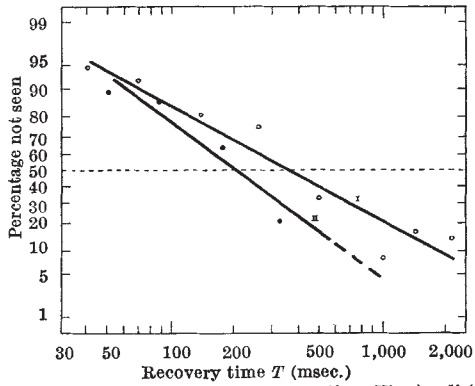

Fig. 2. Percentage not seen versus recovery time. Viewing distance, eight times picture height. I, (○—○) $B_m = 0{\cdot}5$ Mc./s., $S_{max.} = 11{\cdot}4$ min. of arc; II, (●—●) $B_m = 0{\cdot}28$ Mc./s., $S_{max.} = 20{\cdot}3$ min. of arc

experimental points were fitted to a normal distribution versus the logarithm of recovery time (T) as shown in Figs. 1 and 2, using the method of least squares. Each point represents 36 decisions. The permissible recovery times for which the initial lack of sharpness in detail was not seen in 50 per cent of the presentations are listed with the respective experimental conditions in Table 1.

Although within the same viewing distance the permissible recovery time increases approximately in the same ratio as the initial detail size decreases, for the doubling of the viewing distance (that is, halving of detail size for the same B_m) the recovery time increases only by a factor 1·25.

From what is known about human sensual phenomena we cannot expect linear behaviour over any extended range of inputs and stimulus conditions. Hence we consider it unjustified to attempt an extrapolation from the restricted data at our disposal at this time. However, the main conclusions which we may draw from the results of the experiment are that a certain time is required after the presentation of a new and remaining visual display before the perception threshold for fine detail is reached, and that due to this effect it is possible to expand the time interval within which detail in changing complex visual displays is offered to the viewer without noticeably interfering with the normal perception process.

Table 1

Viewing distance (picture height)	4 times		8 times	
Minimum detail (min. of arc)	2·28		1·14	
Maximum detail (min. of arc)	40·6	22·8	20·3	11·4
Recovery time (msec.) for 50 per cent 'No'	160	290	200	360

It must be left to further extended experiments to attempt a determination of the functional relationships between the relevant parameters.

We are indebted to the Supervising Engineer, Research, Postmaster-General's Department of Australia, for permission to publish the material contained in this communication.

[1] Adrian, E. D., "The Physical Background of Perception", The Waynflete Lectures (Clarendon Press, Oxford, 1946).
[2] Monnier, M., *J. Neurophys.*, **15**, 469 (1952).
[3] Brandt, H. F., "The Psychology of Seeing" (Philosophical Library, New York, 1945).
[4] Cherry, E. C., "On Human Communication" (Technology Press, Massachusetts Institute of Technology, 1957).
[5] Quastler, H., "Information Theory in Psychology" (The Free Press, Glencoe, Ill., 1955).
[6] Seyler, A. J., and Korpel, A., *Electronic Eng.*, **31**, 16 (1959).

EFFECT OF OXYGEN TENSION ON HÆM AND PORPHYRIN BIOSYNTHESIS

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THE adaptive synthesis of cytochromes in aerobic and anaerobic conditions of culture is well known[1]. It has been shown by one of us[2] that as the oxygen tension in the culture medium is increased, the synthesis of cytochrome a_2 by *Aerobacter aerogenes* increases to a maximum, and then decreases when still higher oxygen tensions are applied. The maximum was reached when the oxygen concentration in the medium was of the low order of 0·1 M. It was suggested that a self-regulatory mechanism may operate, the formation of cytochrome a_2 being controlled in accordance with the respiratory requirements imposed by the prevailing oxygen tension.

It occurred to us that prosthetic group synthesis might be affected by the oxygen tension. The prosthetic group of cytochrome a_2 is an iron-chlorin[3], and nothing is yet known about the biosynthesis of this cytochrome or its prosthetic group. It has now been found, however, that the biosynthesis of protoporphyrin and hæm, in chicken erythrocyte preparations *in vitro*, appears to be regulated by oxygen tension.

