

suggests the possibility that these might compete for sites on collagen or interfibrillary material with naturally occurring substance resembling cyanide in properties. This, however, is pure speculation.

We thank the Abbott Laboratories for a gift of  $\beta$ -aminopropionitrile.

MARGARET L. R. HARKNESS  
R. D. HARKNESS

Department of Physiology,  
University College, London.

<sup>1</sup> Harkness, Margaret L. R., and Harkness, R. D., *Proc. Fourth Intern. Cong. Rheology*, Providence, Rhode Island (1963). *Symp. Biorheology*, edit. by Copley, A. L. (New York: John Wiley, 1964).

<sup>2</sup> Long, C., *Biochemists' Handbook*, 58 (London: Spon, 1961).

<sup>3</sup> Dixon, A. A., and Webb, E. C., *Enzymes*, 374 (London: Longmans, Green).

<sup>4</sup> Harkness, Margaret L. R., and Harkness, R. D., NATO Advanced Study Conf., St. Andrews, June 1964; in *Structure and Function of Connective and Skeletal Tissues* (Butterworths: London, 1965; in the press).

<sup>5</sup> Levene, C. L., and Gross, J., *J. Exp. Med.*, **110**, 771 (1959).

<sup>6</sup> Fry, Phyllis, Harkness, Margaret L. R., Harkness, R. D., and Nightingale, Margaret, *J. Physiol.*, **164**, 77 (1962).

### Linearization of Evoked Responses to Sine Wave-modulated Light by Noise

THE use of sine wave-modulated light in psychophysics<sup>1,2</sup> has directed attention to problems of linearity in the signal transmission in the visual system.

The first electrophysiological experiments with modulated light have revealed strong non-amplitude dependent distortions<sup>3,4</sup>. One of the most striking phenomena is that in most subjects with the modulation at 5 c/s a nearly pure 10 c/s response is found in the occipital leads of the EEG.

A tentative explanation was presented<sup>4</sup> in which the signal was supposed to be distorted in an early stage of the system. This distorted response, or a combination of it and a rather undistorted response, would then be processed in the cortical areas in a way comparable with selective filtering with the filter frequency set at 10 c/s. It was shown that there are subjects in which indeed resonance effects occurred at approximately 10 c/s, this being at, or near, their  $\alpha$ -rhythm frequency. It was suggested that at low percentages of modulation the quantal and neural noise may exceed the variations occasioned by the modulation.

In an earlier paper<sup>5</sup>, an estimate of the quantal noise near subjective threshold at 10 c/s was given. The conclusion was that with certain suppositions about quantum efficiency, etc., the variations in the light due to quantal noise became of the same magnitude as the amplitude of the modulation. Since this was calculated for a field of 22', it can be expected that for one single receptor the modulation-noise ratio will be considerably smaller. Although such estimates are open to criticism, it was suggested that in a case where the noise exceeds the actual signal, in some non-linear systems the distortion would disappear. This leaves the question open whether and in what way the signal-to-noise ratio in the actual case will have to be improved before the stage of distortion is reached, regarding the large distortions found at modulation depths as low as 3 per cent.

For a number of non-linear systems of the rectifying type the influence of noise on the response functions was calculated and it was found that a sine wave with noise or a non-correlated periodical signal, such as a triangle, sine wave, etc., added, will be less distorted by rectification procedures than a pure sine wave.

