

tion of HFC in the non-tumour-bearing partners, and the figures for gastric mucosa are inconsistent. A similar general elevation of HFC has previously been noted in the tissues of mice dying from Ehrlich ascites tumour<sup>2</sup>, but no indication as to the mechanism of the process was obtained.

It appears that the unusually high excretion of histamine in the urine of female rats bearing the Walker mammary carcinosarcoma may be explained by the ability of the tumour itself to form histamine and also by the increased capacity of the liver in this respect. From the results of the experiments on parabiotic rats it seems that the HFC of several tissues, including the liver, may become elevated and that a blood-borne factor is involved. The observations of high HFC in the tumour and enlarged liver tissue support the view that there is a connection between high rates of histamine formation and certain types of rapid tissue growth<sup>11</sup>.

**Zusammenfassung.** Die Geschwindigkeit der Histaminbildung wurde bei Ratten von experimentellem Walker Carcinosarcom kontrolliert. Bei Parabiosen konnte gezeigt werden, dass der Faktor, welcher diese Histaminbildung auslöst, mit dem Blutstrom übertragen wird.

MARIAN JOHNSTON

*Institute of Physiology, University of Lund (Sweden),  
August 12, 1966.*

<sup>11</sup> This study was supported by U.S. Public Health Service grant No. 5R01 HD00255-06 to Prof. G. KAHLSON, whose interest is gratefully acknowledged. Merck, Sharp and Dohme, Rahway, N.J., USA, kindly gave the  $\alpha$ -methylhistidine.

## Oscillations in the Pigeon's Pupil Servomechanism in Relation to Illumination

The cybernetic approach considers the pupil reflex to light as a self-regulated control device to regulate light impinging on the retina. Similarly to the human eye<sup>1</sup>, the pupil of the chicken continuously undergoes small fluctuations in area even in steady illumination<sup>2</sup>, comprehensible when considered as sustained oscillations in the pupil servosystem because of the time lag of the feedback path which completes the loop. This induced pupillary hippus may originate in, or be modified by, properties of the iris neuromuscular system (i) or central nervous system elements such as reflex centres of the brain stem (ii) or the retina (iii).

Comparison of the frequency spectrum of the pupillary unrest shows values up to 2 c/sec in the smooth muscle of the human iris<sup>3</sup> and up to 15 c/sec for the pigeon's iris consisting of striate muscles, which clearly indicates the effect of the iris neuromuscular system on the spontaneous oscillations of the pupil area. Similarly, the effect of the central nervous system can be inferred from the close correlation of unrest of one iris with the simultaneously recorded unrest of the contralateral iris in humans<sup>4</sup>, and from the effect of brain cooling on the frequency of pupil oscillations in pigeons<sup>5</sup>. The present experiments, which are part of a study of the pupillary reflex to light in the pigeon<sup>6</sup>, were undertaken in order to determine how far the pupil's unrest can be modified by changes at the loop input, i.e. at the retinal level.

Awake, unanaesthetized pigeons were used throughout the investigation. The head of the animal was fixed by holding the skull between the occiput and the beak. The pupil area was measured continuously by reflecting IR-light from the iris onto an IR-photocell shielded with a Kodak 87C filter to eliminate the effects of visible light of the conditioning beam. The output of the photocell was fed into the input of a d.c. amplifier of an oscilloscope (Tektronix type 502A) and recorded photographically on moving film. In order to correct the luminance readings into retinal illumination, it was necessary to measure the actual size of the pupil. This was done by taking photographs of the pigeon's pupil in IR-light. The experiment

started after a dark period of 1 h by determining the threshold of the pupillary light reflex. The experiments were performed by exposing the eye to constant lights of increasingly higher luminances. Records were taken after the adapting light was presented for a period of not less than 10 min.

The Figure, showing records of a typical experiment, gives samples of the fluctuations of the pupillary area at different constant luminances of adaptive illumination. As can be seen from part A of the Figure there are, at low levels of illumination, only a few oscillations of larger amplitude. With increasing luminances of the conditioning light both the amplitude and the frequency of the sustained oscillations increase<sup>7</sup>. Quantitatively (Figure B) the frequency of the pupillary oscillations increases from low values (about 1 c/sec) in dim light (retinal illumination less than 10 Troland) to high values (about 15 c/sec) at high luminances of the conditioning light (1500 Troland). Thus the increase of frequency of oscillations of the pupillary diameter is clearly in the photopic range of luminances of the pigeon's pupillary response to light<sup>8</sup>. While it is commonly believed that the pupillary response to light is mainly governed by the retinal cones<sup>9</sup>, this is certainly untrue in the dark-adapted state and for light stimuli evenly distributed over the entire retinal surface<sup>9</sup>. However, the present experiments indicate it to be true for the oscillatory changes of the

<sup>1</sup> L. STARK, F. W. CAMPBELL, and J. ATWOOD, *Nature*, Lond. **182**, 857 (1958).

<sup>2</sup> H. G. THIENEMANN, *Zool. Jb. Allg. Zool. Physiol.* **57**, 293 (1937).

<sup>3</sup> J. STEGEMANN, *Pflügers Arch. ges. Physiol.* **264**, 113 (1957).

<sup>4</sup> L. STARK, *Proc. IRE* **47**, 1925 (1959).

