length should increase, the more strongly bound is the O_2 group, since electrons are being removed from a bonding orbital of O_2 and replaced in an anti-bonding orbital.

The second bonding model that could be applied to this system is that proposed by Parshall (*6*) for fluoro-alkene derivatives of $IrCl(CO)(PPh_3)_2$. The oxygen species would be O_2^{2-} and this would bond to Ir^{3+} by means of two σ-bonds and no π-bonds. Without further modifications this model does not explain the stronger bonding in the iodo-compound, nor does it predict a change in the O–O bond length on change of ligands to the metal. It appears to us that the first model is more useful in this particular case, and it can be used to make simple predictions: for example, $RhCl(CO)(PPh_3)_2$ does not add oxygen, but perhaps the iodo-compound would. Further experiments are needed to provide more information on bonding schemes and their applicability to different complexes. Specifically, both C_2F_4 (*6*) and $C_2(CN)_4$ (*7*) add to these parent iridium systems, and the structures of these derivatives are under study. In particular, the deviations of the olefin groups from planarity should provide additional insight into the bonding of various ligands, including molecular oxygen, in these complexes.

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Visual Adaptation to Gradual Change of Intensity

Abstract. *The eye can adapt to the rate of change of brightness. After exposure of the eye to a light that grows gradually brighter, a steady light appears to grow gradually dimmer, and vice versa. A field containing shading gives larger aftereffects than a spatially uniform field.*

In the well-known processes of light and dark adaptation, the eye adjusts its sensitivity to the prevailing intensity of illumination. In a new effect reported here, the eye adapts, not to the intensity, but to the rate of change of illumination.

The eye was first adapted by fixating a light which grew gradually brighter. Then the light was switched to a steady intensity, and an aftereffect was seen that appeared to grow gradually dimmer. Conversely, after the eye was adapted to a light that grew gradually dimmer, a light of steady intensity appeared to grow gradually brighter. The effect was confined to the stimulated areas of the retina. The aftereffect from a 30-second adaptation lasted from 1 to 10 seconds.

In practice, it is convenient to vary the intensity in an oscillating, sawtooth wave, so that it brightens or dims repetitively. A single cycle can produce a small aftereffect; many cycles produce a larger one. The brightening or dimming aftereffect is opposite in direction from the slow phase of the sawtooth waveform, and does not itself include any perceived oscillation in brightness (Fig. 1). The effect occurs with white light, and with any visible, monochromatic light. Almost any light source can produce the effect. I used Ferranti R1130B glow modulator neon lamps.

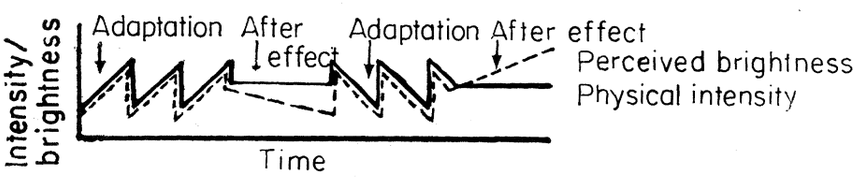

Fig. 1. Adapting light brightens repetitively (solid line, rising sawtooth wave); then, when held at steady intensity (solid horizontal line), it apparently dims (dashed falling line). Or, it dims repetitively (solid line, falling sawtooth wave); then, when it is held steady, it apparently brightens (dashed rising line).

The frequency and intensity of the stimulus, and the area stimulated, are not critical. A cycling rate of 1 cycle/sec and an intensity range of 100 to 1 (2 log units) were about optimum. A pinhole source in a dark room caused a minimum effect in some subjects and no effect in others. The same was true for the entire visual field, secured when half a table tennis ball was fitted over each eye and the subject looked straight into the beam of an intensity-modulated projector. With either the pinhole or the entire visual field, the intensity modulation of the stimulus itself was inconspicuous to the subject.

Different parts of the retina can be differently adapted at the same time. A disc was divided into two halves, and each half was lit uniformly and independently by a separate neon lamp. When the two halves varied in intensity in the same direction (both brightening, or both dimming), but out of phase by any angle, then each half of the retina had an aftereffect in the appropriate direction (both dimming, or both brightening). When the two halves varied in phase, but in opposite directions (left half dimming, right half brightening), then each half had an aftereffect in the appropriate direction (left half brightening, right half dimming).

