natant was removed by suction and discarded. The residuent was dissolved in 20 or more cc. of water (Step 2), an equal volume of saturated ammonium sulfate solution added, and the resultant precipitate centrifuged off and taken up in a small volume of water (Step 3). Glucuronidase activity was determined on specimens removed at Steps 1, 2, and 3 by the method of Talalay, Fishman, and Huggins (*5*). Simultaneous determinations of the protein N of the extracts was also performed (*1*). The results have been arranged in Table 1.

TABLE 1

PARTIAL PURIFICATION OF B-GLUCURONIDASE OF RAT LIVER, KIDNEY, AND SPLEEN

Total weight of organs (grams)	Fraction	Volume (cc.)	Units*/cc.	Glucuronidase activity (total units)	Units/mg. N
34	Liver 1	117	5,700	673,000	1,160
	2	50	6,240	313,000	3,110
	3	20	15,650	313,000	4,280
6	Kidney 1	96	370	35,500	289
	2	25	488	12,300	665
	3	5	1,630	8,150	2,950
4	Spleen 1	100	1,270	127,000	1,270
	2	25	1,990	49,700	22,300
	3	5	7,280	36,300	18,200

* One unit glucuronidase activity will liberate 1 μg. of phenolphthalein in 1 hour at 38°C. from phenolphthalein mono-β-glucuronide at pH 4.5 in 0.1 M acetate buffer (*5*).

Depending on the nature of the tissue being extracted, the activity of the extracts has been increased three to six times, and a 4- to 15-fold purification has been achieved with a preservation of between 23 and 47 per cent of the total original activity. The best purifications were obtained when using spleen, in which the enzyme is present in higher concentration than in either liver or kidney. More powerful preparations were, however, obtained from liver, since this organ contains a greater total amount of enzyme. The application of repeated ammonium sulfate fractionations (*1*) would lead to much purer preparations of the enzyme. Furthermore, the process could be applied unchanged to larger quantities of tissue so that one could achieve even more potent activities. This has been done using a mixture of livers, spleen, and kidneys from 12 animals. However, where it is not important to have highly purified preparations of the enzyme, the product at Step 3 is quite satisfactory.

The present method eliminates the use of an acetone precipitation and the evaporation of the extract in a current of air, two undesirable operations in the original process. The possibility of undue loss of activity here has accordingly been minimized. This method is also more convenient and more rapid than the previous one, since it requires only a few hours for the complete procedure. Good results have been obtained regularly by those inexperienced in enzyme preparative work.

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Frequency Analysis of Electroencephalograms[1]

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Many manual and mechanical types of frequency analyzer are possible, and several have been applied to electroencephalographic problems. The majority are objectionable because they use an arbitrary method of integration, but up to the present time none has received general acceptance and most have been discarded by their authors. It can be presumed that they turned out to be either excessively cumbersome or failed to yield significant information.

Hoagland (*9*) used a map measurer to determine the length of the contour of slow components in the electroencephalographic tracing. This system required accurate control of amplitude and did not distinguish between amplitude and frequency.

Coordinate graphic analysis has been applied to the EEG (*5*), but it is such a tedious process that only an inadequate sample is obtainable. For the few seconds of record considered, the method yields an accurate analysis in which phase relations between harmonics are preserved.

Several different types of electrical filters have been used. One system (*10*) contained constant band-width filters in combination with integrators which measured and recorded amplitude simultaneously. This system was an early prototype of Grey Walter's analyzer and yielded essentially the same type of information. A similar system, employed by Davis (*3*) and his collaborators, had filters with a band-width proportional to the frequency. These were inserted into the oscillographic recording channels and the amplitude of the various frequency components observed. Six frequency bands could be recorded simultaneously by both systems.

Many recording frequency analyzers have been built in the past for use in sound-wave analysis (e.g. *2*, *13*).

Before the analyzer designed by one of us (A.M.G., *8*) was built, all previous systems of analysis were considered. Experience with the application of filter systems to electroencephalography convinced the authors that complete integration by electromechanical means was necessary and could be accomplished only by a system which made a repetitive function (continuous belt) of the sample chosen. Simultaneous registration of the oscillographic and analyzed records was sacrificed to obtain the highest possible accuracy. It was intended to incorporate this feature at a later date if important information was gained and if further study showed that a loss of accuracy could be tolerated.

In the past six years the EEG's of over 1,000 normal persons and 700 patients with nervous and mental diseases have been analyzed. The instrument used for this work (*8*) reduces to a spectrum any desired strip of EEG. Such a spectrum is a plot of the alternating-current voltage at any

[1] A grant for the study of this subject was received from the John and Mary R. Markle Foundation. Certain general costs were met out of funds received from the Rockefeller Foundation. The work of reducing data to lists and transforming lists to punch cards was carried out with the aid of the Works Progress Administration under Project No. 17579 and Official Project No. 665-14-3-515.

integral frequency or fraction of an integral frequency between 1 and 60 cycles/second. It was believed that spectrum analysis might reveal significant features of the EEG which had previously escaped attention, and that exact mathematical data regarding the frequency and amplitude of a large number of EEG's would provide a solid objective basis for electroencephalographic diagnosis.

