farther away than the short lines, and 12 of them reported rivalry at the same time. Only three observers (all of whom had a strongly dominant eye) reported seeing sharp edges without any rivalry, possibly by suppressing the rival contour produced by the nondominant eye. This suggests that the nondominant eye may contribute to stereopsis without producing a rival double image.

Although the periodicity of the patterns in Fig. 1*a* and *b* helps in seeing them in depth (as several contours have similar disparity[9]), it is not a necessary condition for this phenomenon. Figure 1*c* shows two pairs of single bars corresponding to those in Fig. 1*a* and *b*. Now, however, for comparison the sharp bars (bottom) and the 'blurred' bars with a consinusoidal profile (top) are presented simultaneously in the same disparity with respect to the short lines. Some observers find it difficult to fuse the short lines between the bars, but after several attempts it is usually possible to perceive the bars as being closer than the short lines (if the left and right eyes look at the left and right lines, respectively). The sharp edges of the square-wave bars, however, are seen as double.

All the phenomena shown in Fig. 1 suggest that objects with sharply outlined contours and patterns with gradual luminance gradients have different ranges of disparities over which they are seen as single, or at least not seen as rival double images. In other words, the range of single vision in stereopsis is inversely related to the spatial frequencies present in the pattern, as though there were many Panum's areas instead of one determined with fine lines.

Neurophysiologists[10–12] have noted that units with small receptive fields, representing central vision, often have a narrower range of disparities than units with large receptive fields representing peripheral vision. However, the phenomena reported here are concerned mainly with central vision (note that the bars in Fig. 1*c* may be made shorter without affecting the percept). Graham, Robson and Nachmias[13] have demonstrated that central vision has a range of mechanisms tuned to different sizes (or different spatial frequencies). Also, Maffei and Fiorentini[14] noted that cortical cells subserving each part of the visual field are tuned to a range of sizes (spatial frequencies). Although specific neurophysiological investigations relating the range of disparities to the receptive field size in the same part of central vision have not yet been published, some experiments hint that such a relationship may exist. Simple cells in the cat visual cortex responsive to low spatial frequencies tolerate a greater lateral misalignment of line stimuli presented dichoptically than the cells responsive to higher spatial frequencies (D. J. Tolhurst, J. D. Thompson and C. Blakemore, personal communication).

Other psychophysical experiments also point to different binocular processing of sinusoidal and square-wave gratings in antiphase (J.J.K. and I. Wood, in preparation). The binocular contrast thresholds for the detection of sinusoidal gratings were the same whether the gratings were in-phase (identical) or in antiphase for the two eyes. However the thresholds for binocular viewing of square-wave gratings were higher when the gratings were in antiphase as compared with the thresholds for the in-phase presentation. This finding may be of clinical importance, for as the simusoidal gratings do not produce rivalry irrespective of their phase they could be used for exercising binocular vision in patients with squint.

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Telephoto lens system of falconiform eyes

VISUAL ACUITY in falconiform birds has been shown to be higher than man. For instance, vultures with eyes similar in size to those of man have a grating detectability of about twice the spatial frequency of man[1]. This is consistent with measured image quality in an eagle eye similar in size to the human eye[2]. Recently a falcon (*Falco sparverius*) has been shown to have a grating detectability 2.6 greater than that of man[3]. Although the image quality of these falconiform eyes is at least twice as good as man, their minimum intercone spacing is only slightly less than in the human retina. Unless the ratio of focal length to the axial eye length of these birds greatly exceeds that in man, falconiform eyes, unlike man, would be unable to resolve their best retinal image quality. We show here that the presence of a spherical depression in the deep fovea of falconiforms may act like the negative lens component in a telephoto lens system or opera glass. The focal length of the birds' dioptrics can then in theory exceed the axial length of the eye, thus providing the relatively large images necessary for more complete image reconstruction (high resolving power) in a localised region of the retina.

The anatomical resolving power of an eye is set by the image size and by the receptor grain. The image size is specified by the focal length, f, while the receptor grain is specified by the centre-to-centre spacing of foveal cone, d. It is convenient to define an anatomical resolving power, RP, as the reciprocal of the angular separation between cone centres:

$$RP = f/d \qquad (1)$$

In order to determine precisely the intercone distance, d, we made photoreceptor counts by light microscopy on fresh material and by light and electron microscopy on fixed material in the deep foveas of numerous birds ranging from large eagles to small falcons and, for comparison, in human foveas[4]. In all situations shrinkage was carefully monitored and corrected for, and only the most central region of the fovea was examined. In all falconiforms studied $d \simeq 2$ μm, independent of their eye size, while $d \simeq 3$ μm in man. In man, focal length $f \simeq 17$ mm (ref. 5) while in falconiforms f (believed to be accurately estimated from the curvature of the retina[6,7]) measured in all our birds was found to be $f \simeq 0.65L$, where L is the axial eye length. Using equation (1), the anatomical resolving power of falconiforms with eyes the same size as man ($L \simeq 24$ mm) is only 1.38 times that of man. If the resolving power of these birds is to equal twice that of man, then f must equal 22.6 mm or 1.45 times that measured from the retinal curvature. We next show that this amount of image magnification is in fact consistent with the optical function of the bottom of the foveal pit.

