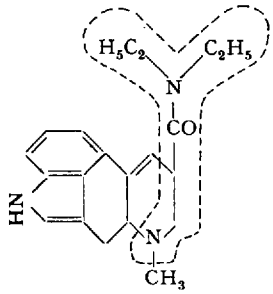
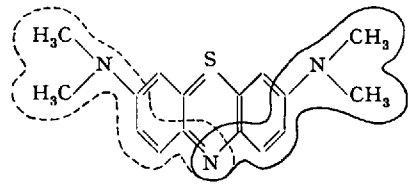
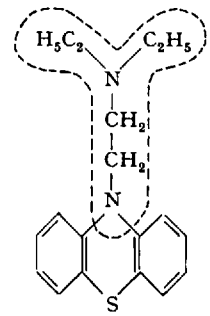


LSD



Methylene blue



"Diparcol"

N-substituted derivatives of mescaline cause model psychosis.

There is a similarity between the psychopathological phenomena caused by 500 mg mescaline and by 100 γ LSD[1], and 300 mg of mescaline or 90 γ or more of LSD cause an apparently similar alteration of the liver function in humans as measured by the glucuronic acid test[2].

Inhibition of an LSD-produced model psychosis may be brought about by previous administration of certain compounds of the phenothiazine series, e.g. methylene blue, β-diethylaminoethyl-N-phenothiazine ("Diparcol", Poulenc Ltd.) etc., displaying some apparently essential features of the LSD molecule[3] (see dotted lines).

LSD[4] has uterotonic properties; mescaline does not exhibit uterotonic action when added to the exsected organ but only when administered *in situ*[5]. Thus, transformation of the mescaline molecule in situ is suggested to be a prerequisite for its activity.

The foregoing suggest that mescaline is transformed *in vivo* to a compound resembling LSD in its main structural features and also having an affinity for wool, and that the observed physiopathological and psychopathological properties of mescaline are due to this LSD-like compound. Whether the biosynthesis is brought about by small amounts of partially demethylated mescaline with a tyramine-like compound, or whether it results, e.g. through condensation of very small amounts of mescaline with *nor*-adrenalin (or 5-hydroxytryptamine[6]) both recently identified in the brain[7], is still in the realm of speculation.

BLOCK[8] has shown that tyramine is the most powerful activator of the enzymatic incorporation of C^{14}-mescaline in the mouse liver without affecting mescaline oxydase. This evidence suggests that the formation of small amounts of a compound derived from mescaline and similar in structure to LSD might occur in the liver and could be connected with the "etiology" of the model psychosis elicited in humans after the administration of mescaline.

Acknowledgment. The stimulating discussions with Professors J. PEPPER, C. MCARTHUR, V. WOODFORD, University of Saskatchewan, Saskatoon, and Dr. M. KATES, National Research Laboratories Ottawa, are gratefully acknowledged.

R. FISCHER

Psychiatric Research Unit, Research Laboratory, Munroe Wing, General Hospital, Regina, Saskatchewan, Canada, August 5, 1954.

Zusammenfassung

Die Hypothese einer Biosynthese von D-Lysergsäurediäthylamidähnlichen Substanzen aus Meskalin in der Leber und im Gehirn wird postuliert.

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[2] R. FISCHER, F. GEORGI, and R. WEBER, Schweiz. med. Wschr., *81*, 817 (1951).

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[4] E. ROTHLIN, unpublished data (1939).

[5] G. S. GRACE, J. Pharmacol. *50*, 359 (1934).

[6] The biogenesis of LSD in the fungus has recently been described, postulating that oxidized 5-hydroxytryptophan is a precursor [*D.* HARLEY-MASON, J. Chem. Ind. *1952*, 172).

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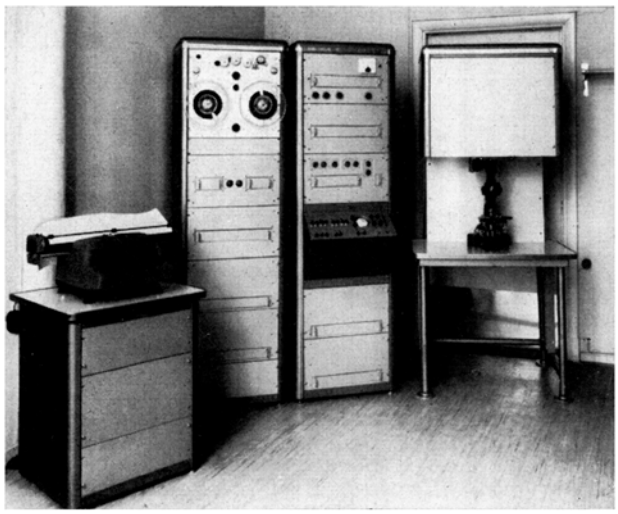
PRO LABORATORIO

