thus unnecessary to calibrate the instrument with each individual artery. One single calibration, once performed without an artery, standardizes the instrument. These results do not depend on the character of the magnetic field used. They are valid for constant as well as for alternating fields; for sinusoidal as well as for nonsinusoidal ones, such as the square wave shape used by Dennison, Spencer, and Green.[17]

The linearity of the calibration is apparent from equation (1) and is verified by experimental results using an excised carotid artery (Fig. 7*A*, reproduced from a previous paper[14]). The same result is obtained when calibration is carried out with a pulsating flow *in vivo* (Fig. 7*B*). The instantaneity of the response of the flowmeter to variations in flow has been confirmed by Inouye and Kuga[18] through careful experimental studies.

It is sufficient to establish the calibration for one single size of pipe. The instru-

ment sensitivity for other diameters follows easily from the following consideration: The emf induced for the rate of discharge $Q = \pi R^2 \bar{v}$ is given by the equation

$$V = 10^{-8}\,\mu H(2R) \cdot \bar{v} = 10^{-8}\,\mu H \frac{2R \cdot Q}{\pi R^2} = \frac{10^{-8}\,2\mu HQ}{\pi R} \qquad (2)$$

V is thus inversely proportional to R at a constant rate of discharge Q. The sensitivity $S = V/Q$ can thus be expressed as follows:

$$S = \frac{K}{R} \qquad (3)$$

where $K = 10^{-8}(2\mu H/\pi)$ is an instrument constant. Having determined S for one particular diameter, we have calibrated the instrument for all artery diameters. In the case of the miniature-magnet method, one has the choice of perfusing the sleeve channel with saline at a known rate prior to cutting the slit *Sl* or of inserting

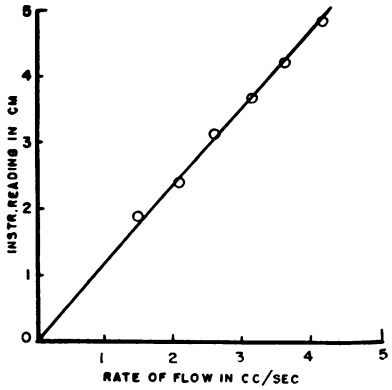

FIG. 7*A*.—Calibration curve for a.c. blood flowmeter. An excised carotid artery is perfused with blood at constant rates. (From A. Kolin, *Rev. Sci. Instr.*, **23**, 235, 1952.)

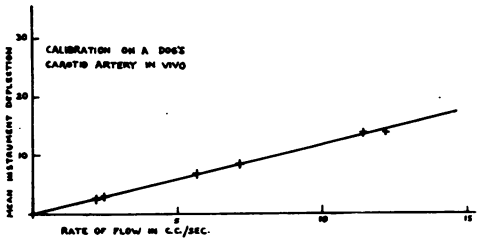

FIG. 7*B*.—Calibration is carried out with a pulsating blood flow through a dog's carotid artery *in vivo*. A constant-field flowmeter is used. (From A. Kolin, *Am. J. Physiol.*, **122**, 797, 1938.)

an excised artery through the slit and perfusing it with blood. Practically, the perfusion consists of ejection of a known volume of saline or blood through the flowmeter unit from a syringe while recording the flow signal. The record thus obtained is shown in Figure 10, *B*, *c*. The injection time is given by the extent of the record along the horizontal time axis. The ratio of the injected volume to this time is the average flow. The average-flow signal is obtained by planimetry of the record of the instantaneous flow and division of the area obtained by the horizontal extent of the curve. The ratio of the average-flow signal thus obtained to the average flow gives the instrument sensitivity in terms of the instrument reading in centimeters per unit flow of 1 cc/sec. In the experiments described below, the sensitivity was 4 mm. per cc/sec, but higher values can easily be obtained by increasing the amplification.

