while both units can act as 'acceptors' of the potential methyne carbon atoms. Such a process would probably involve attachment of the enzyme to the two acidic side-chains which are differently placed with respect to *M* in the two substrates *A* and *B*. It is further postulated that in the final ring closure a reaction which is different in character from the linear condensation of pyrrolic units, the *M* groups of either *A* or *B* units, can be activated. This theory predicts the formation of porphyrins of type I and III and the non-occurrence of those of types II and IV. Initial condensation of *B* with *A* can only be followed by further successive addition of *B* units to give *B—B—B—A*, which on ring closure will give type III. Self-condensation of two *A* units is precluded, while *B—B* condensation can be followed by either further addition of two *B* units giving uroporphyrin I or of one *A* and one *B* unit giving uroporphyrin III. The restrictions placed on the reactions of *A* prevent the incorporation of more than one *A* unit and thus the formation of uroporphyrins II and IV.

The proportions of type I and type III porphyrins synthesized will depend not only on the relative amounts of the units *A* and *B*, but also on the ratio of the velocity constants k_1 and k_2 :

$$\begin{aligned} [B-B] &= k_1[B]^2 \\ [A-B] &= k_2[A][B]. \end{aligned}$$

It is an important consequence of the above postulate that, if $[A]$ and $[B]$ are equal and $k_1/k_2 = 1$, the amounts of uroporphyrin III produced will exceed considerably those of the isomeride of type I. This follows immediately from the fact that while each *AB* condensation leads to porphyrin III, *BB* or *BBB* can add either *A* or *B* and thus give rise to both uroporphyrins. However, the great preponderance of type III porphyrins cannot be entirely explained by such a statistical factor. We shall have to assume that either k_2 exceeds k_1 or that $[A]$ is larger than $[B]$. An excess of *A* may easily arise in the following way. Whatever the relative values of $[A]$ and $[B]$ and of k_1 and k_2 are, the amount of *B* removed from the system by porphyrin formation must be greater than that of *A*. Thus, if the rates of formation of *A* and *B* are approximately equal and if both rates are not very much faster than that of the further condensation, the stationary concentration of *B* in the steady state must be much smaller than that of *A*. This would obviously lead to preponderance of uroporphyrin III. Moreover, owing to the statistical factors discussed above, a ratio of $[A]$ to $[B]$ or k_2 to k_1 of about 15 would be sufficient to produce a ratio in the two uroporphyrins of about 500 to 1.

Congenital porphyria may therefore be explained as a quantitative change in the relative rate of one step in porphyrin synthesis. Thus a decreased rate of production of *A* or an increase in the rate of formation of *B* will favour synthesis of uroporphyrin I. A similar result will be obtained if the ratio k_2/k_1 decreases.

The hypothesis put forward assumes that coproporphyrin III and protoporphyrin IX are derived from uroporphyrin III by successive decarboxylation and dehydrogenation. The fact that uroporphyrin III has not been identified with certainty in the urine, faeces or tissues of normal individuals and possibly not even in cases of acute porphyria may mean that the initial decarboxylation to coproporphyrin is very fast in the III series. Both copro- and uroporphyrin

I occur in porphyria, and it must be supposed that either a separate enzyme is concerned in the transformation of the latter to the former or that the enzyme responsible for the corresponding decarboxylation in the III series is not wholly specific and decarboxylates uroporphyrin I slowly. On the other hand, the enzyme converting coproporphyrin to protoporphyrin appears to be highly specific for the III series, since no meso- or protoporphyrin derived from aetioporphyria I have been found in Nature. This specificity is likely to be due to the spatial arrangement of the propionic acid side-chains in rings III and IV, which presumably are points of attachment for the enzyme(s) concerned with the dehydrogenation and decarboxylation at this stage.

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² *J. Biol. Chem.*, **166**, 627 (1946).

³ Muir and Neuberger, *Biochem. J.*, **45**, 163 (1949). Wittenberg and Shemin, *J. Biol. Chem.*, **178**, 47 (1949).

⁴ Gray, Muir and Neuberger (in the press).

⁵ Altman, et al., *J. Biol. Chem.*, **176**, 319 (1949); Grinstein et al., *J. Biol. Chem.*, **174**, 767 (1948); **179**, 359 (1949).

