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AN APPARATUS FOR MEASURING HUMAN BODY VOLUME

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William E. Siri

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William E. Siri
Donner Laboratory of Biophysics and Medical Physics,
University of California, Berkeley, California

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ABSTRACT

The mean density, or alternatively the volume, of a human body is essential to *in vivo* estimates of body fat, protein, and mineral. A new method and apparatus for measuring body volume, based in principle on gas dilution, was developed to circumvent the disadvantages in applying Archimedes' principle to human subjects. The apparatus consists of two connected chambers forming a closed system. The larger chamber contains the subject in an air atmosphere while the smaller contains pure helium. Since the quantity of air in the system is inversely proportional to the subject's volume, the helium concentration, after the two gases are mixed, is an accurate measure of body volume. With corrections for thermal and respiratory gas effects, a high order of reproducibility was demonstrated by a variety of tests. The probable error in a single volume determination is estimated from tests and analysis to be 0.13 liter.

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INTRODUCTION

The gross composition of the living human body in terms of its principal constituents--water, fat, and nonfat solids--has long interested the clinician and physiologist for its obvious bearing on both normal and abnormal states of the body. Among the three constituents, only total body water is easily measured quantitatively, usually by hydrogen isotope dilution techniques. Neither fat nor solids, the latter consisting chiefly of protein and bone minerals, is amenable to such direct measurement and a more circumspect approach must be taken. The most widely used method is based on empirical formulas relating the amount of fat to the mean density of the body, or to the total body water. The relationships are valid on the average for normal persons, but they are questionable in abnormal conditions. A similar but perhaps more general approach treats the body as a three-component mixture in which the quantities of the constituents can be determined uniquely, whatever their proportions, if both the total body water and mean body density are measured. But whichever method is practiced, mean body density still is needed for the best estimates of fat and lean tissue.

The immersion technique, employing an adaption of Archimedes' principle to humans, was until recently, the only successful means for measuring human density, despite attempts along other lines to circumvent its disadvantages. For the most part alternative methods investigated both in this laboratory and elsewhere have been directed toward measuring body volume, from which the mean density is easily obtained by weighing the subject.[1, 2]

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[1] W. E. Siri, Federation Proc. 12, 488 (1953).

[2] R. J. Wedgwood, J. R. Breckenridge, and R. W. Newman, Federation Proc. 12, 488 (1953)

These methods have included the use of isotopes, gas-dilution techniques, pulsating pressure devices, acoustic resonance in chambers and, of course, a multitude of devices for detecting these effects. Although none of the earlier attempts were wholly successful, the method and apparatus described here for measuring body volume has now proved reliable and accurate during two years of tests and routine measurements of body volume. The procedure is rapid, it does not require trained subjects, and it is well tolerated by aged and ill patients.

PRINCIPLES OF THE METHOD

The apparatus described here for measuring human body volume utilizes a simple gas-dilution technique--namely, the dilution of helium by a quantity of air which is inversely proportional to the volume displaced by the subject. More specifically, the subject is placed in a sealed chamber into which an accurately metered quantity of helium is injected without altering the pressure and total volume of the system. The helium concentration, determined from the increase in thermal conductivity of the gas mixture, is an exact measure of the subject's volume when corrected for thermal and respiratory gas effects. For a system of this kind, shown schematically in Fig. 1, the helium concentration is related to the volume of the subject, V_θ, by

$$c = v/(V_c + v - V_\theta), \qquad (1)$$

where v and V_c are the helium and chamber gas volumes respectively, adjusted to standard temperature and pressure.

The apparatus currently in use has a chamber volume of 413 liters and a helium meter volume of about 12.5 liters. Since adult humans range in volume from 50 to 150 liters, the helium concentration varies from a minimum of 3.4% for the smallest persons to a maximum of about 4.7% for the largest. Consequently, for an error in volume determination no greater that ± 0.1 liter, the helium concentration must be measured with an accuracy in the order of $1:10^5$.

The over-all error of the method, however, is not set by the helium-detecting system, which is both stable and sensitive to about $1:5 \times 10^5$, but

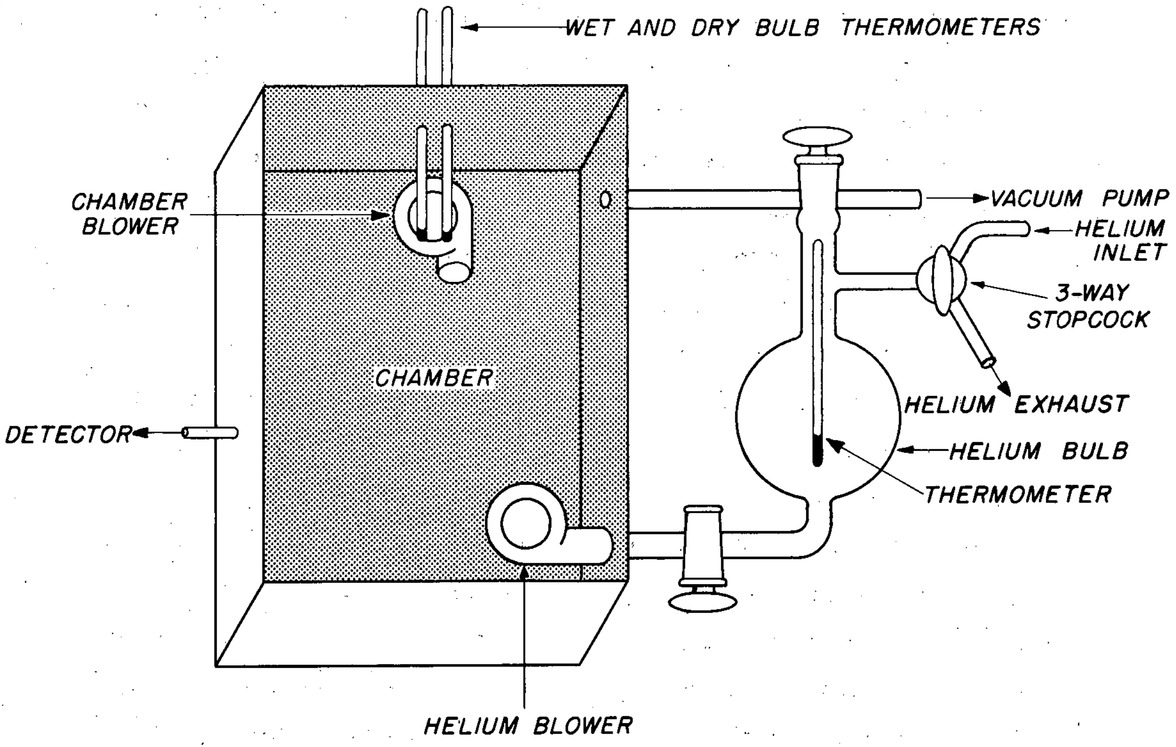

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Fig. 1. Schematic diagram of the chamber and helium-metering system.

rather by instrumental errors introduced through several corrections that are needed to make Eq. (1) exact. An average subject in the course of a run, which requires 15 minutes, consumes 3 liters of oxygen and produces about the same quantity of carbon dioxide, together with variable amounts of water vapor and heat. The detecting device, a thermal conductivity cell, is responsive to changes in concentration of all constituents of the chamber gas, and hence the effect of respiration, in continuously varying the composition, is superimposed on the cell's response to helium. These effects are relatively large compared to the desired accuracy of about ± 0.001% in helium concentration, but they are amenable to correction. The spurious response caused by respiratory gases and also by helium leakage from the chamber is readily corrected by a simple but reliable expedient described later. Explicit corrections, on the other hand, must be incorporated into Eq. (1) for helium and chamber temperatures and for water vapor. The latter correction is needed inasmuch as water vapor constitutes an appreciable and highly variable fraction of the chamber gas diluent, but it is not detected by the thermal-conductivity unit. Water vapor evokes a slow and erratic response and must be removed from the gas sample before it enters the detector.

Pressure corrections are unnecessary because the helium and chamber gas are equilibrated to local atmospheric pressure before they are mixed. The zero setting for the detector is slightly pressure-sensitive, but unless the barometric pressure changes drastically during a run the effect is negligible.