Whole blood (25 ml.) from normal chickens was shaken with glycine (final concentration 0·056 M) and 1 mgm. each of heparin, penicillin and streptomycin, at 38° C. The gas mixtures all contained 5 per cent carbon dioxide and the relevant concentration of oxygen; nitrogen was used as diluent. The mixtures were made in aspirators, and by displacement with water were bubbled through the incubation mixture at the rate of 2 l./hr. The conical incubation flasks were closed with Bunsen valves, and frothing was controlled by a few drops of octanol. When washed cells were used, 25 ml. of blood was centrifuged and the serum and the 'buffy coat' removed. The erythrocytes were washed three times with isotonic sodium chloride and resuspended in isotonic sodium chloride to a final volume of 25 ml. Substrates and

antibiotics were then added, and incubations carried out, as described for whole blood. Porphyrin and hæm synthesis were determined as described by Dresel and Falk[4].

As shown in Fig. 1, the synthesis of copro- and proto-porphyrins and hæm in this system is regulated by oxygen tension. The synthesis of protoporphyrin and hæm is related linearly to time under these conditions (cf. Fig. 3, and Dresel and Falk[4]).

It is not possible, without further experiments, to say whether or not the optimum oxygen tension for the synthesis of hæm is the same as that for protoporphyrin. The situation is complicated by the effects of oxygen upon the incorporation of iron into protoporphyrin. The tissue-catalysed combination of ferrous iron with protoporphyrin is inhibited by oxygen[6], and the liberation of iron from storage in liver ferritin is promoted by low oxygen tensions[7]. Such factors may contribute to the very great inhibition of hæm synthesis at the highest oxygen tensions (Fig. 1).

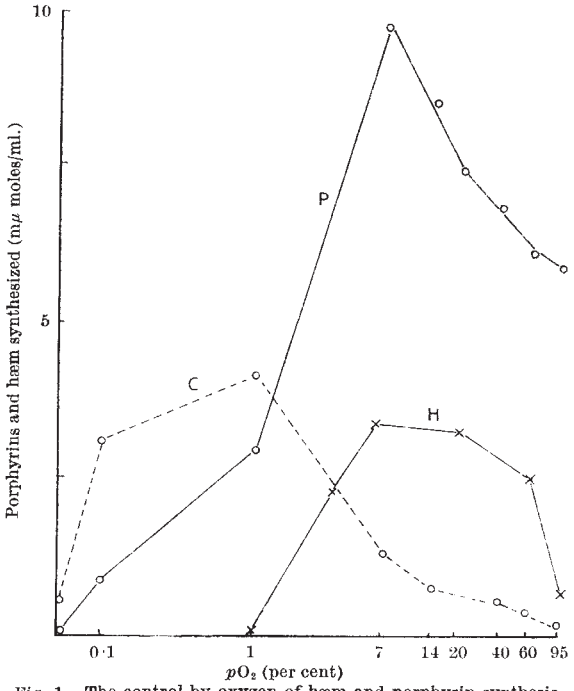

Fig. 1. The control by oxygen of hæm and porphyrin synthesis from glycine in whole chicken blood. Whole blood (25 ml.) was incubated for 8 hr., as described in the text. *P*, protoporphyrin; *C*, coproporphyrin; *H*, hæm

When the erythrocytes were washed three times with isotonic sodium chloride before incubation with glycine, the curve for protoporphyrin formation was found to be similar in form to that shown in Fig. 1, but maximum synthesis was depressed by about 80 per cent (Fig. 2).

That the inhibition of protoporphyrin formation by higher oxygen tensions is reversible is shown in Fig. 3. We have not been able to demonstrate marked degradation of protoporphyrin at 'inhibitory' oxygen tensions.

During the biosynthesis of porphyrins, 'aerobic' reactions are known to be required for the formation of δ-aminolævulic acid, but not again until near the end of the biosynthetic pathway, for the final formation of the vinyl side-chains, and possibly also for the oxidation of a porphyrinogen to the porphyrin level[4,5]. The rising slopes in Fig. 1 reflect these

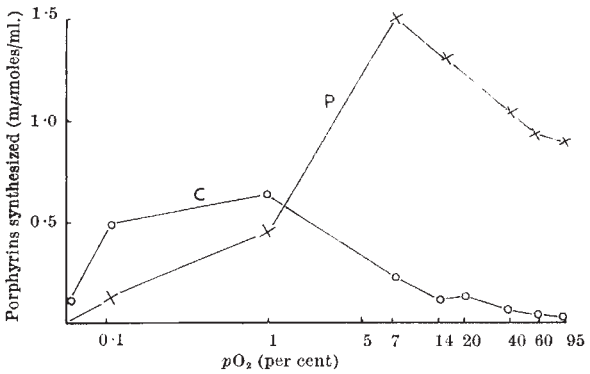

Fig. 2. The control by oxygen of porphyrin synthesis from glycine in washed chicken erythrocytes. The cells from 25 ml. blood were washed and incubated for 10 hr., as described in the text. *C*, coproporphyrin; *P*, protoporphyrin. No protoporphyrin was formed in the complete lack of oxygen