⁶ Muir and Neuberger, *Biochem. J.*, **45**, xxxiv (1949).

⁷ Wittenberg and Shemin, *Federation Proc.*, **9**, 247 (1950).

⁸ Gray and Neuberger (in the press).

⁹ London et al., *J. Biol. Chem.*, **179**, 463 (1949).

¹⁰ Gray, Neuberger and Sneath (in the press).

¹¹ "Untersuchungen über Porphyrine" (Hirzel, Leipzig, 1929).

¹² *C.R. Trav. Lab. Carlsberg, Sér. chim.*, **22**, 454 (1938).

¹³ *Physiol. Rev.*, **20**, 416 (1940).

¹⁴ *J. Lab. Clin. Med.*, **28**, 323 (1940).

¹⁵ *J. Roy. Soc. Arts*, **90**, 795 (1942).

¹⁶ Siedel and Winkler, *Liebigs Ann.*, **554**, 162 (1943).

SUBJECTIVE MEASUREMENTS IN ACOUSTICS

A MEETING of the Acoustics Group of the Physical Society held on April 25 at the National Hospital, Queen Square, London, W.C.1, took the form of a discussion on the technique of subjective measurements. The greater part of the discussion naturally dealt with subjective experiments in acoustics, but there were also certain contributions referring to measurements of vision. The main points dealt with in the discussion were the dimensions of measurement appropriate to subjective experiments in acoustics, the need for an agreed terminology, and the reliability of subjective measurements. A number of contributors reported the great reliability of relative measurements and the comparative unreliability of absolute measurements.

The chairman for the meeting was Mr. H. L. Kirke (chairman of the Acoustics Group) and the discussion was opened by Dr. D. B. Fry, of University College, London, who dealt with a number of fundamental considerations in the making of subjective measurements. He defined an objective measurement as one in which the role of the human being is confined to that of observer, and a subjective measurement as one in which a human sense organ and brain are included in the 'experimental circuit'. The purpose of all subjective measurements is to establish correlations between events in the physical world and events within the human brain, that is to say, correlations between the stimulus and the sensations which it evokes. The technique of such measurements consists in measuring the stimulus along certain dimensions and correlating these measure-

ments with the magnitude of the sensation. The basis of subjective work in acoustics, therefore, is the assumption that the idea of magnitude can be applied to the sensations registered by the human brain. The most commonly used magnitudes of sensation are the minimum perceptible sensation or minimum perceptible change in sensation, which are used in determinations of thresholds of all kinds. Other measurements depend on the idea that the brain can register equal magnitudes of sensation (for example, equal loudnesses) and that it can even decide that one sensation is twice, five times or ten times as great as another. These operations are carried out, for example, in experiments on the fractionation of pitch and loudness.

One of the most important questions in subjective measurements concerns the dimensions of measurement. It is essential that the stimulus and the sensation should be clearly distinguished from each other, and the dimensions of the sensation must be inherent in the subjective world to which the sensation belongs; they cannot be imported from the realm of physical measurements. Dr. Fry suggested that there are three basic dimensions of acoustic sensation: pitch, loudness and quality. These are basic dimensions because two sounds may be presented to the human brain which differ from each other with respect to one of these dimensions, while being the same with respect to the other two. To these purely acoustic dimensions must be added a fourth, which is common to all sensations, namely, a dimension which represents time. The term 'length' might be adopted to express this aspect of the sensation.

The difficulty of maintaining clearly the distinction between the stimulus and the sensation is partly due, Dr. Fry said, to the lack of an agreed terminology in acoustics. Although the various properties of the sensation are not correlated in a simple fashion with a single aspect of the stimulus, it is convenient to have corresponding terms wherever possible. Thus, the term 'length' might refer to the sensation, and 'duration' to the stimulus; 'pitch' to the sensation, 'frequency' to the stimulus; 'loudness' to the sensation, and 'intensity' to the stimulus. The 'quality' of the sensation has no direct counterpart in the stimulus, but the term 'complexity' might be used to denote either a property of the wave-form of the stimulus, or the number of components yielded by any method of frequency analysis which was employed. In addition to these terms for the dimensions, the term 'threshold' might be reserved for the minimum perceptible sensation, and 'limen' for the corresponding magnitude of stimulus, while minimum perceptible changes might be called 'differential threshold' and 'difference limen' respectively.