4. *Apparatus.*—The amplifying and recording apparatus used was essentially the same as described in a previous paper.[14] The magnet was energized by a 60-cycle alternating current. Figure 8 shows the block diagram of the apparatus. The signal voltage derived from the flowmeter *FM* is put in series with the output of the

compensator (*comp.*). The compensator voltage can be varied independently in phase and in amplitude,[14] by one single control knob. This permits rapid compensation of stray 60-cycle pickup in the input circuit which may mask the flow signal to be recorded. This compensation must be accomplished at zero flow. In order to be able to stop the flow through the artery, a pneumatic device was used. It is an improvement upon the occlusion bags described earlier.[14] Figure 9 shows the occlusion unit and its components. A tuning-fork-shaped form figure (*a*) is prepared from a low-melting-point alloy (Wood's metal). By repeated dipping of this form in a solution of polyvinyl in a suitable solvent ("Cadco 201"), a sufficiently strong skin of polyvinyl sheeting is formed on the surface of the metal after the evaporation of the solvent. The Y-shaped form is then dipped into water at 100° C. The metal form melts and flows out of the polyvinyl bag. The open central "tail" of the Y is cemented by polyvinyl cement (solution of polyvinyl in "Cadco 201") to a long polyvinyl tubing which is attached to a syringe, while the two remaining closed legs of the Y are imbedded in the animal, being placed about the artery as shown in Figure 9, *b*. A hull of tygon tubing, shown in Figure 9, *c*, is then pushed over the insert as shown in Figure 9, *d*, to prevent outward expansion of the bags and to insure perfect occlusion of the vessel when the syringe plunger is pushed in. The tygon hull is finally closed by stitches near the end of the split section. Figure 10 illustrates the effectiveness of this occlusion device. Short base lines, like those shown in Figure 10, are obtained frequently throughout the measurements, so that a continuous base line can be obtained by joining them. It is during such occlusion periods that the base line is occasionally rapidly adjusted to zero. Once the adjustment is made, readjustment is rarely required.

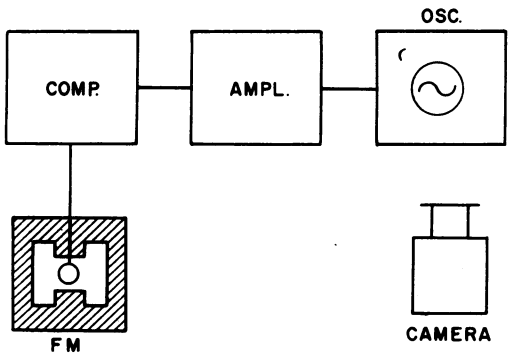

FIG. 8.—Block diagram of the flowmeter circuit. *FM*, the flowmeter transducer; *comp.*, compensator; *ampl.*, amplifier; *osc.*, oscilloscope.

The combined signals of the flowmeter and of the compensator are conveyed in series to the amplifier (RC-coupled single-ended 3-stage) input. The output signal of the amplifier is applied to the oscilloscope (*osc.*) (Dumont type 304), and the oscilloscope reading is recorded by a continuous automatically developing camera, as described in a previous paper.[14]

5. *Examples of Determination of Blood Flow in Unanesthetized Animals.*—Figures 10–12 show records of blood flow obtained with an implanted miniature flowmeter unit of the type described above. These records are not primarily intended to demonstrate physiological results but, rather, are presented as an illustration, obtained with one particular animal, of the possibilities of application of the new modification of the electromagnetic blood flowmeter.