A Scanning and Computing Microphotometer for Cell Analyses

The development of complicated technical tools in cytology automatically produces new technical problems. One of the main problems in quantitative cytology is the time it takes to obtain data from many measurements on each cell, and then to repeat them on many cells in order to get statistically significant results. Every problem on differentiation, cell growth or function involves this difficulty, when the sample is a section through a number of cells. There is little point trying to draw conclusions from observations on a few cells in such studies. The scanning and computing microphotometer described in this paper can be used for quantitative studies of cell sections, and is applicable for the various wave-length ranges now used in cytology. Our aim was to obtain information on transmission values integrated over the cytological preparation point by point with a sufficient resolution and within a short time. For the construction we have used the information theory in its most elementary form, applying a technique commonly used within this field: the pulse technique.

The principle is to convert light intensity to time. The apparatus is thus a type of information machine with a receptor, a microscope system and a scintillation tube with a scanning system, a computing unit, a memory unit, and a printing unit – the effector. 12,000 measurements are made on the sample under examination and the results are computed and recorded in numbers with retained spatial localization. The computation of the 12,000 values takes four minutes. The area of the sample covered by a single measurement is usually 3 μ^2. An ultimate resolution of about 1 μ is possible, and the permissible error of the apparatus has been set to 1%.

Let us consider the general construction (Fig. 1). The unit at *A* contains the microscope system and the scanning mechanism. *B* is the computing unit with its con-



D C B A

Fig. 1. View of the computer. *A* contains the microscope system and the scanning mechanism. *B* is the computing unit with the main panel. *C* is the memory unit and *D* the printing unit.

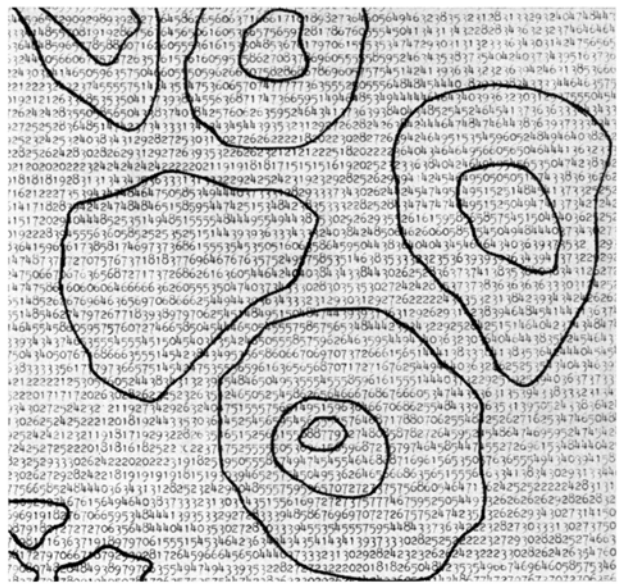


Fig. 3. The result of the scanning of a section through a spinal ganglion. An image of the section has been projected over the transmission values in the same scale.

trols. The whole system is operated from the main panel of this unit. There is ample provision for the localization of faults. The machine is built from sub-units and every unit can be connected with the oscilloscope seen on the rack, tested, and replaced if necessary. *C* is the magnetic memory with its controls, and *D* the printing unit. Figure 2 shows a simplified diagram which demonstrates how the apparatus works. The scanning mechanism, a drawing of which is seen to the left in the diagram, consists of an endless steel band, 50μ thick and perforated with small holes 0·3 mm in diameter. The holes scan the microscope image in line after line for 120 lines. When one hole has been moved 100 diameters the scan-