Strips of EEG 30 seconds in length from the frontal, parietal, occipital, and temporal leads (indifferent electrode on the ear lobes) were analyzed. The voltages in each frequency and half-frequency between 1 and 60 cycles/second were read and listed. To facilitate statistical treatment, the data were transferred to IBM punch cards. Three 80-column cards, 10 holes to a column, were used for each spectrum. Since at least 4 spectra were obtained in each case, a minimum of 12 cards/case were required. By running the punch cards through a tabulator, any class of patients or normal controls could be sorted out and the range and distribution of voltage at any integral frequency or half-integral frequency determined. It was an easy matter with an automatic tabulating and calculating machine to obtain averages, mean deviations, and totals of voltage in a wide or narrow frequency range.

Much experimentation with the data finally leads to the conclusion that, although frequency analysis has advantages for revealing certain general features of the EEG, it is not satisfactory for clinical purposes. No index, either simple or complex, based on one or on many spectra from a given case, can express the highly specific detailed information contained in the EEG. Nothing of diagnostic or prognostic significance could be brought out by spectrum analysis that was not readily discernible by an experienced person from inspection of the unanalyzed record.

The reason for the failure of frequency analysis was easier to see by hindsight than by foresight. Such analysis necessarily disregards phase.[2] In the single unanalyzed tracing, phase is an essential component of wave form. In the multichannel record, it manifests itself as presence or absence of simultaneous, synchronized activity and also as identity or difference in pattern of waves in different leads. These aspects of phase, all taken together, convey a large part of the intelligence in the EEG. Any type of frequency analysis gives a partial expression. It is possible that such an expression might suffice for certain purposes; what was lost might be more than compensated for by an increase in objectivity or ease of quantification. However, experience shows that this is not true for clinical studies.

The analyzer developed by Grey Walter (*4, 11, 12*) is attractive in that it permits constant registration of alternating-current voltage in various frequency bands, and the registration is superimposed on the unanalyzed EEG. This is merely a practical advantage, however. The analyzer used in our work will integrate the voltage in any selected strip of EEG (*7*). The length may vary, as desired, from 1 minute to 1 second. The standard integration in most of the work referred to here covered 30 seconds. Moreover, this instrument analyzes the *electroencephalogram*; it is possible to go back over the record and choose for analysis any number of strips, sequence of strips, or overlapping sequence from any lead (*7*).

[2] Phase as used here does not refer to the artificial reversal of phase that occurs in bipolar recording when leads are connected from a common electrode (or neighboring electrodes) to opposite inputs of adjacent channels.

Voltage can be read to three places and frequency to 0.1 cycles/second. Thus, this instrument has considerably greater flexibility and resolving power than that used by Walter.

The report by Dawson and Walter (*4*) gives a satisfactory exposition of the general principles that are subsumed in all forms of sine-wave analysis. However, the authors do not sufficiently stress the fact that to regard the electrical activity of the cortex as composed entirely of sine waves is arbitrary and artificial. The specific nonsinusoidal patterns, illustrated in their report as constructed of sine waves, are so constituted only when the sine-wave components have a specific phase relation to each other. When a method of harmonic analysis disregards phase, it is possible to obtain entirely different nonsinusoidal wave forms with identical sine-wave formulas, as Dawson and Walter show.

Walter and Dovey's report (*12*) on the value of the frequency analysis for diagnosing deep tumors is unconvincing. The medium low frequency, "gamma," activity which is supposed to indicate a deep tumor is found in many conditions in which there is a slight degree of cortical involvement and is easily seen without an analyzer.

Frequency analysis facilitates the reading of differences in the predominant frequency, but a competent electroencephalographer from casual inspection of the record can read frequency to within 1 cycle/second in the range between 1 and 8 cycles/second and can see all significant differences in frequency above that range, either from measurements of wave lengths or from wave counts. It is possible with proper recording to distinguish at a glance between cortical activity and muscle potentials. This difference is difficult to see on an analyzed record, particularly if the analysis does not extend to 100 cycles/second. A more serious drawback arises, however, from the fact that the EEG cannot be correctly regarded as a repetitive function. The 20-minute multichannel recording with a 2-minute period of hyperventilation, which experience shows is necessary if the EEG is to have approximately full significance, contains thousands of nonrepeating second-to-second variations of extreme importance; because of these transients, each part of the record is different. In essence, therefore, a complete EEG is a large, detailed, and highly complicated picture. The visual analysis and correct interpretation of such a picture is a fairly easy intellectual task; for a machine it is almost impossible.