This suggested the following experiment: A well-trained subject was stimulated with white light from a television projection tube which could be modulated electronically<sup>6</sup>. The stimulation was performed with a large field at moderate intensity, in the range of 50–200 lux equivalent. The level of illumination had little influence on our results. The responses of the subject for 10 per cent modulation were averaged by a *CAT* computer and are presented for

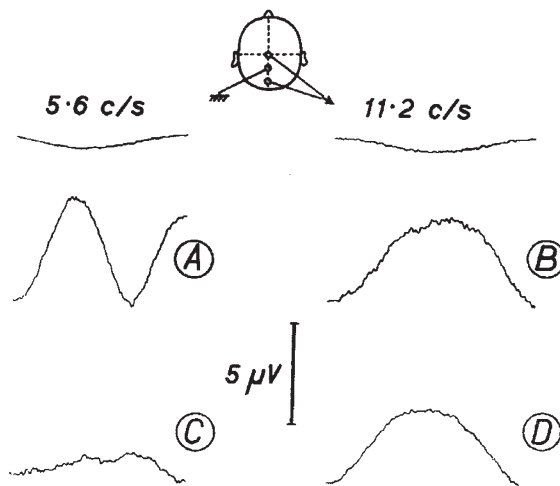


Fig. 1. Occipital responses to 5.6 and 11.2 c/s. Diffuse illumination, 10 per cent modulation, natural pupil, approximately 200 lux equiv. Upper trace: modulated light. Medium trace: responses to sinusoidal stimulation (A and B). Lower trace: responses to sinusoidal stimulation and noise (C and D)

two-eye stimulation in Figs. 1A and B for 5.6 and 11.2 c/s. It is seen that the 5.6 c/s gives a pure second harmonic response, whereas the response at 11.2 c/s displays mainly the fundamental frequency. If now gaussian noise resulting in a signal-noise ratio  $A^2/2\sigma^2 = 0.04$  ( $A$  being the amplitude of the sine wave,  $\sigma$  being the standard deviation of the noise) and a band-width 15–25 c/s is added to the modulating signal (1C and 1D) the second harmonic at 5.6 c/s stimulation nearly disappears, whereas the fundamental response at 11.2 c/s stimulation is much less affected, if at all. This may depend on the influence of saturation phenomena.

If one eye is stimulated with the sine wave modulation and the other eye separately at the same time with only noise, not much change in the responses to 5.6 and 11.2 c/s is found, compared with responses to stimulation of one eye with sine wave modulation and the other eye with steady light. This, and other arguments, suggest that most probably the distortion is not caused at a late stage in the system. If these results are valid also for the spontaneous noise inherent in the retinal processes, a kind of integration has to be assumed to increase the signal-noise ratio before the distorting stage is reached.

The possibilities for further work with this method are evident, and one of these is the adding of high-frequency sine waves to get an impression of the high-frequency attenuation up to the stage of distortion. By comparing responses at 5.6-c/s stimulation with the addition of non-related high-frequency sine waves we could deduce that the high-frequency attenuation from 25 to 60 c/s is less than would be expected from the so-called De Lange curves, a problem discussed earlier by Van der Tweel<sup>7</sup> and Levinson<sup>2</sup>.

Part of this work was supported by contract N 62558–2701 of the U.S. Navy European Research Program and project MFA 282–A–21 of the Organization for Health Research T.N.O.

H. SPEKREYSE  
L. H. VAN DER TWEEL

Laboratory of Medical Physics,  
University of Amsterdam.

<sup>1</sup> Lange, H. de, thesis, Delft (1957).

<sup>2</sup> Levinson, J., *Docum. Ophthalm.* (Den Haag), **18**, 36 (1964).

<sup>3</sup> Clynes, M., Kohn, M., and Lifshitz, K., *Ann. N.Y. Acad. Sci.*, **112**, 468 (1964).

<sup>4</sup> Tweel, L. H. van der, *Docum. Ophthalm.* (Den Haag), **18**, 287 (1964).

<sup>5</sup> Tweel, L. H. van der, *Ann. N.Y. Acad. Sci.*, **89**, 829 (1961).

<sup>6</sup> Denier van der Gon, J. J., Strackee, J., and Tweel, L. H. van der, *Phys. in Med. Biol.*, **3**, 164 (1958).

<sup>7</sup> Tweel, L. H. van der, *Acta Physiol. Pharmacol. Neerlandica*, **11** (1962)