Temperature and water vapor corrections are the only factors that must be written explicitly into Eq. (1). The volume of helium and chamber gas at standard temperature T are vT/t_h and $(V_c - V_\theta)T/t_c$, where t_h and t_c are the respective gas temperatures at the time they are mixed. The volume of water vapor, corrected to temperature T, is $(V_c - V_\theta)Tp/Pt_c$, where P is local atmospheric pressure, and p the water vapor pressure at chamber temperature t_c. If these quantities are inserted into Eq. (1), the helium concentration sensed by the thermal conductivity unit is then

$$c = \frac{vT/t_h}{(V_c - V_\theta)T/t_c - (V_c - V_\theta)T/t_c + vT/t_h} \qquad (2)$$

or $$c = \frac{v}{(V_c - V_\theta)\,\delta + v} \qquad (3)$$

where $$\delta = \frac{t_h}{t_c}\left(\frac{P - p}{P}\right). \qquad (4)$$

The thermal conductivity unit's response S, in millivolts, is not a linear function of helium concentration but diminishes in sensitivity with increasing concentration. Confining the operating range to a small segment of the curve at low concentration, however, eliminates the need for constructing a calibration curve accurate to 0.001% and also takes advantage of the region of highest sensitivity. Deviation from linearity over a range in helium concentration of 1% is small, and no appreciable error is incurred by assuming $S = kc$, where k is a constant of proportionality. To justify use of a linear relation, however, an unknown volume V_θ can be determined only by extrapolating between two accurately known volumes which bracket more or less the operating range. Reference volumes now in use consist of Pyrex carboys with their openings sealed and their volumes measured gravimetrically. Substituting $c = S/k$ and designating by subscripts 1 and 2 quantities associated with reference volumes and by θ those associated with the subject, three equations in the form of Eq. (3) are obtained which can be solved simultaneously for the volume V_θ:

$$V_0 = \frac{1}{R_0(R_2 - R_1)}\Big[V_2R_2(R_0 - R_1) - V_1R_1(R_0 - R_2)$$

$$+ v(S_0 - S_1)(R_2 - R_1) - v(S_2 - S_1)(R_0 - R_1)\Big] \qquad (5)$$

The quantities R_i are the corrected values of the direct instrument readings S_i, i.e., $R_i = S_i\delta_i$ where δ_i is given in explicit form above. The volume V_θ is now expressed in terms of the reference volumes and instrument readings. The last two terms on the right of Eq. (5) are small correction terms and normally contribute about 0.1 liter to the total.

In principle, Eq. (5) is somewhat simplified if the empty chamber is used as a reference point because $V_1 = 0$ and one term vanishes. In practice, this stretches the linear relation $S = kc$ further than is justified by the thermal conductivity unit's actual nonlinear characteristics.

CHAMBER DESIGN

The essential features of the chamber are illustrated in Fig. 1, and the completed chamber now in use is shown in Fig. 2. Earlier experience with a horizontal chamber into which the subject was placed in a supine position led to the present design in the form of an enclosed chair because it is better tolerated by aged and ill subjects and more efficient in its operation. Nevertheless, nearly any form of enclosure will serve the purpose provided it is rigid and reasonably airtight. Rigidity is the more important factor since an indeterminate alteration in volume produces a proportional error in the measured value of the subject's volume. However, the chamber is never subjected to a pressure differential and only deflection under the subject's weight need be avoided. For the same reason the chamber need not be sealed as thoroughly as a vacuum system, since it is necessary only to guard against excessive leakage of helium by diffusion. The procedure, to be described later, for extrapolating the helium concentration back to its initial value becomes troublesome when the leakage rate is too great or if it is variable. On the other hand, the chamber cannot be wholly airtight, for it is essential to equilibrate continuously the chamber gas with local atmospheric pressure during the run as the temperature rises continuously from the subject's body heat. A total leak equivalent to an orifice 3 to 5 mm in diameter appears to be adequate.

Auxiliary chamber equipment includes two induction-motor-driven blowers mounted on the inner wall near the top and bottom of the chamber. To minimize noise and heat production in the chamber, the motors are mounted on the outside wall with their shafts projecting through leather-washer seals to the rotors. The blowers are essential to insure a homogeneous gas mixture and uniform temperature. Without them, layering of CO_2, air, and helium becomes immediately apparent to the detector, which thereupon responds erratically.

A small high-speed blower, also mounted on the inside wall, is used for flushing chamber air through the helium-metering system. The blower exhaust is piped directly through a right-angle tube into one of the two connections between the helium flask and chamber.

A wet-and-dry-bulb psychrometer consisting of a pair of matched precision thermometers with 0.1°C divisions (5° to 30°C) is currently used to

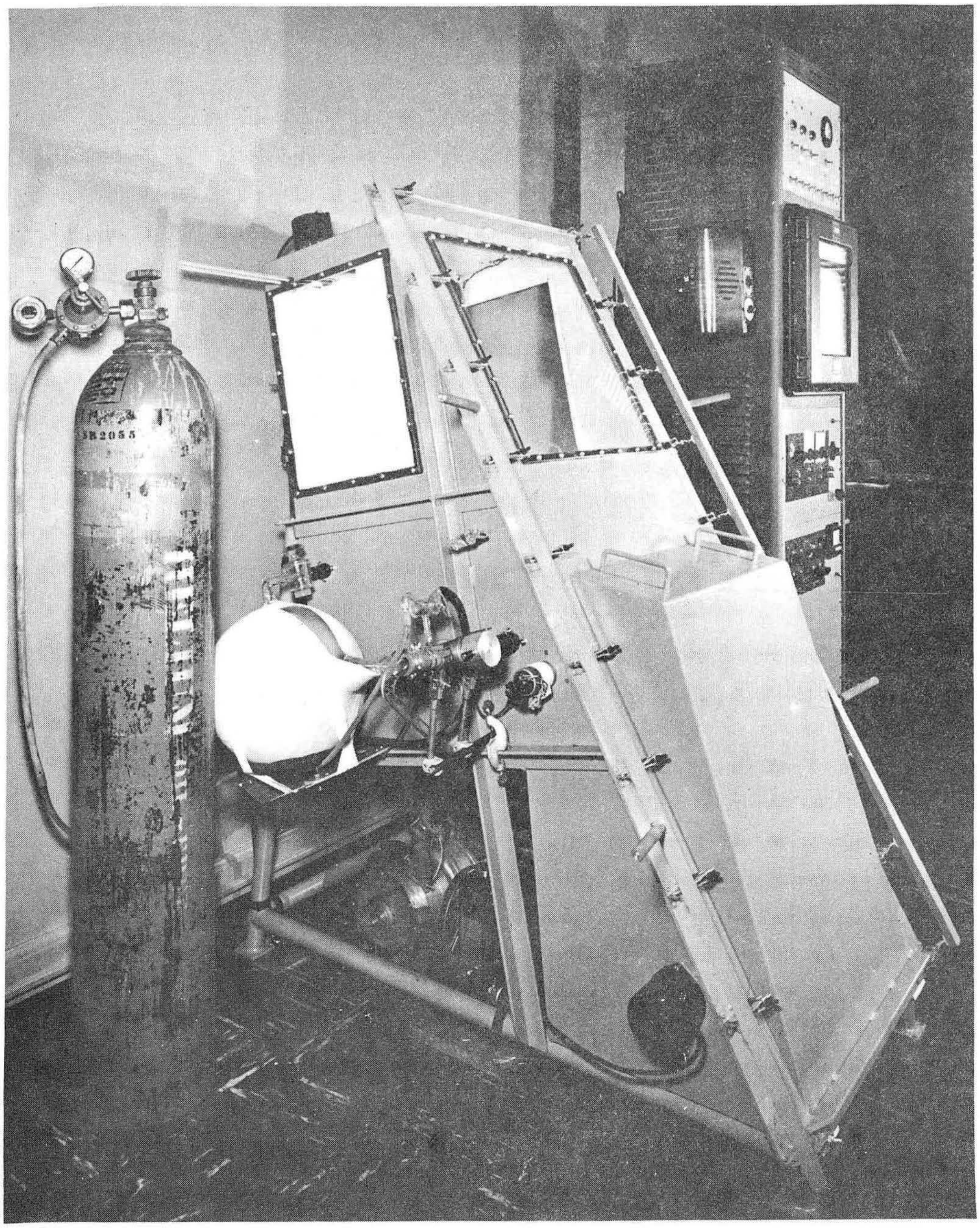

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Fig. 2. Photograph of the completed human volume apparatus.

measure water vapor in the chamber. The thermometer bulbs, one of which is covered with a cotton wick and kept moist by a test tube water reservoir, are mounted at the intake of one of the blowers. The stems project through the chamber wall to facilitate temperature observations during a run. The thermometers should be matched or calibrated with the metering system thermometer within ± 0.01°C for the range from 10°C to 30°C.