In dealing with various techniques of subjective measurement, Dr. Fry suggested that a distinction might usefully be made between the experiment which requires an effort of introspection from the subject, and that in which he is allowed to make some automatic reaction such as he makes in everyday life. Most techniques for determining limina are 'introspective', whereas articulation-testing methods, for example, depend on a quasi-reflex response from the subject. The subject is generally more at ease in experiments of the second type, but quite stable results can nevertheless be obtained with the introspective method. Whichever technique is used, the part played by the subject in the experiment should be as simple as possible, and he should not be allowed

any control over the stimulus, since this gives rise to a spurious reliability in the results. The observer needs much skill and judgment in the conduct of the experiment if the measurements are to yield reliable results.

Mr. T. Somerville (B.B.C.) also spoke of the need for an agreed terminology in this field and cited the use of the term 'resonance' by musicians as leading to much confusion. He did not agree with Dr. Fry that the subject should not be allowed to control the stimulus; there are many cases in which it is important that he should do so. He pointed out that there are a number of difficulties in subjective measurements. A subject must not be asked to continue the measurements for too long; a test lasting twenty minutes is generally the maximum which should be allowed. In all measurements it is necessary to carry out a pilot experiment to show up the various difficulties which could not be foreseen. Then there is the question whether subjects should be selected or not. This would depend very much on the type of experiment which is visualized; in the use of a questionnaire, for example, it is necessary to use a large number of subjects, and these would normally be unselected. It has been found by the B.B.C., however, that much valuable information can be obtained by using a group of specialists as subjects for particular measurements.

Mr. P. Denes (University College, London) stressed the fact that the measurement of sensations is possible only along the appropriate dimensions, and that subjective measurements cannot measure along physical dimensions. With regard to quantitative subjective scales, he distinguished the rank-order scale from the numerical scale and cited the scale of phons and the scale of sones as examples of the two types. He also suggested that relative subjective measurements should be made in preference to absolute ones, since they give greater reliability. Referring to the general basis of subjective measurements, Mr. Denes said that there is always a considerable number of links in the chain which connects stimulus with sensation, and that influences of various kinds operate on these different links; one is therefore never dealing with a single cause and effect, and it is not justifiable to draw conclusions from subjective measurements about any single link in the chain. He also put forward a plea for the fullest possible description of the experimental conditions in published accounts of subjective measurements.

Subjective measurements of visual effects were described by Dr. R. G. Hopkinson (Building Research Station), who dealt with the degree of reliability which may be achieved in such measurements. His experiments have been concerned with the glare set up by lighting systems, and employ a 'multiple criterion' technique; that is, the subject is given a limited number of judgments (in this case 'just imperceptible glare', 'just acceptable' and so on) and he then adjusts the stimulus himself to match the given judgment. It has been found that the absolute level of the adjustment varies considerably even with one subject on different occasions, but as relative measurements the results show a high degree of reliability.

Mr. C. R. Maguire (Metropolitan-Vickers Electrical Co., Ltd.), in describing experiments involving equal loudness judgments, mentioned several important points of technique. Experience has shown that in this field it is advisable to take all control of the

stimuli away from the subjects, and the question which the subject has to answer should be reduced to the simplest possible terms. Where the subject is asked to make a comparison, the experiment should begin with cases in which the difference between stimuli is large and the subject has no difficulty in answering the question. An interesting and so far unexplained result was obtained in the experiments described; it proved to be of some importance whether the reference tone or the test tone was varied when presenting the stimuli, as a change in this respect introduced a consistent change of about 4-5 phons in the results.

The chairman (Mr. H. L. Kirke) stressed the need for keeping random variations in equipment small in comparison with the quantities to be measured. He also mentioned that the 'multiple criterion' technique has been successfully used by the B.B.C. in measuring the unpleasantness of interference in radio reception. In this particular experiment, six criteria were employed. The discussion, he said, had indicated a real need for some consideration of the terminology to be used in connexion with subjective work.