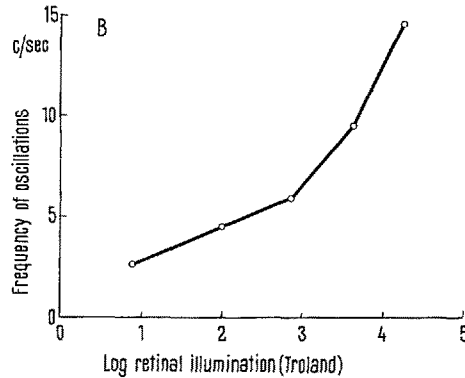
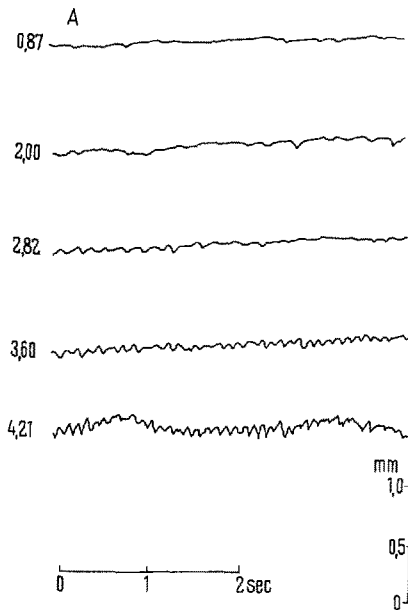
<sup>5</sup> Unpublished data of the laboratory. A full account will be published elsewhere.

<sup>6</sup> E. ALEXANDRIDIS, *Pflügers Arch. ges. Physiol.* **289**, R 63 (1966).

<sup>7</sup> A similar phenomenon has been described previously in the chicken<sup>2</sup>. However, for technical reasons neither the frequencies of oscillations nor the photometric quantities are comparable with the present results.

<sup>8</sup> H. HARMS, *Albrecht v. Graefes Arch. Ophthal.* **149**, 1 (1949).

<sup>9</sup> N. M. J. SCHWEITZER, *Documenta ophth.* **10**, 1 (1956).



(A) Records of area fluctuations ('oscillations') of the pupil of a previously dark-adapted unanaesthetized pigeon at increasingly higher levels of adaptive illumination (values in log Troland beside records). (B) Ordinate: Frequencies (in c/sec, averaged over a period of 10 sec) of oscillations of the pigeon's pupil in relation to state of adaptation. Abscissa: Adaptive illumination (values in log Troland). Measurements of an experiment as in A.

pupillary diameter, reaching a change of up to 16% in retinal illumination (cf. Figure A, lowermost record). Changes like these may play a role in the visual process in the pigeon's eye with its high resolving power in time<sup>10</sup> and space<sup>11</sup>, such as preventing the disappearance of a stabilized image.

**Zusammenfassung.** Die oszillatorischen Änderungen der Pupillenweite wacher Tauben wurden infrarot-reflektometrisch gemessen. Gleichzeitig mit einer Amplitudenzunahme steigt die Frequenz der Pupillenoszillationen von 1/sec bei einer adaptiven Beleuchtung unter 10 Troland bis auf 15/sec bei 1500 Troland.

E. ALEXANDRIDIS

*Abteilung für Experimentelle Ophthalmologie  
(II. Physiol. Abteilung) des W. G. Kerckhoff-Instituts  
der Max-Planck-Gesellschaft, Bad Nauheim (Germany),  
September 13, 1966.*

<sup>10</sup> E. DODT and A. WIRTH, *Acta physiol. scand.* 30, 80 (1953).

<sup>11</sup> G. L. WALLS, *The Cranbrook Institute of Science*, Bloomfield Hills, Michigan (1942), 785 p.

## STUDIORUM PROGRESSUS

### Light Sensitivity of Melanophores in Neural Crest Explants

Changes in the state of contraction (concentration of pigment) or expansion (dispersion of pigment) of amphibian melanophores resulting from alterations in illumination have been studied frequently. In some cases, as in the tail melanophores of *Xenopus* larvae, the action of light is direct<sup>1,2</sup>, while in others it presumably operates through indirect hormonal mechanisms. One body of information, recently discussed by BURGERS et al.<sup>3</sup>, reveals that color variation may depend upon the release of intermedin from the hypophysis. Another group of experiments<sup>4-6</sup> indicates that the blanching of amphibian larvae which are placed in darkness may result from the action of a pineal hormone. In order to ascertain whether these indirect hormonal effects are influenced by responses attributable to direct action of light on melanophores, the following experiments on isolated melanophores were performed.

Pieces of trunk neural fold from open neural plate stages of 3 anurans, *Xenopus laevis*, *Rana esculenta* and *R. pipiens*, and 2 urodeles, *Ambystoma mexicanum* (axolotl) and *Pleurodeles wallii*, were excised and wrapped in sheets of ventral-lateral epidermis (with accompanying mesoderm) from the same embryo. *Xenopus* explants were made and cultured in Niu-Twitty solution, while for all the others, the initial operation was performed in full strength Holtfreter's solution followed by subsequent culture in 50% Holtfreter's solution with addition of an

<sup>1</sup> J. T. BAGNARA, *Proc. Soc. exp. Biol. Med.* 94, 572 (1957).

<sup>2</sup> B. VAN DER LEK, J. DE HEER, A. C. J. BURGERS, and G. J. VAN OORDT, *Acta physiol. pharmac. néerl.* 7, 169 (1958).

<sup>3</sup> A. C. J. BURGERS, K. IMAI, and G. J. VAN OORDT, *Gen. comp. Endocr.* 3, 53 (1963).

<sup>4</sup> J. T. BAGNARA, *Science* 132, 1481 (1960).

<sup>5</sup> J. T. BAGNARA, *Gen. comp. Endocr.* 3, 86 (1963).

<sup>6</sup> J. T. BAGNARA, *Prog. Brain Res.* 10, 490 (1965).