A checkerboard of 1-inch squares (12 by 12) of Polaroid was fixated through a piece of Polaroid which turned steadily through 90°, then returned sharply to 0°, so that the white squares gradually turned black, and vice versa. The appropriate aftereffects were observed in each square.

Contrast can influence the effect. A square subtending a visual angle of 4° and held at a steady intensity, was centered in a square adapting field subtending a visual angle of 45°. The intensity of this field continually increased, following an oscillating, sawtooth waveform. Owing to the contrast in brightness, the steady central square appeared to be continually dimming, in contrast to the surrounding square. After 30 seconds the intensities of both the central square and the adapting, surrounding area were held steady. The surrounding area now appeared to grow dimmer for 10 to 15 seconds, and the

central square appeared to brighten, even though its objective intensity had remained constant throughout the experiment.

Correspondingly, when the area surrounding the square grew continually dimmer during the stimulation period, the steady central square apparently grew brighter. During the aftereffect the surrounding area apparently grew brighter, and the central square apparently grew dimmer.

The aftereffect can be greatly increased by a spatial intensity gradient (shading) across the field. The shading can be either on the oscillating field to which the subject adapts, or on the steady afterfield against which he sees the aftereffect. A square, uniform adapting field, subtending a visual angle of 2°, was repetitively increased in intensity over an intensity range of 100 to 1. The aftereffect (mean of 8 subjects) lasted 5.7 seconds. With a shaded adapting field, the mean aftereffect lasted 6.5 seconds; with a shaded afterfield, 8.4 seconds, and with both adapting and afterfield shaded, 8.6 seconds (Fig. 2). The shaded afterfield made a greater contribution than the shaded adapting field to the aftereffect.

There was apparent movement from the bright edge to the dark edge in a continually brightening, spatially shaded adapting field. During the aftereffect, apparent movement in the opposite direction was seen. These movements correspond to the movement of imaginary "contours of equal brightness" across the field. However, the brightness aftereffect described here is quite distinct from the well-known negative aftereffect of movement (*1*).

A continually brightening, spatially uniform adapting field, containing no directional component, gave a dimming aftereffect on a uniform afterfield. The dimming aftereffect occurred here in the absence of any movement.

A continually brightening adapting field, spatially shaded to be darkest on the left, apparently moved to the left during stimulation (Fig. 3). The gaze was then transferred to a steady afterfield, shaded to be darkest on the right. The reported aftereffect was of dimming plus apparent movement to the left. This was appropriate to the stimulus of changing intensity. The aftereffect appropriate to the stimulus of perceived movement would have been an apparent movement to the left. So the aftereffect reported was one of brightness, not of movement.

The effect is not due to pupillary responses, since it was still observable through an artificial pupil 2 mm in diameter. Also, dimming and brightening effects could be seen simultaneously, side by side, on a checkerboard, but the pupil cannot expand and contract simultaneously.

The effect is probably retinal rather than central. If the left eye viewed a dimming light, and the right eye viewed a brightening light, visually superimposed in a stereoscope, binocular rivalry was reported. Then, if both eyes were closed, or both were open viewing a steady light, no aftereffect was seen. But if one eye was opened, this eye had its own aftereffect, though more feebly than if the other eye had not been stimulated. Also, when one eye was adapted monocularly, little or no aftereffect was observed with the other eye.

The effect appears to be a newly discovered one. It is distinct from the aftereffect of movement. It may represent selective adaptation of "on" and "off" receptors, but its physiological mechanism is not yet known.