The chamber interior equipment is completed with a shallow removable lucite tray mounted near a blower exhaust; in the current apparatus it is placed above the subject's head. During each run the tray holds a fresh charge of 100 g of an absorber of CO_2 and water, such as "Caroxite" or "Ascarite". It is not intended to absorb these gases completely but rather to reduce their rate of accumulation, and ideally to maintain a steady concentration during a run by compensating, in part, the CO_2 and water vapor produced by the subject. Corrections for these gases are then somewhat easier and more reliable.

The chamber shown in Fig. 2 was fabricated from 1/8-in.-thick aluminum alloy sheet, butt welded at the seams and stiffened with angle sections welded to the outside. The assembly forms an enclosed chair, tilted back 15° for comfort, and designed for adequate head and knee space without greatly exceeding 400 liters volume.

The door spans the full height of the chamber to allow easy entry for subjects, and is locked and sealed into position with two rows of clamps. Each row of clamps is actuated with a single lever. Soft rubber tubing, 0.25 in. in diameter, cemented to the door frame forms the airtight seal.

Ample window space, paneled with 0.25-in.-thick lucite, on both sides of the chamber and on the door eliminate any feeling of claustrophobia.

HELIUM-METERING SYSTEM

The importance of constancy in the quantity of helium injected into the chamber may be judged by the fact that any uncertainty in quantity is reflected as a 100-fold error in the volume being measured. The helium-metering system, consequently, must be capable of delivering on every run a volume of helium that is reproducible within $1:10^5$. With a volume that is essentially constant, the quantity, so far as it affects the helium concentration in the chamber, depends solely on the temperature and can then be corrected to about 1: 3 x 10^4, if the temperature is measurable to 0.01°K. On the other hand, while the volume of helium must be constant, its absolute value need not be determined accurately because it appears explicitly only in the those terms of Eq. (5) where it is a factor in a small correction.

A simple vacuum system such as that shown in Fig. 1 is the most dependable of a variety of methods tested for constancy of volume and quantitative delivery of helium. It consists of a 12-liter Pyrex flask equipped with stopcocks for evacuating, filling, and discharging the system. A 6-in.-long neck on the flask terminates in a 1-cm-bore hollow-plug "T" stopcock, one arm of which connects with the chamber, and the other with a mechanical vacuum pump. A 1-cm straight-bore stopcock attached to the side of the flask and connected to the chamber with a short length of tube completes the closed circuit between the helium flask and chamber. A third stopcock, preferably the Y-type with a 3-mm bore, serves as the helium inlet and as a means for equilibrating the flask to atmospheric pressure after it is filled. Helium expelled through the stopcock should be vented through tubing and released outside of the room to avoid contaminating the reference gases.

The helium temperature at the time it is discharged into the chamber is a significant factor in the corrections discussed above and should be recorded with an accuracy of ± 0.02°C. Immersing the flask in a water bath would hasten thermal equilibration and perhaps improve the accuracy with which the temperature is measured, but this was not done with the present apparatus. Instead, the flask is air-cooled until a constant temperature is reached. The temperature is given by a total-immersion thermometer graduated in 0.1°C divisions, which is supported by wire clips with its bulb located at the center of the flask. The thermometer stem projects into the neck of the flask where the scale is clearly visible.

When the system has been evacuated to 0.05 mm Hg, or better, the flask is filled from a high-pressure helium cylinder through a standard regulator, after air has been flushed from the filling and exhaust lines with helium. During the five to ten minutes required for the temperature to stabilize within ± 0.01°C, the connecting lines are occasionally flushed with helium and the flask is opened briefly to the exhaust line through the Y stopcock to equilibrate the helium to atmospheric pressure. After the temperature is recorded and the two large stopcocks are set for flow through the chamber connections, air from the chamber is forced through the flask by a 2-in. high-speed blower mounted in the chamber. With the device now used, mixing is complete in approximately 2.5 min.

HELIUM DETECTOR

The high thermal conductivity of helium lends itself to an effective yet simple method for detecting small changes in helium concentration in air. A heated filament whose temperature--and hence resistance--depends upon the thermal conductivity of the surrounding gas forms a highly sensitive detecting device for helium, and when operated in the form of a Wheatstone bridge, is capable of measuring changes in helium concentration of 1:5 x 10^5. Nevertheless the effective use of a thermal conductivity unit at a high level of sensitivity requires care in its installation and operation. With a bridge circuit whose elements consist of nearly identical filaments, an unwanted response to environmental factors other than thermal conductivity is greatly reduced but not wholly eliminated. The requisite accuracy for detecting helium can be achieved, however, through careful regulation of the thermal conductivity unit's temperature and operating current and of the gas pressure and flow rate, and avoidance of severe vibration and gas contamination.

The thermal conductivity unit now in use is a commercial product[3] somewhat modified for immersion in a constant-temperature oil bath. It consists of eight helical filaments, each with a nominal resistance of 30 ohms, mounted in separate cells in a brass block. Two filaments in series form each arm of a Wheatstone bridge, and alternate arms, as shown schematically in Fig. 3, are exposed to a reference gas, whereas the remaining pair monitors the chamber gas for helium concentration.

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3. Thermal Conductivity Unit Type M/T-T-8, Gow-Mac Instrument Company, Newark, N. J.

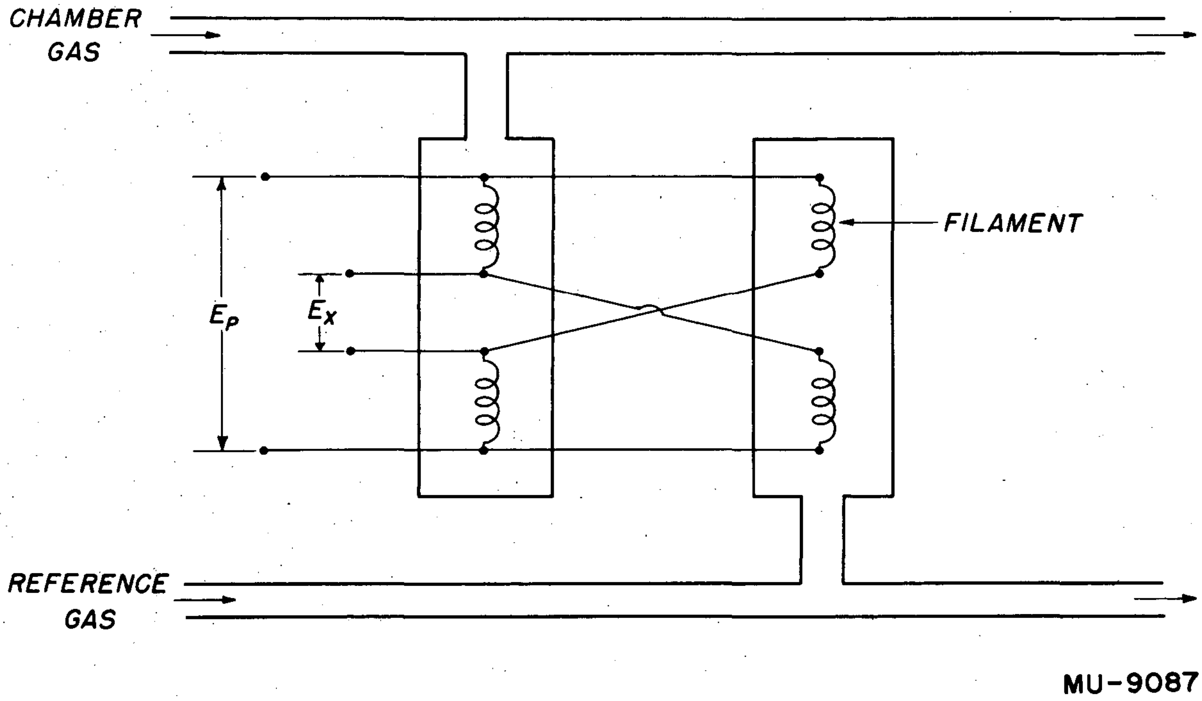

Fig. 3. Schematic diagram of the helium-detecting unit. Ep, input voltage; Ex, output voltage.