An account of experiments on the adaptation of the ear to sound stimuli was given by Dr. J. D. Hood (Otological Research Unit, Medical Research Council), who suggested that adaptation might have an important bearing on many subjective acoustic measurements. His experiments have demonstrated a difference between the results obtained by alternate and simultaneous loudness balances.

Mr. D. L. Richards (Post Office Research Station) dealt with the application of probit analysis to the calculation of confidence limits with respect to the results of subjective measurements. The experiments discussed were designed to determine the loudness-level necessary to provide a usable telephone system. When the proportion of subjects who judged the system to be usable was plotted against the loudness level, the results gave a probability integral. The standard deviation of the corresponding normal distribution gives the measure of reliability of the judgments. The experiments also showed that the judgments of one subject are very reliable in the course of a single experiment, but that the absolute levels for that subject vary on different occasions.

A comprehensive account of the part played by subjective measurements in clinical work on deafness was given by Dr. T. S. Littler (Wernher Research Unit, Medical Research Council). He pointed out the difference between measurements in which the subject has to interpret what he hears, and those in which he has simply to register that he hears something. In the deafness clinic, both types of measurement are made in the forms of pure tone audiometry and speech audiometry. Certain limitations are imposed by the conditions in which such tests are carried out. The time available is short and so the tests must require little conditioning of the subject. With deaf patients, it is particularly necessary that all instructions should be precise and simple; in articulation tests employed in speech audiometry, only meaningful words can be used, and the material has to be suitable for the particular patient. Care is necessary to avoid unwanted subjective effects, such as the setting up of transients in the ear through the sudden onset of a pure tone signal, or excessive practice effects in speech audiometry. Assessing the true performance of hearing aids is an operation which must be based on subjective measurements; and, where objective methods are used for the

purpose, their results should be correlated with subjective judgments.

Mr. J. G. Holmes (chairman of the Colour Group of the Physical Society), in commenting on the need for an agreed terminology, gave a résumé of the work done by the Colour Group in drawing up a suitable terminology for use in its own field.

Mr. R. L. Dadson (National Physical Laboratory) discussed the technique of loudness-balance experiments particularly, and said that the order in which different stimuli are presented to the subject should be random. Experiments at the National Physical Laboratory in which the subject was allowed control of the stimulus gave results which agreed well with those of measurements in which he had no control, although the scatter of the latter was rather greater.

D. B. FRY

GROWTH AND FORM

ON March 16 the Royal Society held an all-day discussion meeting on the "Measurement of Growth and Form". Prof. S. Zuckerman introduced the ten formal contributors by saying that this was the fourth symposium having growth as its subject-matter that had been held during the past five years. The first¹ had taken the form of a *Festschrift* for Sir D'Arcy Wentworth Thompson, whose lasting influence on current thought would be apparent throughout the proceedings; the second, a conference at Princeton in 1946, the proceedings of which had just been published²; the third, the Summer Conference of the Society for Experimental Biology in 1947³. The present conference was to be deliberately narrower in scope than these last two, since it was less concerned with growth mechanisms than with the measurement of growth and form. This restriction might make it possible to reach agreement on a variety of technical problems. What, for example, was the status of growth equations: were they empirical or could they be arrived at deductively? What was the relationship between the curve of growth of a single organism and that compiled from the means of massed statistics? Was the allometry equation a valid formulation of differential growth, and what was its relationship to D'Arcy Thompson's method of transformations? Prof. Zuckerman called for a clear statement of the differences between the modes of growth of plants and animals, and asked how far methods appropriate to the description of animal growth were applicable to the growth of plants.

Prof. F. G. Gregory took up the last question. Plant growth, he said, is in a sense permanently embryonic, in that change of form endures throughout the plant's life-history. In the main, the form of the higher plant is governed by the relative development of leaf and stem; the tendency for secondary axes or branches to be produced; the absolute sizes and shapes of leaves and their arrangement in the stem; and the duration of growth of primary and secondary stems. The form of the leaf was the subject of mathematical description by D'Arcy Thompson; but such a description did not illuminate the actual mechanism of growth, for the shape of the leaf is independent of cell size or shape and is a function of local variations in the rates of cell division, apparently related to the distribution and synthesis of auxins. The comparison of the growth processes of different organisms promises to be more rewarding. A study