The experiments presented below were obtained with a mongrel dog (weighing 14 kg.) two days after the implantation of the measuring unit. The dog was unanesthetized and was strapped in standing position to avoid moving too far from the

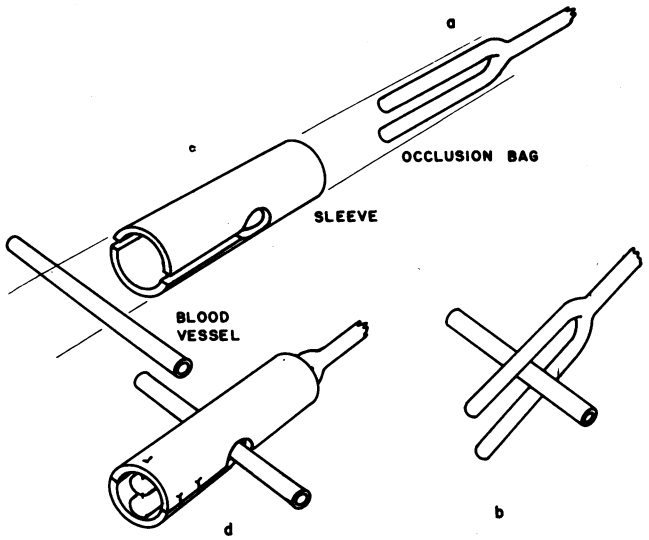

FIG. 9.—Components of the occlusion bag in relation to the artery

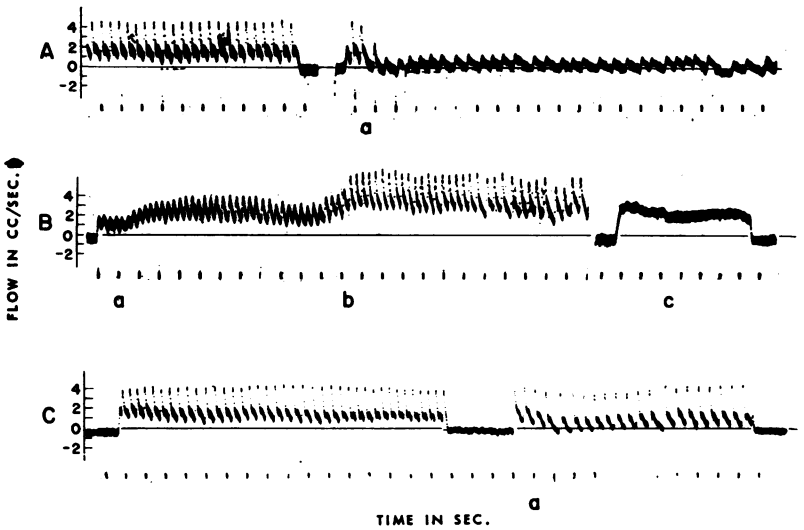

FIG. 10.—Effect of ether anesthesia upon blood flow in dog's left carotid artery and effect of inhalation of smoke. *A*, onset of ether anesthesia (mask applied at *a*). *B*, recovery from ether anesthesia (mask removed at *a*; dog regains consciousness at *b*; *c*, calibration record). *C*, effect of inhalation of smoke upon carotid blood flow; inhalation begins at *a*. The base line is obtained by pneumatic occlusion of the artery.