Improvements will come in electroencephalography when more attention is given to the selection and training of electroencephalographers and to the taking of easily interpreted, undistorted, artifact-free records.[3] Considerable skill and much training is required to take a satisfactory EEG. Interpretation requires at least as much intellect and training as general X-ray diagnosis, because the EEG is a registration of a highly complex form of structural functioning more akin to an X-ray picture than to an electrocardiogram. The electroencephalographer must obtain his professional competence by studying for at least a month a large number of normal

[3] This means (1) recording that is unaffected by fluctuations in line voltage or changes in temperature, (2) equal amplification of all frequencies between 1 and 80 cycles/second, (3) monopolar recording from at least 8 cortical areas on 6 channels simultaneously (more are desirable), (4) a paper speed of 3 cm./second to give adequate resolution, (5) the center line of each tracing not more than 3 cm. from its neighbor in order to permit close comparison of the activity in neighboring leads, and (6) a record free of artifacts and almost entirely clear of extraneous body potentials.

and abnormal cases in a center where such cases have already been collected and classified. An equivalent training will require 5 or 10 years if the beginner tries to collect the requisite normative and pathological data for himself. He will certainly encumber and embarrass himself if he places major reliance on any type of electromechanical frequency analyzer.

It should not be concluded from these remarks that electromechanical analysis of the EEG is altogether unprofitable. For special purposes and under limited conditions quantification of certain aspects of the EEG is desirable. New types of electromechanical analyzer will doubtless be developed which will be as useful or possibly more so than the one which we have employed or the one devised by Walter. However, experience has shown that in electroencephalography great significance attaches to transient wave forms, wave patterns, and differences in phase relations between leads; for the analysis of this type of data even a supermachine is defective as compared with a trained eye and mind.

Addendum: Since the completion of this manuscript two monographs on frequency analysis of the EEG have been received from France. The first, by Bertrand and Lacape (*1*), discusses the advantages of graphic Fourier analysis. The second, by Drohocki (*6*), deals with the electrical activity of the cortex as reviewed through band-pass frequency filters of the type originally used by Loomis, *et al.* (*3, 10*). Nothing in these reports requires a modification of the point of view expressed in the present article. Both are valuable contributions but do not consider the limitations of the method employed, nor does either give sufficient credit to the resolving power of the human eye and intellect.

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Book Reviews

Science, liberty and peace. Aldous Huxley. New York-London: Harper, 1946. Pp. 86. $1.00.

In the second half of the 18th Century and throughout the 19th, many scientists and political philosophers believed that liberty and peace were so linked to science that they must always advance with it. This belief has become constantly harder to hold as the succeeding years have shown a great advance of science with little gain for liberty and less for peace. In the opinion more often expressed today, science is a powerful but morally indifferent engine, which can be used as well to enslave men as to make them free, to kill as to make alive.

This is the opinion of Mr. Huxley in the book here reviewed. But he adds a further and more somber judgment, that the social system under which scientific research began in Europe and, even more, the conditions the world over in which it is practiced today imposed and still impose a tremendous bias toward the use of science for oppression and war.

The book begins with a quotation from Tolstoy: "If the arrangement of society is bad (as ours is) and a small number of people have power over the majority and oppress it, every victory over Nature will inevitably serve only to increase that power and that oppression. This is what is actually happening," to which the author adds: "On many fronts Nature has been conquered; but, as Tolstoy foresaw, man and his liberties have sustained a succession of defeats." To account for this, he says that in the early years of modern science economic power was already maldistributed. Those who held the greater share of it naturally employed inventors and technologists to apply scientific discoveries in a way to increase their profits and their power. In this way the methods of mass production were improved and those of small production neglected. Consequently, mass production now has an advantage, partly inherent, partly artificial, but able in either case to consolidate more and more power in fewer and fewer hands. Unemployment is both a result and a secondary cause of this concentration. There is now, as there was in the precarious days between the fall of Rome and the rise of feudalism, "a general wish to exchange freedom for protection, independence for guaranteed subsistence in the service of the holders of great power."

Whether this power is held by a ring of financiers or an oligarchy professing socialism is, in the author's view, beside the main point, because the excesses of power will in time mold all oligarchies to a common likeness. And because the craving for power is never satisfied, every such power group will be menaced by every other, and, when it controls the state, it must maintain an armed society. In this its social resources are a hypertrophied industry and fluid labor force, in which both machine parts and people are interchangeable, so that the industry may be quickly converted to the making of munitions and the people readily conscripted and subjected to the mass propaganda of state-worship, an idolatry with practices as revolting as the worship of Moloch.