The unit received from the manufacturer was stripped of fittings and electrical connections and the filaments were carefully removed. Four lengths of copper tubing, long enough to extend several inches above the oil bath, were soldered to the pipe fittings on the brass block for gas inlets and exhausts. The filaments, matched in resistance to give the best bridge balance, were replaced with the addition of an O ring inserted under each filament mount, as illustrated in Fig. 4, to form an oil seal. After lengths of bare copper wire are soldered to the filament leads, the unit can be suspended in the oil bath.

A rectangular glass tank 6 by 7 by 10 in., which serves as the oil bath (Fig. 5), is mounted adjacent to the chamber wall so that the gas connection between chamber and detector is as short as possible. The tank is wrapped with aluminum foil and further insulated with a layer of 0.25-in.-thick cork. To minimize transmission of vibration to the unit, the tank rests freely on a thick pad of felt supported by a shelf attached to the chamber. The thermal conductivity unit, electrical terminals, the oil bath accessories are mounted on a 0.5-in.-thick lucite plate which covers the tank. A small stirring motor for circulating oil in the tank, however, is mounted independently on a bracket attached to the chamber or shelf. Accessory equipment includes a thermometer graduated in 0.1°C divisions, a sensitive mercury thermostat, and a 10-watt heater made from a wire-wound resistor. Heater current is supplied through an electronic switch controlled by the thermostat.

The oil bath temperature is most effectively regulated when maintained a few degrees above the highest expected ambient air temperature. While selection of the operating temperature is arbitrary, once it has been set stable operation of the conductivity unit at high sensitivity requires thermal regulation within ± 0.01°C.

The extrapolations that are needed in compensating for helium leakage and for the change in chamber gas composition due to respiration require continuous gas sampling during a run. This introduces, at least as potential factors in the design of the apparatus, the delay time in the gas-sampling system, the response time of the thermal conductivity unit, and the influence of gas flow rate on stability. If both the delay and response times are very small compared to the mixing time for helium in the chamber (which for our apparatus is about 2.5 minutes) their influence is negligible. The length and volume of the gas line and the flow rate can all be adjusted to give a

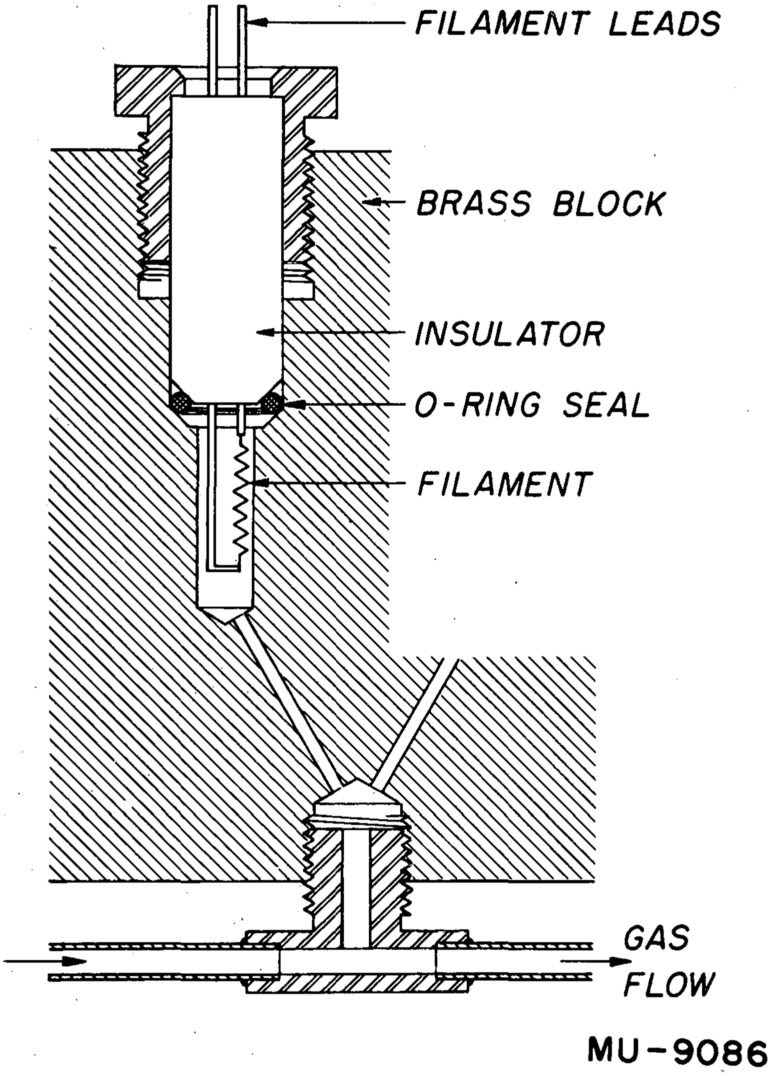

Fig. 4. Diagram of a thermal conductivity cell showing O-ring location.

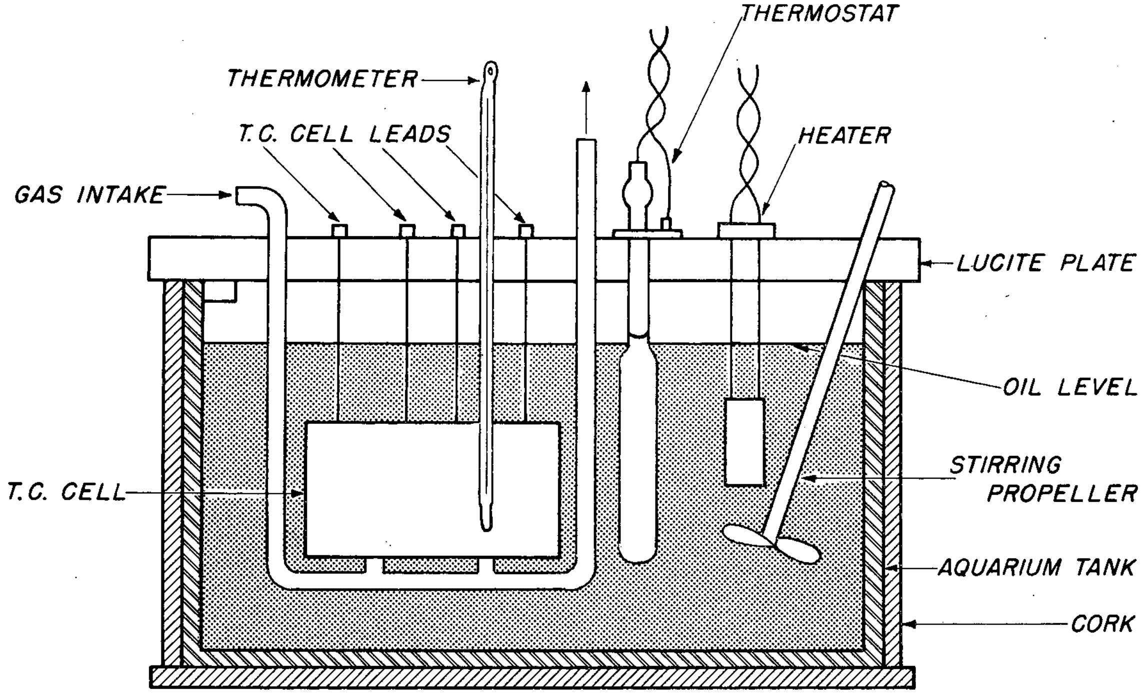

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Fig. 5. Oil bath and accessories for the thermal conductivity unit.

delay time of 10 sec. or less. The response of the conductivity unit, on the other hand, is roughly exponential because it depends upon diffusion of the gas into the cells of the unit, which are removed from the direct gas flow, as shown in Fig. 3. The half time for helium, however, is less than 5 sec., and the effect of so short a response time may be disregarded.

The flow rates of reference and chamber gases, if constant, have little effect upon the calibration of the thermal conductivity unit, at least for rates less than 100 cc min^{-1}. The calibration is also unaffected by normal excursions in atmospheric pressure although the initial bridge reading may change slightly with pressure. The conductivity unit is highly responsive, however, to changes in pressure between the reference and chamber gases. Regulation of gas flow rates is consequently needed to avoid, or at least to stabilize, pressure differentials between cells containing reference gas and those whith chamber gas.

