Group	Rat	Daily food intake (gm.)
Group A (No thiouracil)	Rat 40*	6.6 – 8.2 – 7.4 – 7.3 – 7.3 – 7.0 – 6.7 – 7.7 – 6.5 – 5.9 – 5.5 – 4.8 – 4.2 – 2.6†
	Rat 43*	8.3 – 9.7 – 9.4 – 9.2 – 8.5 – 7.5 – 6.3 – 9.2 – 2.9†
	Rat 44*	9.0 – 11.2 – 11.7 – 12.2 – 10.8 – 9.7 – 7.0 – 9.4 – 7.6 – 6.3 – 7.0 – 6.0†
	Rat 45*	8.6 – 10.4 – 10.0 – 8.1 – 9.0 – 8.3 – 7.3 – 10.2 – 8.0 – 6.0 – 6.2 – 5.1 – 5.1 – 4.8 – 4.1 – 3.4 – 0.7†
	Rat 53*	5.2 – 6.9 – 6.6 – 5.9 – 6.3 – 6.3 – 5.4 – 6.4 – 5.3 – 1.4 – 4.4 – 4.4 – 5.5 – 2.7 – 2.3 – 2.0†
	Rat 68*	6.3 – 7.4 – 7.4 – 6.7 – 6.4 – 7.6 – 6.5 – 7.7 – 6.4 – 7.0 – 7.4 – 6.9 – 8.4 – 6.0 – 5.2 – 6.3 – 6.5†
Group B (With thiouracil)	Rat 55**	8.8 – 7.8 – 6.6 – 5.6 – 5.8 – 6.5 – 6.2 – 6.6 – 6.7 – 6.3 – 7.1 – 7.4 – 7.9 – 7.5 – 7.3 – 7.1 – 7.4†
	Rat 59‡	6.1 – 5.7 – 7.0 – 6.8 – 6.6 – 8.0 – 5.7 – 7.6 – 6.2 – 6.1 – 5.9 – 5.6 – 6.4 – 7.5 – 5.8 – 6.3 – 7.7†
	Rat 60‡	7.2 – 6.9 – 6.6 – 7.0 – 6.6 – 4.9 – 4.5 – 7.5 – 6.7 – 6.0 – 5.7 – 5.2 – 5.9 – 6.7 – 5.8 – 6.6 – 6.1†
	Rat 63‡	6.6 – 6.1 – 6.4 – 6.3 – 5.9 – 6.0 – 4.7 – 8.0 – 6.2 – 6.1 – 6.5 – 6.4 – 6.0 – 6.1 – 7.4 – 7.9 – 8.1†
	Rat 64‡	6.6 – 7.2 – 7.0 – 5.1 – 5.5 – 6.3 – 5.7 – 6.4 – 5.9 – 6.5 – 5.5 – 5.5 – 5.5 – 6.4 – 6.5 – 7.7 – 8.6†

* Cirrhosis.
** Mild cirrhosis.
‡ No cirrhosis.

Average daily food intake Group A: 6.7 gm. Group B: 6.5 gm.

animals kept on a severe cirrhosis-producing regime is in good accord with the protective action of sulfanilamide against the hepatic cirrhosis due to chronic poisoning with carbon tetrachloride.[6] Both sulfanilamide and thiouracil inhibit the formation of thyroxine in the thyroid gland[5] and their effect on the liver might be based on this common denominator. Methionine protects the liver not only from purely dietary (trophopatic)[7] but also from postnecrotic (toxipathic)[7] cirrhosis, such as is caused, for instance, by carbon tetrachloride.[8] It can be assumed that the possible saving effect of lowered metabolic rate on methionine may, therefore, manifest itself not only in trophopathic but also in toxipathic cirrhosis.

The clinical implications of the above observations are obvious: Thiouracil presents itself as a supporting measure in the treatment of cirrhosis in combination with a diet rich in protein and methionine. The high incidence of injurious manifestations following thiouracil therapy does not militate against its use in cirrhosis for which condition any possible improvement in prognosis, even if only on account of prevention of progress of the disease, would represent a distinct advantage. Constant clinical observation, with repeated blood counts (leukopenia), is indispensable. It may be surmised that jaundice, seen in very few cases as a toxic complication of thiouracil medication in the clinic, is more the expression of allergic reaction than direct hepatic injury. How far these experiments on animals will prove to be valid in therapeutic clinical studies, only experience will teach.

Conclusions. Thiouracil mixed to a cirrhosis-producing synthetic diet in amount of 0.1 per cent. has a preventive effect on the production of cirrhosis in rats.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE APPLICATION OF GEOPHYSICAL OSCILLOGRAPHS TO MULTIPLE RECORDINGS IN PHYSIOLOGY

THE simultaneous recordings of several physiological phenomena is facilitated by the use of appropriate pick-up units that convert the events into electrical signals which are capable of actuating galvanometers, oscillographs, inkwriters or other recording devices. When a number of phenomena such as blood pressure, respiration, blood flow, body temperature, the activity of the heart, the activity of nerve fibers, the contraction of muscles, etc., are to be accurately and simultaneously recorded, severe instrumental difficulties arise because of the variety of pick-up units that are required for the recording of these several phenomena. The ideal recorder should be compact, permanently aligned, sensitive; yet rugged and simple to operate. Under these conditions atten-

[6] J. C. Forbes, B. E. Leach and G. Z. Williams, *Proc. Soc. Exp. Biol. and Med.*, 51: 47, 1942.