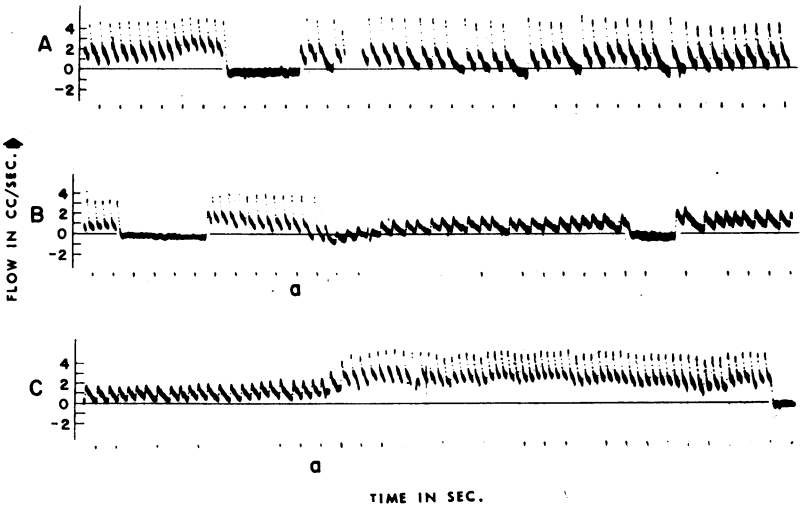

FIG. 11.—Effects of a visual stimulus and of a pharmacological agent upon blood flow through left carotid artery in dog. *A*, reaction to flame (a torch is presented to the dog at the interruption of the record). *B*, effect of amyl nitrite (inhalation begins at *a*). *C*, recovery from effect of amyl nitrite. The inhalation ends at *a*.

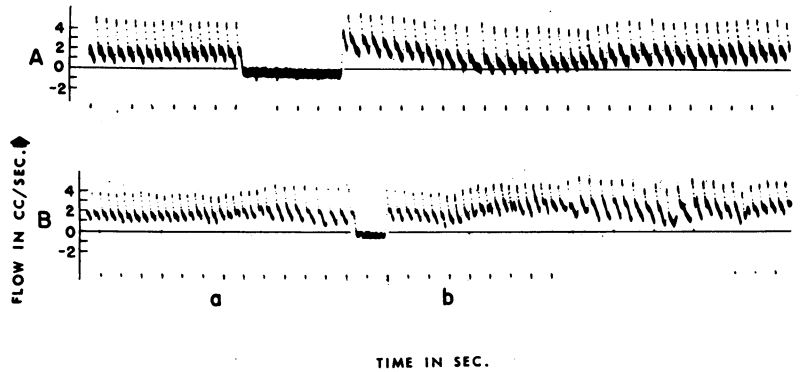

FIG. 12.—*A*, effect of occlusion of carotid artery interrupting the flow signal upon the subsequent carotid blood flow. Record taken in left carotid artery. The other carotid was tied. *B*, reaction to food. Blood flow in left carotid artery. Food is presented at *a*. Chewing and swallowing of the food begin at *b*.

recording apparatus. Blood flow was recorded in all the subsequent tracings in the left carotid artery; the right carotid artery was ligated. In Figure 10, *A* and *B*, the profound effect of anesthesia upon the blood flow in the carotid artery is illustrated. The first section of Figure 10, *A*, represents the normal control tracing. It is followed by a brief occlusion of the carotid artery to establish the base line at zero flow. The ether mask is then applied to the dog at *a*, which results in a marked reduction in blood flow. Figure 10, *B*, shows the increase in carotid blood flow during recovery from ether anesthesia. The mask is removed at *a*. The sharp increase in flow upon regaining consciousness at *b* is noteworthy (*c* is a calibration record). Figure 10, *C*, shows a marked effect of inhalation of cigarette smoke (inhaled at *a*) upon the carotid blood flow.

In Figure 11, *A*, the effect of excitement by presentation of a flame (torch) upon the carotid blood flow is illustrated. In Figure 11, *B* and *C*, a pharmacological effect is depicted. At *B*, *a*, the animal begins inhaling amyl nitrite. The reversal of the normal direction of diastolic flow during the initial diastoles is noteworthy. At *C*, *a*, the inhalation of amyl nitrite is discontinued and the blood flow goes up. In Figure 12 the filmstrip *A* shows the effect of a brief occlusion of the carotid artery upon the subsequent blood flow through it. As can be seen from this record, the initial brief increase in flow following release of the artery is substantial (approximately 45 per cent). Figure 12, *B*, shows the effect of stimulation by food upon carotid blood flow. At *B*, *a*, food is presented to the dog. There is an immediate noticeable increase in flow; at *b*, as the animal begins to chew the food (ground meat), the flow increases and becomes somewhat less regular.

Other types of stimuli have been tried, such as frightening the animal by a light flash. It was interesting to note the very rapid conditioning which occurred. The carotid blood flow was reduced upon the presentation of the light bulb to the animal prior to flashing it for the second time.