Adequate regulation is achieved with a gas-sampling system such as shown in Fig. 6. The flow rate is set at about 50 cc min^{-1}, and while fluctuations may exceed ± 1 cc min^{-1}, they are necessarily the same for both the reference and chamber gas, and have little influence. The oil bubbler and needle valve assist in adjusting and stabilizing the flow rates, but the exhaust pump is the more critical part of the system in maintaining long-period stability. A high-speed exhaust pump with multistage impellers has given good performance, although other air-pumping devices may be substituted if sufficiently stable to have no effect on performance of the conductivity unit.

Dry, CO_2-free air is used as a reference gas because it is always at the same pressure as the chamber. To be certain that it is not contaminated with helium and traces of other fumes sometimes present in the laboratory, the air is piped from outside the building. Contamination in itself is not objectionable provided it remains constant during a run. Contamination of the chamber gas has no effect other than merely shifting the initial and final bridge balance by a constant voltage. The H_2O and CO_2 absorption cell for the reference gas holds a 50-cc charge of "Ascarite", "Caroxite", or an equivalent absorber. Water vapor, but not CO_2, is removed from the chamber gas-sampling line by a 3-cc absorption cell which holds sufficient anhydrous magnesium perchlorate for one day's operation; a larger cell

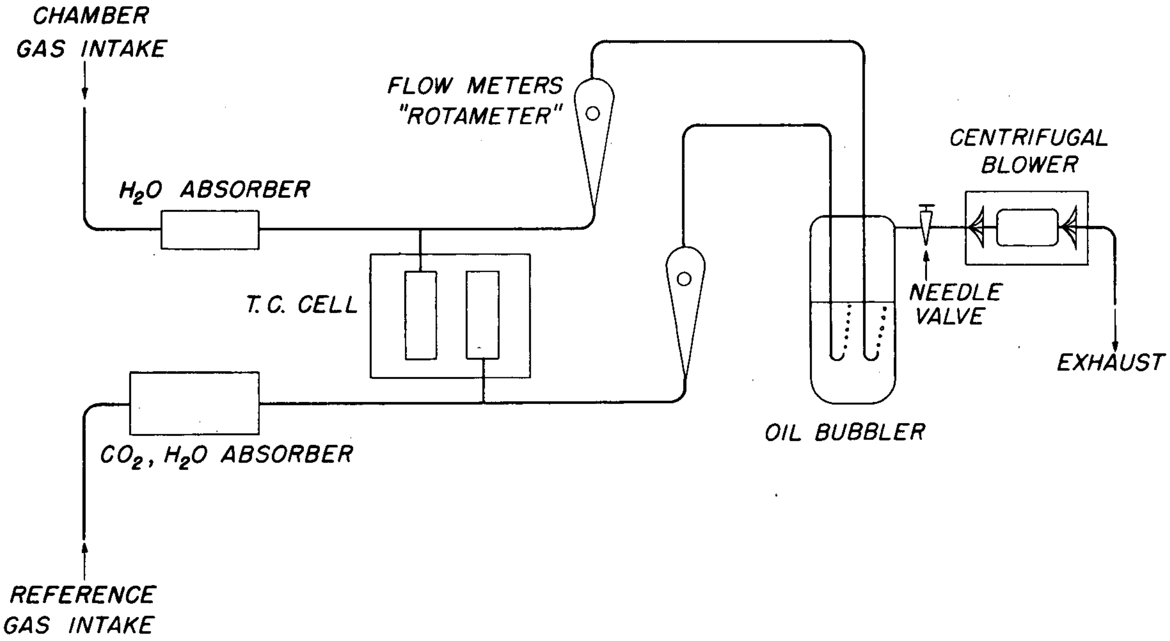

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Fig. 6. Reference and chamber gas-sampling systems.

volume needlessly increases the delay time of the system. However, when the apparatus is on stand-by for an extended period, a larger absorption cell may be inserted and the exhaust pump stopped.

POWER SUPPLY

The thermal conductivity unit is no less sensitive to its operating current than it is to its environment. A workable sensitivity for helium concentration in air of $1{:}10^5$ requires regulation of the bridge current in the same order of magnitude. The successful use of the device consequently is more dependent upon achieving the requisite stability in the power supply than on any of the other factors affecting it operation.

An elementary form of power source proved to be the most reliable and stable after several unsuccessful attempts to use electronic circuits. The circuit now used, shown in Fig. 7, consists of a full-wave selenium rectifier powered by the 110-volt service line, a simple filter for reducing ac ripple, and a set of storage batteries.

Ripple and line voltage fluctuations are undetectable at the output, and the drift rate with a constant load is in the order of 0.01 mv day^{-1}. It may be noted that batteries alone are inadequate because their discharge rate, even with no load, far exceeds the tolerable rate of 0.01 mv hr^{-1}. However, with the selenium rectifier current set 0.1 amp higher than the battery current that is drawn, the output voltage remains remarkably constant for periods of several months--usually until one of the batteries shows signs of deterioration. At installation the batteries should be new and fully charged, with the area about the terminals coated with grease to prevent the formation of semiconducting surface deposits.

The thermal conductivity unit is operated at 0.138 amp at about 8.3 volts as recommended by the manufacturer. The 12-volt output from the batteries is reduced to the required operating voltage through resistances R_1, R_2, and R_3. Resistances R_1 and R_2 are decade resistance boxes connected in parallel, each adjustable by increments of 0.1 ohm from 0 to 999.9 ohms. One decade, set at 25 ohms, passes a large fraction of the current so that the other, set at about 400 ohms, functions as a fine control for the bridge current. The

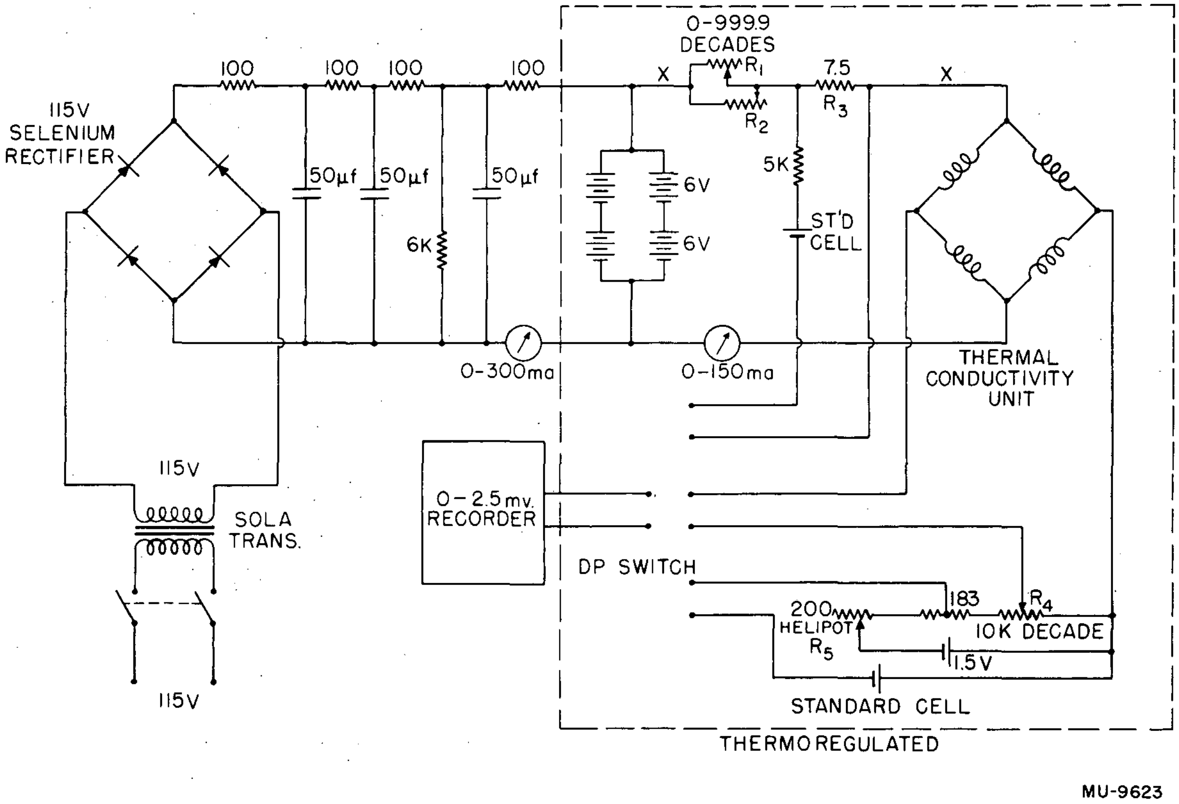

Fig. 7. Power supply and potentiometer circuits for the thermal conductivity unit. All resistances except those in the rectifier circuit are precision WW, 1 Watt. The automatic current regulator, shown in Fig. 8, may be inserted between points marked X-X, replacing the corresponding portion of the circuit shown above.