[7] H. P. Himsworth and L. E. Glynn, *Lancet*, I: 457, 1944.

[8] P. György, J. Seifter and R. M. Tomarelli. Unpublished experiment.

tion can be devoted to physiological problems being studied rather than to the care and maintenance of some make-shift apparatus. Geophysicists are able to make multiple recordings through the use of small, rugged and sensitive galvanometers aligned in banks of twelve or more and incorporated into compact, photographically recording oscillographs. These instruments are widely used in the recording of strains and vibrations in mechanical structures, in the detection of seismic disturbances and in a number of other physical and engineering applications. The galvanometers are ordinarily of the moving coil type and a variety of sensitivities are available from those giving a deflection of only a fraction of a millimeter per milliampere (at one meter optical distance) to others which give a 700–1,000 millimeter deflection per milliampere. The sensitivity of these galvanometers is inversely proportional to the square of the natural frequency and a variety of galvanometers with a variety of frequency responses are obtainable. The most sensitive types have a natural frequency in the neighborhood of 40 c.p.s., while others going up to several thousand c.p.s. are also available. Oscillographs may be ordered which incorporate several types of galvanometers in one instrument, making possible the application of the most suitable galvanometer for a particular recording. It is of course necessary to employ a galvanometer having a response which is flat over the entire frequency range which is liable to be encountered in any one recording, but the frequency requirement should not be unnecessarily extended because of the lower sensitivity which is then obtained. Many features useful for the physiological laboratory are included in the various oscillographs, such as: paper speeds which may quickly be varied from a fraction of an inch per second to several feet per second; a built-in camera which does not require a darkened room for recording; a built-in timing system which places an accurately aligned time line completely across the record; and, in the more elaborate instruments, attenuators which individually control the galvanometers. Details of the galvanometers and oscillographs may be obtained from current geophysical literature, from texts[1] and from the technical data supplied by the companies making these instruments.

It is important to note that these galvanometers are low impedance instruments and the problem of feeding into them must be solved differently for the various pick-up units. If a low impedance input unit is employed, matching to the galvanometer is obtained and enough sensitivity may then be available so that no amplification is required. A low impedance device that is especially adapted for coupling to these galvanometers is the wire strain gage,[2, 3] which is now available commercially. There is no reason why the strain gage can not be applied to the recording of such physiological phenomena as blood pressure, intra-arterial pulse, isometric muscle contractions, etc. Use of the strain gage has already been made in recording the human finger pulse[4] and strains in the skull.[5] When high impedance pick-up units are used, special matching stages are required. The geophysical practice of using stepdown transformers is not possible in physiology because of the low frequencies often encountered, and special vacuum tube matching stages may be required. One useful method of matching is to include the galvanometer in a cathode follower circuit.[6] The authors have found a simple and satisfactory arangement to be two tubes in parallel as shown in the output stage of the amplifier of Fig. 1A. The load resistance is made equal to the internal

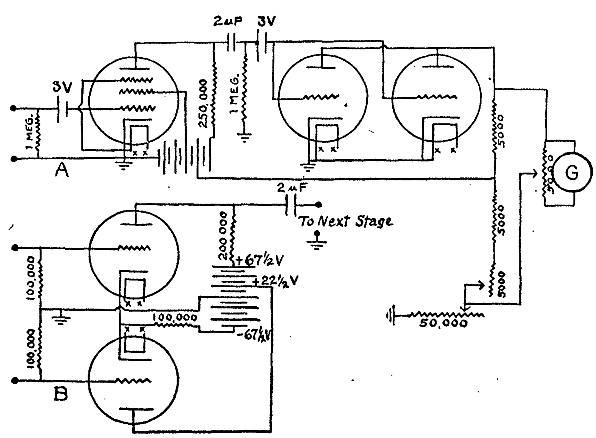

FIG. 1. A. A battery operated condenser coupled amplifier. The plate supply is 225–270 volts and the screen supply is 45 volts. B. Modification of Matthews' differential input stage using 6C6 as triodes. Other tubes, such as 6SC7, may be used.

resistance of the tubes. A fixed resistance equal to the load resistance is connected to ground through a variable resistance, which is several times the combined plate and load resistances. This arrangement eliminates the use of bucking voltages in balancing out the plate current. A second variable resistance may be added to serve as a finer balance control. The current that passes through the galvanometer is controlled by a variable potentiometer acting as a shunt. The output tubes are type 6C6 connected as triodes, but others, such as type 42, 6F6 or 6SC7, are

[1] J. J. Jakosky, "Exploration Geophysics," 1st edition, Times-Mirror Press, Los Angeles, California, 1940.

[2] D. M. Nielsen, *Electronics*, 16: 106, December, 1943.