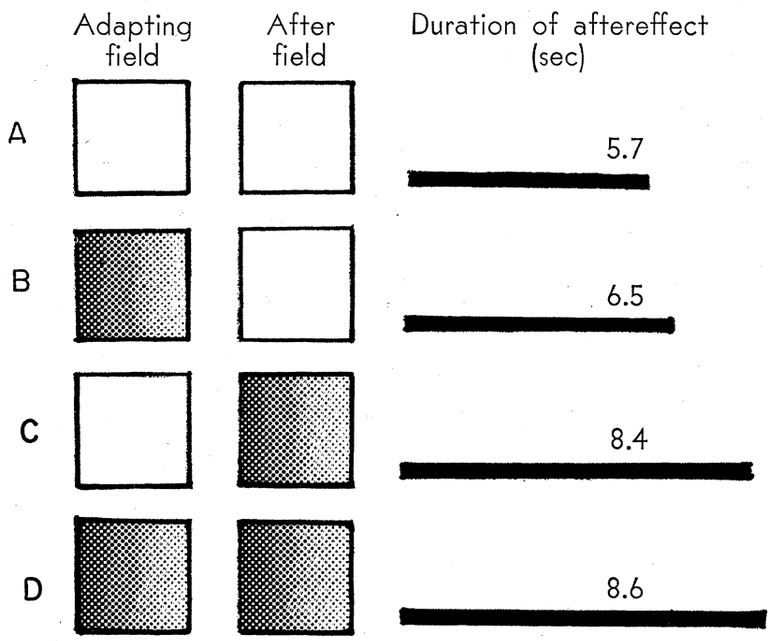

Fig. 2. Spatially uniform adapting field and afterfield produce aftereffect of 5.7 seconds. Shaded adapting field increases aftereffect to 6.5 seconds; shaded afterfield, to 8.4 seconds; shaded adapting field plus shaded afterfield, 8.6 seconds.

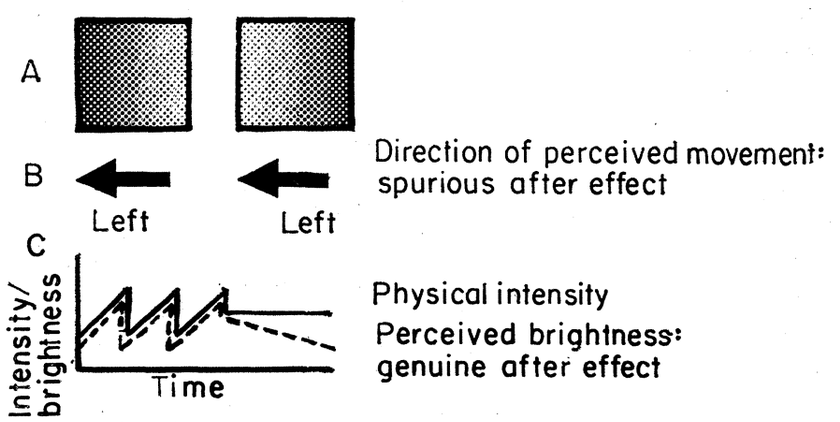

Fig. 3. Brightening adapting field, shaded to be darkest on the left, apparently moves to the left. Steady afterfield, shaded to be darkest on the right, apparently dims and apparently moves to the left. Dimming aftereffect is genuine. But movement aftereffect is an artifact. Genuine aftereffect would apparently move to the right.

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2. The glow modulator lamps were loaned by Dr. F. C. Campbell, and the amplifier to power them was designed by Dr. J. F. Robson, both of the Physiological Laboratory, Cambridge. This work was supervised by R. L. Gregory and supported by a D.S.I.R. (S.R.C.) research studentship.

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Glutathione Reductase in Red Blood Cells: Variant Associated with Gout

Abstract. *A variant of red cell glutathione reductase, characterized by greater electrophoretic mobility, increased enzyme activity per unit of hemoglobin, and an autosomal mode of inheritance, has been found in Negro populations. There appears to be an association of this variant with primary gout.*

During a survey of 1473 Negro male outpatients for variants of red cell glucose-6-phosphate dehydrogenase (G-6-PD) (*1*) by starch-gel electrophoresis (*2*), the extra slabs of most gels were stained for glutathione reductase by a two-stage procedure (*3*). This procedure results in a dark stain, whereas the reduced nicotinamide-adenine dinucleotide phosphate (NADPH) applied to the gel remains unaltered. The three light bands which appear for each samples (Figs. 1 and 2) are assumed to represent regions where NADPH has been oxidized. The light band nearest the origin of the sample on the gel is the location of glutathione reductase since this band does not appear unless oxidized glutathione is present in the staining mixture. The middle band, with migration identical to that of hemoglobin A, and the distal band appear with or without oxidized glutathione in the staining mixture. Presumably these two bands do not represent glutathione reductase. That they do not reflect some action of hemoglobin on NADPH is suggested by the presence of apparently identical bands on electrophoresis of serum or plasma.