fixed resistance R_3, about 7.5 ohms, is part of the current-standardizing circuit. With a 0-to-2.5-mv recording potentiometer switched into the circuit, the voltage drop across R_3 is balanced against the full voltage of a Weston standard cell by adjusting R_2. An exact voltage balance is unnecessary, and, on the contrary, it is convenient to leave a residual voltage of 1 mv to be balanced by the recorder. However, the current is afterwards always maintained within 0.5 μamp (0.005 mv on the recorder) of the arbitrarily selected setting.

The power supply possesses the virtue of great internal stability for a fixed load but is not at all regulated with respect to a variable load. As the thermal conductivity unit functions best when operated at constant current, it is necessary to make frequent manual current adjustments as the resistance of the unit shifts with changing gas composition. Manual adjustment can at best give a close approximation of constant-current operation, but it is a potential source of error and, in a sense, an incomplete utilization of an otherwise highly stabilized supply. The electromechanical system shown in Fig. 8 provides the needed automatic regulation but it has not yet been thoroughly tested.

All the components of the power supply except the rectifier and filter are maintained at constant temperature. A standard Budd rack-cabinet is adequate for this purpose if the space housing the power supply is lined with 0.5-in.-thick plywood, with cork sheet cemented to the inside faces of the front panels through which the controls project. The enclosure is completed with a plywood top and bottom and removable rear panel, which supports a 4-in. blower with its induction motor mounted on the outside. The temperature is controlled by a sensitive mercury thermostat that actuates a 60-watt bulb through an electronic relay, Fig. 9. Care should be taken, however, to shield the batteries and resistances against direct radiation from the bulb. A second bulb can be switched into the heating circuit in the event the first fails, thus avoiding a lengthy shutdown for replacement and return to thermal equilibrium. The air temperature within the enclosure can be regulated within $\pm 0.2^{\circ}C$ if the thermostat is set about $5^{\circ}C$ above the highest expected room temperature.

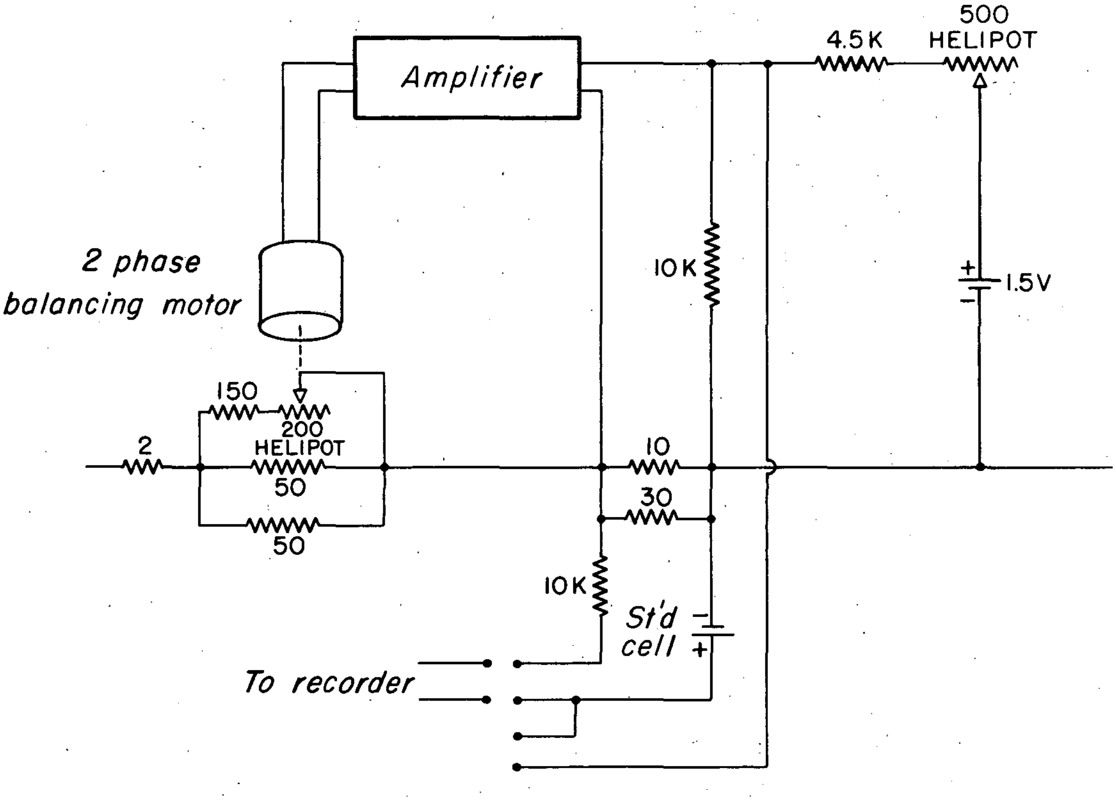

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Fig. 8. Proposed automatic current regulator.

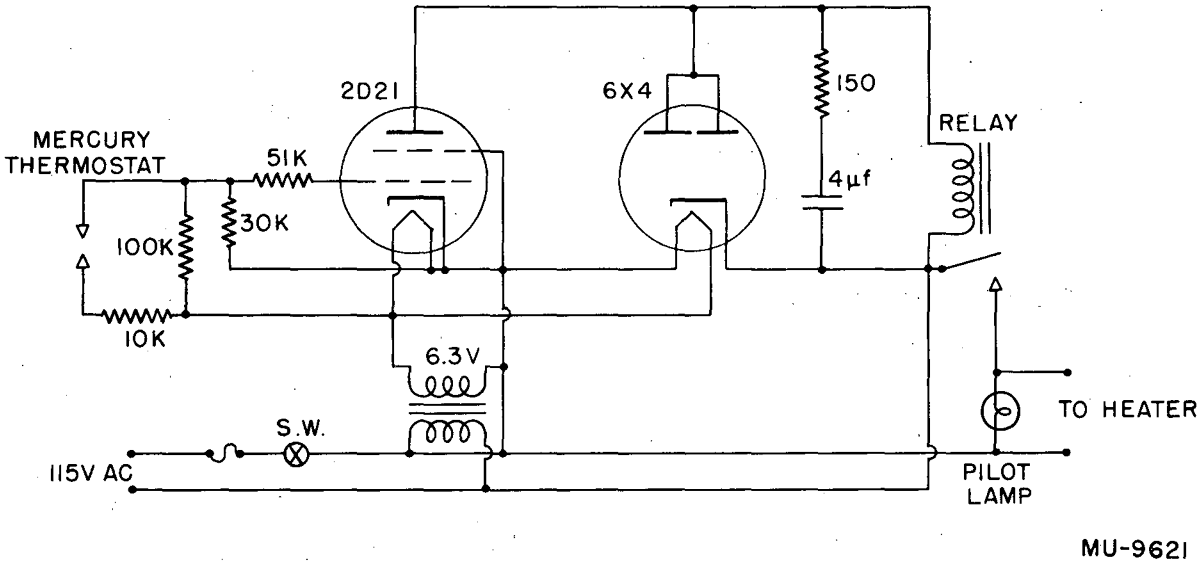

Fig. 9. Electronic relay switch.