[3] R. O. Fehr, *Electronics*, 18: 112, January, 1945.

[4] H. Grundfest, J. J. Hay and Sergei Feitelberg, SCIENCE, 101: 255, 1945.

[5] E. S. Gurdjian and H. R. Lissner, *Jour. Neurosurgery*, 1: 393, 1944.

[6] W. Richter, *Electronics*, 16: 112, November, 1943.

also satisfactory. Figs. 2A and 2B illustrate the responses of two different geophysical galvanometers (Miller) to a 200 millivolt signal applied to the grids of the output tubes. The current change is approximately 15 microamperes. With a single pentode (6C6) RC-coupled to the output tubes to provide amplification (Fig. 1A), a 500 microvolt signal gives a good deflection, as shown in the records (Fig. 2C) ob-

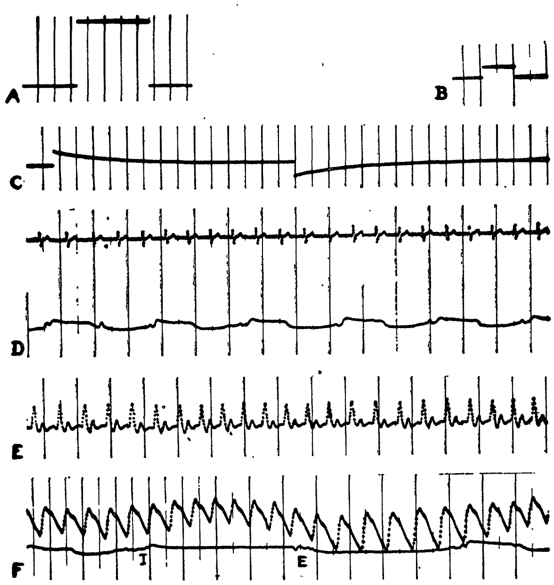

Fig. 2. A and B. A 200 millivolt square wave applied to the output tubes of amplifier (1A) and recorded by two different Miller galvanometers. C. The "on" and "off" of a square wave (500 microvolts) applied through amplifier (1A). D. The electrocardiogram (lead 1) and respiration recorded simultaneously. A thermocouple mounted in a nose piece was used to record respiration, the thermocouple operating the galvanometer directly. Upward deflections represent inspiration. E. Pulse in the right index finger recorded by the use of the hot wire-thermocouple method.[6] F. Pulse in the right finger recorded by means of a phototube and showing the effects of a prolonged inspiration (beginning at I) and the effect of a prolonged expiration (beginning at E). Time throughout is in half seconds.

tained in response to the "on" and "off" of a 500 microvolt square wave. The voltage amplification, as measured with the cathode ray oscillograph, is about 100. The time constant of this amplifier is about 1.5 seconds, but this figure could be increased by the use of a double RC coupling[7]; or even direct coupling could be employed. The ability of this amplifier and the Miller galvanometers to record such physiological processes as the electrocardiogram and finger pulses is shown in Fig. 2 (D, E, F). The finger pulse records are similar to those taken with the cathode ray oscillograph.[8]

The special advantage of these geophysical galvanometers is that they combine, as few other galvanometers do, the qualities of sturdiness, sensitivity and good frequency response. Many pick-up units such as strain gages, thermocouples, thermopiles, photocells, etc., can be used either coupled directly to the galvanometer or through a simple matching stage. This makes unnecessary the need of high-gain amplifiers, which, especially in the low frequency (subaudio) range, involve special design problems or special precautions in order to achieve a reasonable degree of stability. For some types of physiological recording it may be necessary to utilize a balanced or differential input stage. Quite adequate is Matthews's[9] circuit employing two tubes with a common cathode resistor and a negative cathode voltage. A slightly modified arrangement (Fig. 1B) is very satisfactory and possesses a high differential action. When added to the amplifier (Fig. 1A) the total voltage amplification is about 1,000, and 50 microvolts gives a good deflection.

It would seem that the use of these oscillographs in physiology would simplify many instrumental problems and give to the physiologist and biologist a convenient and useful tool for simultaneous multiple recording of many physiological changes in either one or several organisms.

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DISCUSSION

THE AMINO ACID COMPOSITION OF PROTEINS

In a recently published monograph on methods for the amino acid analysis of proteins,[1] the practice is advocated of computing the results of the determinations upon the uniform basis of a hypothetical substance that contains 16 per cent. of nitrogen. Comprehensive tables of data are presented, in all of which the original figures from the literature have been recalculated. The authors state that this is done

[1] R. J. Block and D. Bolling, "The Amino Acid Composition of Proteins and Foods." Springfield, Illinois. 1945.

[7] F. E. Terman, *Radio Engineers' Handbook*, 1st edition, p. 374. McGraw-Hill Book Co., Inc., New York, 1943.

[8] F. Crescitelli and E. Gardner, *Jour. Lab. Clin. Med.*, 30: 63, 1945.

[9] B. H. C. Matthews, *Jour. Physiol.*, 93: 25P, 1938.

[10] Now with the Department of Anatomy, College of Medicine, Wayne University, Detroit.