requirements for oxygen; it appears that much lower oxygen tensions suffice for reactions prior to coproporphyrin formation than for the formation of protoporphyrin. If the decreased amounts of protoporphyrin found at higher oxygen tensions are not due to degradation reactions, they would appear to be due to an inhibition by oxygen of some step in the synthetic pathway. As pointed out above, this inhibition is reversible, and it must lie far back in the pathway because coproporphyrin synthesis also is decreased at those high levels of oxygen (Fig. 1) at which protoporphyrin synthesis is decreased.

It appears possible that the control of porphyrin synthesis by oxygen tension may play an important part in cytochrome adaptation in bacteria, though the production of some cytochromes by obligate anaerobes must be considered. There is also evidence[8] that the synthesis by micro-organisms of some colourless enzymes is controlled by oxygen tension.

It is interesting to relate the present findings to animal physiology. The stimulatory effect of anoxia upon erythropoiesis in higher animals[9] and in Crustacea and other invertebrates[10] is well known, and it has also been shown that high tissue-oxygen tensions lead to decreased erythropoiesis[11]. In physiological studies, it has been difficult to separate the effects upon erythropoiesis of oxygen tension from those of endocrinological or other 'plasma'

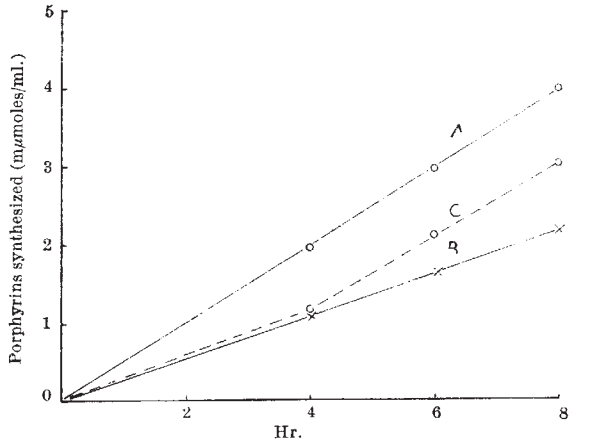

Fig. 3. The reversibility of the inhibition by high oxygen tension of protoporphyrin synthesis. Whole chicken blood was incubated as described in the text. Curve *A*, 5 per cent oxygen; curve *B*, 95 per cent oxygen; curve *C*, 95 per cent oxygen for 4 hr., then 5 per cent oxygen for 4 hr.

factors[9]. The present experiments indicate that there is an oxygen effect exerted directly on a step or steps in the biosynthetic pathway to hæm. In studies *in vitro* of bone marrow from rabbits damaged by X-irradiation, and of normal marrow[12], it has been demonstrated that hæm synthesis precedes that of globin; oxygen tension, by limiting directly the synthesis of hæm, may be expected to limit hæmoglobin synthesis. That the rate of maturation of erythrocyte precursors *in vitro* increases with oxygen tension to a maximum and falls with further increases of oxygen has been demonstrated[13], and it appears possible that maturation of these cells may be linked to hæmoglobin synthesis.

Since the above was written, Lascelles[14] has shown that the formation of bacteriochlorophyll in *Rhodopseudomonas spheroides*, incubated in the dark, reaches a maximum at a pO_2 of about 6 per cent and is depressed at higher oxygen tensions. The formation of δ-aminolævulic acid, and the conversion of this to porphobilinogen, were both found to be sensitive to oxygen tension in *R. spheroides*. We have not investigated the sensitivity of these particular reactions to oxygen in chicken erythrocyte preparations, but we have clear evidence (to be published) that some reaction after the formation of porphobilinogen and prior to the formation of uroporphyrin is inhibited by oxygen tensions higher than about 7 per cent. A preliminary report of this work has been given[15] and it will be described in detail elsewhere. It thus appears that in tetrapyrrole biosynthesis, oxygen may control a number of sensitive steps which could vary both qualitatively and quantitatively from tissue to tissue.