POTENTIOMETER CIRCUIT

The sensitivity of the thermal conductivity unit to helium in air at concentrations near 4% is about 30 mv for a 1% change in concentration. With the instrument parameters described earlier, the maximum output voltage that needs to be measured is therefore about 150 mv, while the sensitivity in terms of the subject's volume is approximately 0.3 mv ℓ^{-1}. The desired over-all accuracy of ± 0.1 ℓ for the method calls for an equivalent accuracy in voltage determination of ± 0.03 mv, but in view of small errors accumulated in the corrections for temperature and humidity, the actual output should be measured with an error no greater than ±0.005 mv over the entire working range from 0 to 150 mv.

The standard recording potentiometers such as the "Speedomax" (Leeds and Northrup Co.) and "Electronik" (Brown Instrument Co.) with a 0-to-2.5-mv range on 10-in. charts possess adequate sensitivity for this purpose, and it remains only to extend the range of the recorder with an external potentiometer circuit, such as that shown in Fig. 7. The output from the thermal conductivity unit is then balanced to the nearest millivolt by manual adjustment of the precision decade divider R_4 and the remaining fraction of a millivolt is balanced automatically and charted by the recorder with an accuracy for the total voltage of ± 0.005 mv or better. The recorder, however, serves a dual purpose in that it not only possesses the required precision but also gives a continuous record of balance voltage for the duration of a run, which is needed to compensate, by a simple extrapolation described later, for the continuous change in voltage caused by helium leakage and alteration in gas by the subject's respiration. These extrapolations are more easily and reliably made on recorders with a 0-to-2.5-mv range than on instruments of greater or lesser range.

The external potentiometer is an elementary voltage-dividing circuit adjustable in whole units of millivolts from 0 to 1 volt, with provision for standardizing its potential against a Weston cell. With the recorder switched into the standardizing circuit to serve as a null indicator (Fig. 7), the potential across the decade R_4 is adjusted to 1 volt ± 5×10^{-6} volt with helipot R_5. This adjustment is made prior to each run. When the apparatus is assembled, the decade divider should also be calibrated to determine the actual voltage within ± 0.002 mv for each decade step. An appropriate correction voltage can then be added to the indicated value of each decade setting in subsequent operations. The calibration is most conveniently performed by observing with the recorder the differences between successive millivolt steps of the decade, using an adjustable external voltage to balance all but the last millivolt.

The entire potentiometer circuit, except for the recorder, is placed in the thermo-regulated chamber along with the power supply for the conductivity unit. The constancy of the reference voltage cannot otherwise be maintained because of large thermal coefficients of batteries and of some resistance elements. It is also essential to minimize contact resistance and other juction effects in assembling the circuit, particularly in the switches.

OPERATING PROCEDURE

A brief description of the operating procedure will give a more integrated view of the apparatus and help clarify details omitted in preceding sections. When the apparatus is first put into operation, the output from the thermal conductivity unit reaches a steady state in one to two days. The long starting time is caused by the storage batteries which, because of their large mass and poor thermal conductivity, approach thermal and charge equilibrium slowly. Once the apparatus has been placed in operation and adjusted, the most practical course is to maintain continuously the bridge current and thermo-regulation of the electrical circuits and conductivity unit, even if the apparatus is used infrequently. The equipment shown in Fig. 2 has in this way remained in continuous operation for two years and is always ready for immediate use.

The subject, after a brief rest to stabilize CO_2 production, is placed in the chamber wearing a minimum of clothing, preferably only a light hospital gown, and instructed to remain quiet but relaxed. The tray containing carbon dioxide and water vapor absorber is inserted and the chamber door is clamped into place. The helium flask, evacuated to 0.05 mm Hg or better, is filled to slightly more than atmospheric pressure after the connections between the helium tank and metering system have been flushed thoroughly with helium. The flask is immediately equilibrated to atmospheric pressure through the exhaust valve, Fig. 1. While the helium approaches thermal equilibrium, the reference voltage and bridge current are adjusted. The recorder is then switched back to the potentiometer circuit to record the changing carbon dioxide and oxygen concentrations. When the helium is equilibrated in temperature and pressure with the ambient air, its temperature is recorded within 0.01°C and it is then discharged into the chamber with the aid of the small blower. Immediately after the helium injection is started, the wet- and dry-bulb temperatures are recorded. These temperatures, together with that of the helium, are used later for the thermal and water vapor corrections.

Mixing is complete in less than three minutes. Near the end of the interval, resistance R_2 (Fig. 7) is again adjusted with the aid of the recorder to restore the bridge current at its original value if automatic regulation is not incorporated in the circuit. The recorder is again inserted into the potentiometer circuit and the decade R_4 adjusted to balance, to the nearest millivolt, the detector's response to the helium. The chart again shows a straight line of negative slope in response to the increasing carbon dioxide and diminishing oxygen concentrations.

In effect, the chart line has been merely interrupted and displaced by the introduction of helium into the chamber and it remains only to extrapolate, on the chart paper, the two lines to a common time. In practice, the point selected is that time at which the detector first responds to helium, because the final curve, with the added effect of small but perceptible helium leakage, may have a slightly greater slope than the initial line. By this procedure the effects of respiration on the chamber gas composition are eliminated, leaving only the direct response to helium, i.e.,

S = final mv (decade + chart) – initial mv (decade + chart).

This value is then corrected for temperatures and water vapor as described earlier, namely

$$R_i = \delta_i S_i = St_h(P - p)/Pt_c,$$

where t_h and t_c are helium and chamber temperatures respectively, P the atmospheric pressure, and p the water vapor pressure.[4]

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[4] The water vapor pressure may be obtained from the well-known formula

$$p = p_w - 0.00066P(t - t_w)\left[1 + 0.00115(t - t_w)\right],$$

where t and t_w are the dry- and wet-bulb temperatures respectively, p_w is the saturated water vapor pressure at temperature t_w, and P is barometic pressure. Tables of p_w will be found in Handbook of Chemistry and Physics, Chemical Rubber Publishing Co, Cleveland, Ohio.

The same procedure is followed in securing the detector response R_1 and R_2 for the two reference volumes. This need be repeated only occasionally as a check on the calibration of the apparatus. The volume of the subject is calculated with Eq. (5).

ESTIMATION OF ERRORS

The factors that have an appreciable influence on the precision of the apparatus are sufficiently well-defined to justify an analysis of their contribution to the over-all error. The analysis is, of course, most useful in the sense that it establishes the magnitude of error that can be tolerated in each critical detail of design and operation if a probable error in volume no greater than ± 0.1 liter is to be achieved.

The measured volume of a subject was shown by Eq. (5) to depend upon the corrected potentiometer reading R_0 for the subject, and the corresponding values R_1 and R_2 for the reference volumes. This equation may also be used now to evaluate the effect upon V_0 of both systematic and random errors in the apparatus and method. For this purpose, the last two terms in the equation, which contribute less than 2% to the volume, may be omitted, and the reference volumes, V_1 and V_2, can be regarded as constants inasmuch as they can be measured with negligible error by gravimetric methods. The equation is then

$$V_0 = \frac{V_2 R_2 (R_0 - R_1) - V_1 R_1 (R_0 - R_2)}{R_0 (R_2 - R_1)} . \qquad (6)$$

Consider first the effect of systematic errors in the R_i. This may be seen in the differential of Eq. (6), written in the form

$$\Delta V_0 = \frac{R_1 R_2 (V_2 - V_1)}{R_0 (R_2 - R_1)^2} \left[\frac{R_2 - R_1}{R_0} \Delta R_0 + \frac{R_0 - R_1}{R_1} \Delta R_1 + \frac{R_0 - R_1}{R_2} \Delta R_2 \right] . \qquad (7)$$

If the "errors" R are systematic, we may expect them to have the same sign and same order of magnitude. Furthermore, since the whole operating range of R is only about 5% of R, the denominators of the terms in brackets may be replaced with a mean value of R without altering the values of the separate terms by more than a few percent. Except for these differences of a few percent, it is seen that the factor in brackets tends to vanish, and with it, also ΔV_0.

This will be more evident on substituting values taken from actual runs with the apparatus, choosing as an example, 119.55 mv for a 67.5-liter man, and 115.07 mv and 121.37 mv for the 52.04- and 73.84-liter reference volumes respectively:

$$\Delta V_0 = 3.38\, \Delta R_0 - 1.16\, \Delta R_1 - 2.37\, \Delta R_2, \tag{8}$$

or, assuming that $\Delta R_0 \cong \Delta R_1 \cong \Delta R_2$, then we have $\Delta V_0 = 0.15\, \Delta R$. Obviously the effect of systematic error on V_0 is negligible; ΔR may be as great as ± 0.7 mv before compromising the desired accuracy of ± 0.1 liter. This suggests that substantial errors in procedure, such as in the extrapolations to obtain S and in corrections for temperatures and water vapor, may be tolerated provided they are consistent.