Falconiforms are well known to have a deep nasal fovea[8,9], see for example, Fig. 1, where Fig. 1*b* shows the deep fovea of the red-backed hawk, *Buteo*, which also has a 'man-sized' eye. We call attention here not to the steep sides of the fovea[8,10], but rather to the fact that the bottommost portion of the pit is a well formed hemisphere. Our hypothesis is that this concave portion of the foveal pit (labelled by the arrow in Fig. 1*b*) functions as a negative lens which, together with the positive power of the cornea and lens, acts like the telephoto optical system of Fig. 2. This system has an effectively long focal length which, in

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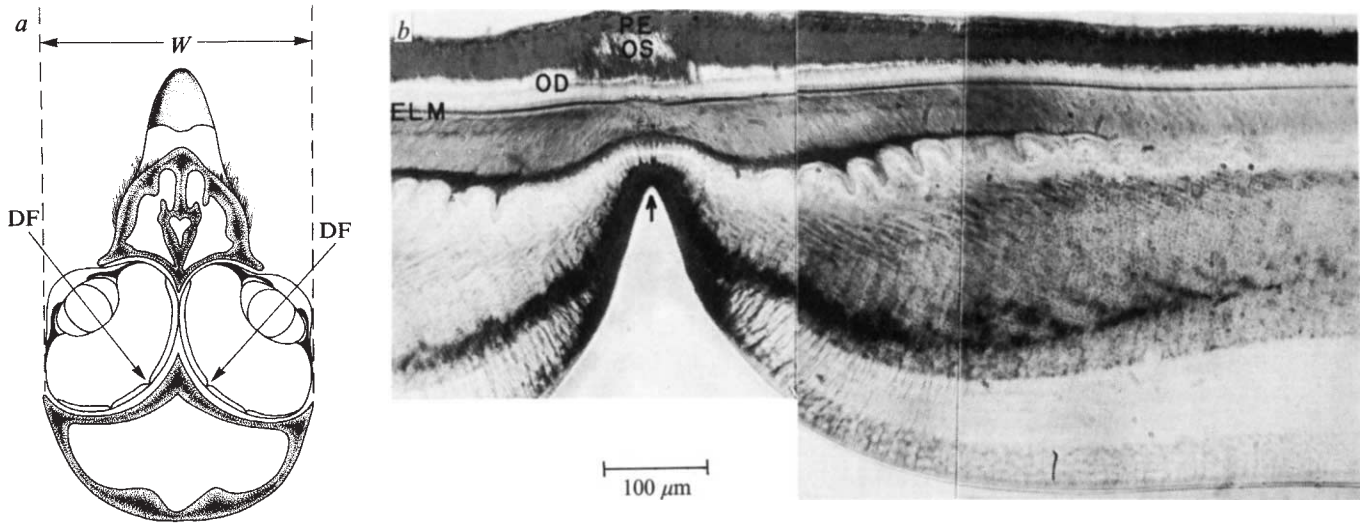

Fig. 1 *a*, Schematic of an avian eye viewed ventrally, illustrating the relative position of the deep or nasal fovea (DF). The figure is adapted from the hawk *Buteo latissimus*[14]. *W*, the head width, approximately equals twice the axial eye length *L*. *b*, Unstained 10-μm thick section of glutaraldehyde-fixed retina of red-backed hawk in region of deep fovea. Section photographed using interference contrast. Increasing darkness indicates higher refractive index. Arrow indicates concave region of foveal pit which we hypothesise may function as a diverging optical element to project magnified image on receptors at centre of fovea. Note that *n* is uniform between internal and external limiting membranes outside of fovea on extreme right of figure. Dark densities sclerad to ELM are the result of pigment and do not necessarily relate to *n*. ELM, external limiting membrane, OD, oil droplets; OS, outer segments; PE, pigment epithelium. Scale bar, 100 μm.

theory[11], can even exceed the physical length of the eye. Walls[8], ignoring the bottommost portion of the pit, suggested that the steep sides of the foveal pit magnifies the image, but Pumphrey[10] showed that instead they cause distortion.

Thus, from Fig. 2 the effective focal length of the bird eye is given by mf, where m is the magnification[11] of the foveal pit, defined in the legend of Fig. 2*b*, and f is the focal length used in equation (1). Therefore, from equation (1), the resolving power of falconiforms is mf/d. The magnification m increases the smaller the radius of curvature R of the concave pit and/or the greater the distance s of the bottom of the pit from the photoreceptors. From our above discussion, m must equal about 1.45 for the man-sized falconiform eye to have twice the resolving power of man.