[1] Knox, W. E., Auerbach, V. H., and Lin, E. C. C., *Physiol. Rev.*, **31**, 345 (1951).
[2] Moss, F., *Aust. J. Exp. Biol. Med. Sci.*, **34**, 395 (1956).
[3] Barrett, J., *Biochem. J.*, **64**, 626 (1956).
[4] Dresel, E. I. B., and Falk, J. E., *Biochem. J.*, **63**, 72 (1956).
[5] Falk, J. E., Dresel, E. I. B., and Rimington, C., *Nature*, **172**, 292 (1953). Dresel, E. I. B., and Falk, J. E., *Biochem. J.*, **63**, 388 (1956).
[6] Krueger, R. C., Melnick, L., and Klein, R. J., *Arch. Biochem. Biophys.*, **64**, 302 (1956).
[7] Green, S., and Mozur, A., *Science*, **124**, 1150 (1956).
[8] Slonimsky, P. P., Proc. Internat. Congr. Biochem., Brussels, 242 (1956).
[9] Grant, W. C., and Root, W. S., *Amer. J. Physiol.*, **150**, 618 (1947).
[10] Fox, H. Munro, *Proc. Roy. Soc.*, B, **143**, 203 (1955).
[11] Jacobson, L. O., Goldwasser, E., Fried, W., and Plzak, L., *Nature*, **179**, 633 (1957). Toko, J., Eskuche, I., Abarea, F., Salvatore, F., and Hodgson, G., *Nature*, **175**, 167 (1955).
[12] Richmond, J. E., Altman, K. I., and Salomon, K., *J. Biol. Chem.*, **190**, 817 (1951). Thorell, B., in "The Biosynthesis of Porphyrins and Porphyrin Metabolism", Ciba Foundation Conference (Churchill, London, 1955).
[13] Magnussen, J. D., *Acta Pharmacol. Toxicol.*, **5**, 153 (1949).
[14] Lascelles, J., *Biochem. J.*, **72**, 508 (1959).
[15] Falk, J. E., Moss, F. V., and Porra, R. J., *Aust. J. Sci.*, **21**, 187 (1959).

POSSIBLE ROLE OF HIGHER PROPRIOCEPTIVE CENTRES IN THE PERCEPTION OF VISUAL SPACE AND IN THE CONTROL OF MOTOR BEHAVIOUR

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THE variability of oriented motor acts may lead to the assumption that the transformation of proprioceptive impulses into signals for the appropriate regulation of a movement going on greatly depends on temporary changes produced by the conditioning stimulus in the higher centres to which they are flowing. Admitting that orientation in space is mainly based on ontogenetic experience, we are led to suppose that the 'Pavlov feedback'[1]—the temporary connexions of the higher proprioceptive centres—play an important part in the organization of the perception of space.

This view is not generally accepted. Thus, in visual space perception theory, Sherrington's concept[2] identifying the 'muscle sense' of the eyes with the inflow of impulses from the sensory nerve endings in the extrinsic eye muscles is opposed by the generally accepted Helmholtz's theory[3] affirming that we evaluate the direction of our sight on the basis of "the innervation impulses we must apply to transfer the eye in the intended position".

According to a recent suggestion[4], the normal human perception of space "is organized on the conservative principle of a null-hypothesis" and should require no analysis in terms of specific neural events. Such a rather paradoxical view will scarcely satisfy the physiologists interested in the investigation of nervous mechanisms subserving normal life functions.

Now, from Helmholtz's typical 'outflow' theory it would follow that for every eye rotation a corresponding innervation pattern is quantitatively 'predetermined' by the 'sense of innervation'. Hence, as the eyes in their movements (especially horizontal) constitute a system with constant mechanical load, equally directed eye fixation movements of a subject in equal conditions ought to follow the same course.

To study eye rotations under the action of the 'muscle sense', conditioned fixation movements have been systematically investigated in 14 normal subjects. In response to the conditioning sound stimulus (400/sec., 30 db. above audibility threshold, applied during $1\frac{1}{2}$ sec.) the subjects had to turn their eyes in total darkness and to maintain them in the directions in which formerly visible points appeared and were fixed. A total of 14,000 large-scale electrooculographic records were examined, and the results analysed statistically.

Previously, it has been shown[5] that conditioned eye 'muscle sense' has significant directional power, for, in the mean, 40 per cent of all conditioned eye movements were found to be as precisely directed towards the goal as fixation movements to visible objects, and, once attained, a given position of the eyes was further as exactly maintained in complete darkness.

It was no less significantly demonstrated (Fig. 1) that even in a series of successive trials, the saccadic movements of the same subject's conditioned eye fixation, transferring the line of regard into one and the same exact final direction, nevertheless differ essentially one from each other as regards characteristics and composition of the saccade, and namely as