On the other hand, random errors in the R_i are far more critical to the accuracy of V_0 because they may vary independently and possess either sign with equal probability. To establish the magnitudes of the errors that can be tolerated in the R_i, designate by r_0, r_1, and r_2 the probable errors in R_0, R_1, and R_2 for human subjects and reference volumes. The probable error in V_0 is then given explicitly on applying the law of propagation of errors in Eq. (6):

$$r_v^2 = \left(\frac{R_1R_2(V_2 - V_1)}{R_0^2(R_2 - R_1)}\right)^2 r_0^2 + \left(\frac{R_1(R_0 - R_1)(V_2 - V_1)}{R_0(R_2 - R_1)^2}\right)^2 r_1^2 + \left(\frac{R_2(R_0 - R_2)(V_2 - V_1)}{R_0(R_2 - R_1)^2}\right)^2 r_2^2. \tag{9}$$

Inserting the values for the R_i given above, we have

$$r_V^2 = 11.42\, r_0^2 + 5.57\, r_1^2 + 1.27\, r_2^2.$$

If $|r_0| \cong |r_1| \cong |r_2|$, the probable error in R needed to limit the probable error in V_0 to ± 0.1 liter is $r_R = \pm 0.024$ mv. It is reasonable to expect to have $|r_1| \cong |r_2|$, since they are derived from identical runs on inert reference volumes, but it is more realistic to expect that we will get $|r_0| \cong 2\,|r_{1,2}|$ because of the slightly greater error introduced by more rapid excursions in temperature and humidity during runs with human subjects. The required probable errors are then

$$r_0 = \pm 0.028 \text{ mv and } r_1 = r_2 = \pm 0.014 \text{ mv}.$$

With the values of the r_R established, criteria are provided for estimating the stability required of the apparatus and the accuracy with which water vapor pressure and temperatures must be measured. The explicit form of R in terms of observable quantities was given in Eq. (4) as $R = S\delta = St_h(P - p)/Pt_c$.

Applying the law of propagation of errors to this expression, we find the probable error in R is

$$r_R^2 = S^2 \frac{t_h^2}{t_c^2}\left(\frac{P - p}{P}\right)^2\left(\frac{r_s^2}{S^2} + \frac{r_{t_c}^2}{t_c^2} + \frac{r_{t_h}^2}{t_h^2} + \frac{r_p^2}{(P - p)^2} + \frac{p^2 r_P^2}{P^2(P - p)^2}\right). \tag{10}$$

No significant error is committed on inserting the approximate values $t_h \cong t_c \cong 300^\circ$K, $S \cong 120$ mv, $p \cong 10$ mm Hg, and $P \cong 760$ mm Hg, hence

$$r_R^2 = r_s^2 + 0.16\, r_{t_h}^2 + 0.16\, r_{t_c}^2 + 0.026\, r_p^2 + 4.4 \times 10^{-6}\, r_P^2. \tag{11}$$

The most likely values for the r that one may expect in runs with the reference volumes, based upon the inherent reliability of the separate items of apparatus involved, are $r_s = \pm\, 0.01$ mv, $r_{t_h} = \pm\, 0.015^\circ$C, $r_{t_c} = \pm 0.02^\circ$C, $r_p = \pm\, 0.05$ mm Hg, and $r_P = \pm\, 0.1$ mm Hg. The last term of Eq. (11) obviously is negligible. An error in barometric pressure as great as 1.0 mm Hg does not introduce a significant error into R. Substituting these values in Eq. (11) gives a probable error in $R_{1,2}$ of $r_{1,2} = \pm\, 0.016$ mv.

In runs with human subjects, slightly greater error is encountered in measuring the chamber temperature and water vapor pressure and also in the extrapolation for S. For these runs, the probable errors are $r_s = \pm\, 0.015$ mv, $r_{t_h} = \pm\, 0.015^\circ$C, $r_{t_c} = \pm 0.04^\circ$C, and $r_p = \pm\, 0.1$ mm Hg. Hence the probable error in R_0 is $r_0 = 0.028$ mv.

Admittedly the selection of numerical values for the probable errors was guided, in part, by the desired end result, for when these values of r_0 and $r_{1,2}$ are substituted in Eq. (8), the probable error in V_0 is $r_V = \pm\, 0.1$ liter. Nevertheless, this was the intended purpose: to estimate the precision required of critical parts of the apparatus. This precision is, in fact, very nearly achieved in routine operation of the apparatus, and the indicated errors are entirely reasonable when it is recalled that large systematic errors may be tolerated in parts of the apparatus without greatly affecting the over-all error.

It is not important if the thermometers are in error, relative to true temperature, provided the several thermometers are matched and that they, and the procedures for reading them, are consistent over the small range in which the temperature normally varies. This applies also to the response of the thermal conductivity unit, and more particularly to the validity of the extrapolation for compensating respiratory effects.

The ultimate test of precision can be found only in actual performance of the apparatus. An evaluation of its accuracy was based upon a variety of tests for reproducibility and on measurements of inert reference objects whose volumes were accurately determined gravimetrically. The definitive test of accuracy in measuring human volumes would involve comparison with volume determined by an independent means, but underwater weighing, the only alternative method, was not practicable. The immersion method requires skill and experience to achieve high accuracy and, moreover, the inherent error in the method is comparable to that expected for the helium-dilution method.

The inert reference volumes, which are the basis for calculating human volume, consist of three sealed Pyrex carboys with volumes of 21.80, 22.73, and 52.04 liters. Normally they are run in combinations that give volumes of 52.04, 73.84, and 96.57 liters, which bracket the range for most humans. Repeated runs on these three volumes during a two-year period provided a check on consistency and a measure of the accuracy of the apparatus. From each set of three reference runs, the indicated volume for any one of them, calculated by Eq. (5), can be compared directly with its known volume. When the smallest and the largest reference volumes were used as standards in 45 sets of three runs, the average value indicated for the 73.84-liter reference volume was 73.83, liters for which the probable error from the mean was ± 0.024 liter. An error of similar magnitude was found for small differences in volume, as when the volume of a reference was augmented by the addition of a 1-liter flask.

A greater random error is anticipated in measuring human subjects than in the runs on inert reference volumes. The production of heat and water vapor by the body leads to a somewhat greater uncertainty in the true mean chamber temperature and humidity. However, the variability to be expected in volume determinations may be estimated in part from duplicate measurements on human subjects made within a sufficiently short interval to avoid transient changes in true volume. Fourteen such pairs of runs, in which the second measurement was made within two hours of the first, yielded an average difference between the first and second determinations of -0.04 liter and a probable error for the differences of ± 0.09 liter.

Although the foregoing result suggests a high order of reproducibility in measuring human subjects, it cannot be construed as a measure of over-all error. The two volume determinations of each pair were based on one set of reference volume runs for that day and therefore do not include the variability in the indicated values of the R_i for the references. A more indicative test of over-all error is given by measurements repeated after more extended intervals, which then involve repeated runs on the references as well. For this purpose body density rather than volume must be used, since transient real changes in volume of at least 1/2 liter occur in even the most stable persons.

Data were selected for 34 subjects whose individual weight variations did not exceed ± 1 kg of their average weights. The interval between runs varied from two days to six months. The difference in density between the first and second runs was 0.0006 g cm^{-3}, while the probable error of the differences about the mean difference for the group was ± 0.0017 g cm^{-3}. The group as a whole was highly heterogeneous, consisting of both men and women with densities varying from 0.990 to 1.076, and weights ranging from 55 to 97 kg.

An exact estimate of error in a single determination of human body volume cannot easily be evaluated because of the difficulty in assessing the contributions of many small factors, both instrumental and biological. In view of the reproducibility of the instrument and the apparent abscence of significant systematic error, the probable error for a single measurement of volume would appear to be no greater than about ± 0.13 liter. Since the error is little affected by absolute volume, the corresponding error in density would range from ± 0.0026 g cm^{-3} for 50-kg subject to ± 0.0013 g cm^{-3} for a person who weighs 100 kg.

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