These examples illustrate the possibility of studying the effects of physiological and psychological stimuli as well as of pharmacological agents upon essentially normal conscious animals. Chronic research in experimental pathology also appears to be within the realm of possibility. Until now, the implants have not been left in the animal for more than a week, because of thrombosis caused probably by excessive constriction of the artery. There are good reasons to expect that, after elimination of this condition, the implants could be left in the animal indefinitely. The demonstration of the absence of objectionable biological effects of the implants, when properly used, as well as of physical artifacts affecting the measurement of flow, will be presented in a subsequent publication.

The preceding examples demonstrate some of the main advantages of the new modification of the electromagnetic method over the traditional methods of blood-flow determination. The possibility of obtaining a continuous flow record showing instantaneous responses without interference with the flow enables one to detect phenomena which are not observable by means of conventional methods. The possibility of making chronic implantations of sensing elements suggests the applicability of this method to research in experimental pathology and therapeutics. The use of conscious animals promises pharmacological results of greater validity than those obtained in earlier studies on anesthetized animals and permits the application of this method to problems in physiological psychology. Finally, the possibility of implanting miniature flowmeters simultaneously about several different arteries will make it possible to study the correlation between the functions of several different organs and their simultaneous response to a variety of stimuli.

The next step in this work will consist of improving the apparatus and procedure so as to make it adaptable to the measurement of blood flow in human beings and in animals in any accessible blood vessel of sufficiently large diameter. It will be possible to measure blood flow in arteries $^1/_2$ mm. in diameter. This is not necessarily the lowest attainable limit.

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[1] M. Faraday, Bakerian lecture, *Phil. Trans.* I, 1832.
[2] E. J. Williams, *Proc. Phys. Soc. London*, **42** 466–78, 1930.
[3] P. Fabre, *Compt. rend. Acad. Sci.*, **194**, 1097, 1932.
[4] A. Kolin, *Proc. Soc. Exptl. Biol. Med.*, **35**, 53, 1936.
[5] A. Kolin, *Am. J. Physiol.*, **119**, 355, 1937.
[6] L. N. Katz and A. Kolin, *Am. J. Physiol.*, **122**, 788, 1938.
[7] A. Kolin, *Am. J. Physiol.*, **122**, 797, 1938.
[8] E. Wetterer, *Z. Biol.*, **98**, 26, 1937.
[9] E. Wetterer, *ibid.*, **99**, 158, 1938.
[10] The best nonpolarizable electrodes for this purpose seem to be calomel half-cell electrodes as described by Jochim, in Glasser's *Medical Physics*, **1**, 377, 1944.
[11] A. Kolin, *Proc. Soc. Exptl. Biol. Med.*, **46**, 235, 1941.
[12] A. Kolin, *Rev. Sci. Instr.*, **12**, 555, 1941.
[13] A. Kolin, J. L. Weissberg, and L. Gerber, *Proc. Soc. Exptl. Biol. Med.*, **46**, 235, 1941.
[14] A. Kolin, *Rev. Sci. Instr.*, **23**, 235, 1952.
[15] A. Kolin, *ibid.*, **24**, 178, 1953.
[16] A. Kolin, *ibid.*, **16**, 109, 1945.
[17] A. B. Dennison, M. P. Spencer, and H. D. Green, *Circ. Research*, **3**, 39, 1954.
[18] A. Inouye and H. Kuga, *Japan. J. Physiol.*, **4**, 205, 1954.

ON THE BINDING OF ADENOSINE TRIPHOSPHATE BY ACTOMYOSIN

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Several attempts[1–4] have been made to study the combination between adenosine triphosphate (ATP) and actomyosin quantitatively, by determination of the viscosimetrically or turbidimetrically measurable change induced in the protein by its combination with ATP. The first efforts [1, 2] were preliminary, in that the available methods did not permit sufficiently rapid measurement of these transient phenomena. But even the measurements performed with a rapid technique[4] are