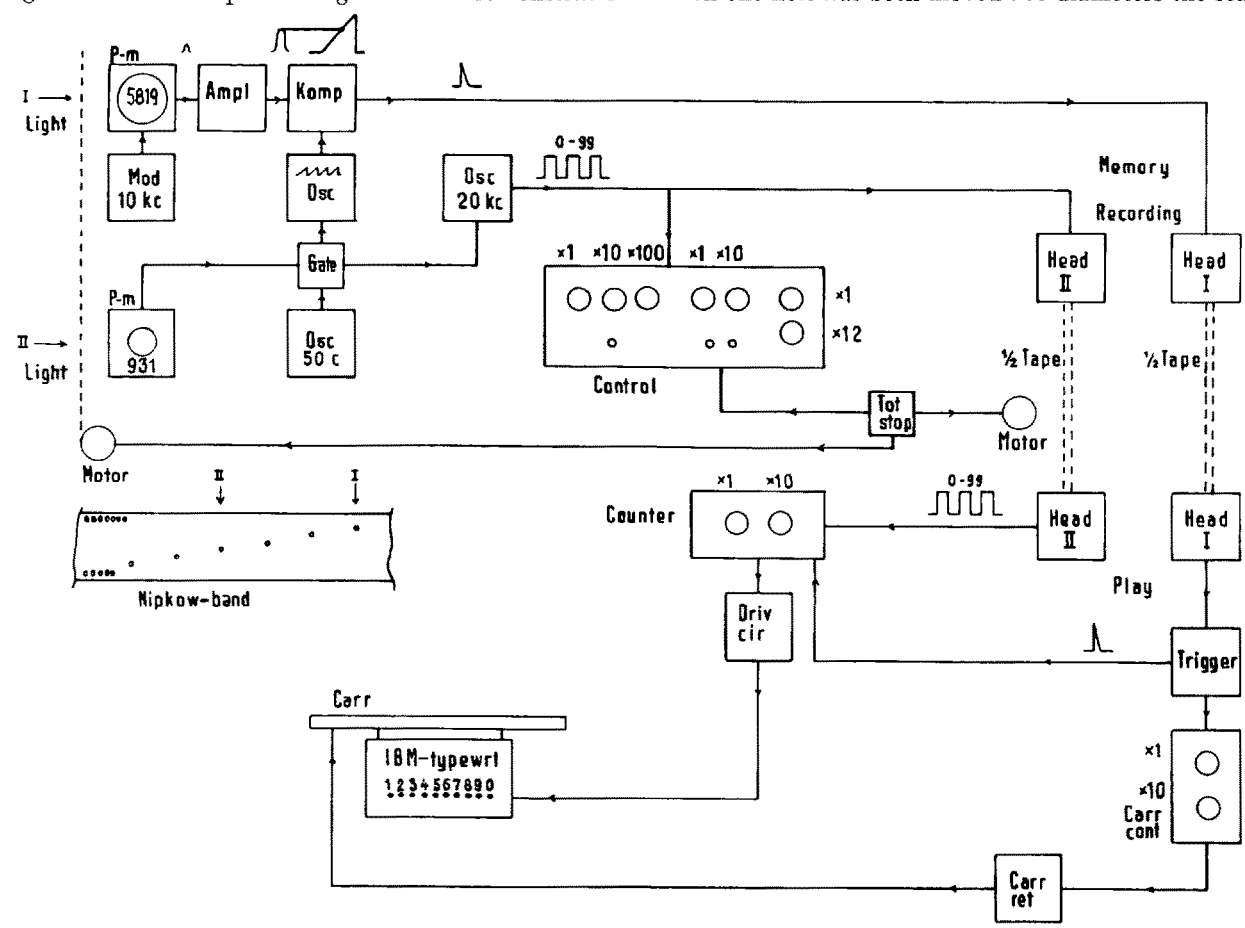


Fig. 2. Simplified block diagram.

ning of one line is complete. A section of the steel band is seen to the left in the diagram, in front of the phototubes.

The electronic problem was to achieve a linear amplification of the *DC* from the phototube. This was solved in the following way. The *DC* generated in the phototube is modulated by an oscillator and the rectified amplitude is then proportional to the light intensity. The *AC* from the phototube is amplified and rectified and fed into a comparator together with a sawtooth voltage. When the sawtooth voltage has attained the value of the above-mentioned, amplified and rectified *AC* amplitude a synchronizing pulse is emitted. Thus, during the time needed for the sawtooth voltage to increase, a pulse train is emitted with a certain number of pulses proportional to the light intensity. This computation is a synchronised process governed by another phototube. At the moment when the 3 μ^2 area of the sample is to be measured, the sawtooth voltage is started. The values of the light intensities and the synchronizing pulses are stored in the heads of the memory.