For the G-6-PD study (*1*), hemolyzates were adjusted to a hemoglobin concentration of 0.2 g per 100 ml of hemolyzate before application to gels, and electrophoresis was carried out for 12 hours in the cold room. Under these conditions glutathione reductase in some samples migrated definitely faster and in other samples questionably faster than in most samples. When electrophoresis of the 196 samples most recently obtained from individuals included in the G-6-PD study (all from Negro male medical outpatients) was repeated and conducted for 14 to 15 hours instead of the usual 12 hours, the variant moved farther from the usual, more slowly migrating form (Fig. 1); most of the bands previously recorded as questionably fast spread into a wide band suggestive of the fast and slow bands merged together (Fig. 2).

Samples from 6 of these 196 individuals showed the electrophoretically fast band; 40 showed the wide band thought to represent the heterozygous state; and 150 showed the usual more slowly migrating band of glutathione reductase. If the fast and slow bands represent homozygotes and the wide band the heterozygote, gene frequency for the variant is .133, and for the usual form of the enzyme it is .867 with a standard error of .017. From this data, 3.5 individuals homozygous for the variant, 45.2 heterozygous for the variant and the usual form, and 147.3 homozygous for the usual form would theoretically be expected, a distribution which does not differ significantly from the observed distribution. Chi-square is 2.4334; P is less than .2 and greater than .1, with one degree of freedom. Since gene frequencies calculated for hospital patients do not necessarily reflect the frequencies in the population from which the patients are drawn, electrophoresis was subsequently performed on blood samples from 125 presumably healthy Negroes, 79 males and 46 females, randomly selected in Austin, Texas. In this group gene frequencies of .132 for the glutathione reductase variant and .868 for the usual form of the reductase, with standard error of .021, are almost identical with those found for the 196 outpatients.

Electrophoresis of red cell glutathione reductase from both parents and all children of nine Negro families (*4*) is consistent with the assumption that the wide band represents the heterozygous state and that there is an autosomal mode of inheritance for the enzyme. Among these families are three unrelated individuals who are homozygous for the variant enzyme and whose parents are each heterozygous. A fourth individual homozygous for the variant has a father homozygous for the variant and a heterozygous mother. For family studies, enzyme activity was determined as described (*5*), and each sample was then adjusted to the same enzyme activity per unit volume for application to the gels.

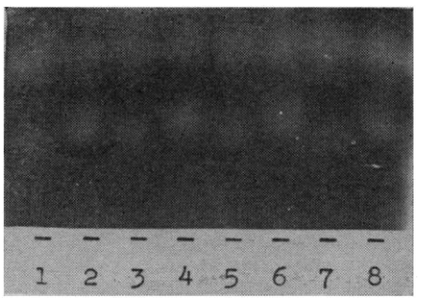

Fig. 1. Row of light bands nearest origin (bottom) indicates location of glutathione reductase on starch gel after electrophoresis with samples adjusted to the same enzyme activity. The same sample of the usual form of glutathione reductase in the odd-numbered positions is alternated with the same sample of the faster moving variant form in the even-numbered positions.

There was no association between the common G-6-PD variants and the glutathione reductase variant among the 196 Negro male outpatients. Twenty-five with G-6-PD of type A, 19 with type A(−), and 105 with type B were homozygous for the usual form of glutathione reductase. Seven with G-6-PD of type A, 5 with type A(−), and 34 with type B were heterozygous or homozygous for the glutathione reductase variant. Chi-square was 2.041 and P was about .9 (two degrees of freedom).

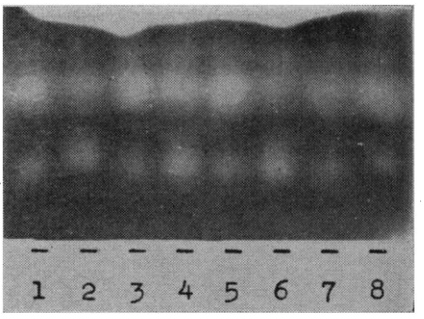

Fig. 2. The usual form of glutathione reductase is in positions 1, 3, 5, and 7. The electrophoreticaly fast variant is in positions 2 and 8. The broad band thought to represent the heterozygote for the usual and variant forms is in position 4 and 6. Samples are adjusted to the same enzyme activity.