When it is convenient, these values are printed as per cent transmission point by point as they occur in the sample. One must be sure, however, that the transmission values never exceed 100%, and an initial control is therefore necessary. The apparatus has an advance control and an operation control. The advance control renders the transmittance visible on the dekatrone tubes of the panel. Individual values can also be computed. The operation control, seen to the right of the panel, is a continuous register of the localization and the number of measured values that have been registered.

The printing system consists of a pulse-counting device and an IBM writer. Trigger circuits ensure that the dekatrones emit their information in the right order.

Figure 3 shows an example of values obtained from a section through a spinal ganglion which has been exposed at 8–10 Å in an X-ray microspectrograph. The radiogram was then inserted in the computer and scanned. When the transmission values have been printed on the square of paper, the image of the preparation is projected over this area in the same scale and the outline of the cells are drawn. Details of this information machine will be published elsewhere.

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Department of Histology, Medical Faculty, University of Göteborg, December 17, 1954.

Zusammenfassung

Der vorliegende Artikel beschreibt einen Zellenanalysator, der die Lichttransmission in einem mikroskopischen Präparat absucht und quantitativ berechnet. Das Präparat, das in einem wahlfreien Teil des elektromagnetischen Spektrums untersucht werden kann, teilt sich in 12000 Messpunkte ein, gewöhnlich jedem 3 μ^2 im Präparat entsprechend. Die Transmissionswerte in Prozenten werden automatisch in der Ordnung, wie sie im Präparat vorkommen, ausgeschrieben, wobei sowohl die Verteilung als auch die Menge der untersuchten Substanz leicht aus dem Ziffernbild, das die Maschine gibt, berechnet werden kann. Die Berechnung der 12000 Messwerte dauert 4 min.

PRO EXPERIMENTIS

A Simple Paper Chromatographic Method for the Study of Serum Protein Patterns in Health and Disease[1]

Franklin and Quastel[2] applied paper chromatography to the separation of plasma proteins and showed that the patterns exhibited in chromatograms of pathological plasma vary greatly, according to the disease, indicating distinct changes from the normal. The chromatographic patterns obtained by Franklin and Quastel were criticised and shown to be artefacts by Hall and Wewalke[3]. Recently Tauber and Petit[4] have described a two-dimensional paper chromatographic method for the separation of a portion of each fraction of albumin and γ-globulin from a mixture of the two. Complete separation of the proteins was not possible by this method.

A simple circular paper chromatographic method for the separation of serum proteins is described in this note in the hope that it may prove useful for clinical diagnosis and prognosis of diseases.

The procedure adopted for obtaining the chromatograms was similar to the one described by Giri *et al.*[5] for the separation of amino acids in blood. 40 μl of the serum is spotted at the centre of a Whatman No. 1 filter paper (18·5 cm diameter). Immediately after spotting, the "wick" is inserted at the centre of the paper and the chromatogram is developed with about 40% of aqueous alcohol as the solvent. The spot should not be allowed to dry on the paper before development. After the solvent front reaches a distance of about 8 cm from the centre of the paper, it is dried at 90–100°C for about 5 min. The protein fractions are dilineated as chanelled and circular zones by staining with the dye bromophenol blue as follows:

(1) Dipping for about 3 min in 0·2% bromphenol blue in saturated alcoholic $HgCl_2$ solution for staining and fixing the serum proteins on the paper;
(2) Rinsing in 0·5% acetic acid solution;
(3) Final washing in water to remove acetic acid and drying at 60–70°C.

Figure 1 is the typical pattern of normal serum.

For better comparision of the difference in the patterns showing the variation in Albumin-globulin ratio, it is convenient to run a mixed chromatogram which may be carried out by spotting 10 μl of normal and pathological serum on the circumference of a circle (3 cm diameter) drawn at the centre of the paper, diametrically opposite to each other and developing the chromatogram as described above. Figure 3 is the chromatogram of the patterns of normal and liver cirrhosis sera. The difference in composition of the serum protein fractions-

[1] Presented before the symposium on "Chromatography" held on 3rd and 4th April 1953 under the auspices of the Society of Biological Chemists, India, and published in an abstract form in the Proceedings of the Society of Biological Chemists (India) *11*, 33 (1953).

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