Using the deep fovea of the red-backed hawk in Fig. 1*b* as an example, with $s = 110$ μm and $R = 6$ μm, then the refractive index n_r of the deep fovea must equal 1.369 if m is to be 1.45. This result is found from the equation in the legend of Fig. 2*b* assuming the refractive index of the vitreous humor[12] is the same as man and cat[5], that is, $n_c = 1.336$. There are several convincing reasons why n_r should equal or exceed 1.369. First, the vitreal surface of the foveal pit is formed by Müller cells only. From our electron micrographs, these Müller cells are seen to be exclusively and densely packed with microfilaments. Similar protein, for example, collagen in the cornea, has a refractive index[12] $n_r \simeq 1.55$. Second, interference microscopy of the red-backed hawk fovea, (Fig. 1*b*) indicates an n_r similar to that of the cone outer segments[13] for which $n_r \simeq 1.4$. Since the regions of highest n in Fig. 1*b* are shown as the darker areas, the region below the pit has a nonuniform refractive index. Thus, Fig. 2 represents only a crude model of the optics. We emphasise that the high refractive index region surrounding the spherical pit in Fig. 1*b* is absent in extrafoveal regions and in all primate foveas and less apparent in the shallow foveas of falconiforms. Third, measurement of interference fringe displacement in the deep fovea of a glutaraldehyde fixed, Spurr's media embedded specimen (Fig. 1*b*) indicates a minimum value of 1.379 for the refractive index of both the pit and sides of the deep fovea. However, this value is a lower bound because we have not adjusted for the fact that the high n Spurr's medium infiltrates the denser tissue more than the less dense tissue. The measured n value is consistent also with the intensity of the foveal reflex believed equal to that of myelinated nerve fibres of the optic disk[14]. Thus, the very high refractive index below the spherical pit and its radius of curvature are consistent with the pit functioning as a negative element in a telephoto lens system.

The deep fovea may also act as a focus indicator; however, both the nail polish and the ray models used to test this hypothesis[15] were not scaled to give the correct magnification factor as determined by our interference microscopy and anatomical measurements (L. Harkness, personal communication). When appropriately scaled, we have observed the magnification predicted by the telephoto lens model and furthermore, the entire 'retinal' image is in focus in the same plane that magnification occurs.

There are distinct disadvantages associated with the telephoto lens system described above, including a narrow field of view for high resolving power and susceptability to aberrations caused by the steep sides of the fovea. Why is it then that the avian eye did

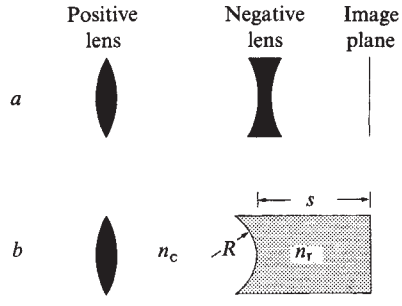

Fig. 2 Schematic of the telephoto lens. *a*, Classical design. *b*, Equivalent system of avian eye where the negative lens is replaced by a spherical (concave) surface. The magnification of the system,

$$m = 1 + \frac{s}{R}\left(\frac{n_r - n_c}{n_c}\right)$$

where n_r and n_c are the refractive indexes of the medium to the right and left of the spherical surface respectively, R the radius of curvature of the surface and s the distance from the apex of the spherical surface to the image plane. The position of the oil droplets is taken as the image plane in Fig. 1*b*.

not simply have a higher cone density, avoiding these difficulties? The answer may be found in the constraints imposed by the wave nature of light. Because of frustrated total internal reflection[11], photons within one outer segment have a probability of crossing over into neighbouring outer segments. This optical 'cross talk'[16] increases the more densely packed the cones become, manifesting itself by an increased reduction in contrast sensitivity. If high resolving power is the animals' primary objective, the deep fovea, acting as the magnifier of a telephoto lens, may be a strategy superior to a fine receptor grain.

Although our arguments have been applied mainly to falconiforms with man-sized eyes, they should hold more generally. In all of the falconiforms we have studied, the focal length f of equation (1) is directly proportional to axial eye length L while the minimum inter-cone spacing d and magnification m due to the deep fovea are independent of eye length. Consequently the resolving power, RP, of these birds should be directly proportional to L or equivalently to the animals' head width W of Fig. 1*a*. Our finding that the birds' pupil diameter, as measured in bright natural conditions, is directly proportional to L is also consistent with the RP being directly proportional to L. This follows assuming, as in man[17], that the birds' best image quality (minimum line spread) is nearly diffraction limited and occurs at the smaller (bright light) pupil diameters.

Finally, recall that grating detectability provides only a limited assessment of bird visual superiority. Alternatively consider a distant point object. The most crucial determinate of detection is then maximum image brightness which also equals the two-dimensional polar area under the modulation transfer function of the optics[11]. From the modulation transfer function for the optics[2,17], we calculate that the man-sized eagle eye can, in theory, detect a distant point object at a distance 3 to 8 times greater than man. This ratio is nearer to 8 when the object is significantly brighter than its surround, and ~3 when the object brightness is equal or less than its surround. Such superior visual acuity is in better agreement with the reported observations[18] than the value of twice that of man found from grating detection[1].

Thus man-sized falconiform eyes have an image quality at least twice as good as man[2], yet their minimum inter-cone spacing is only slightly less than man[4]. Nevertheless, our anatomical findings and refractive index measurements are consistent with the hypothesis that the spherical portion of the deep fovea acts like the negative lens component in a telephoto lens system. The focal length of the dioptrics may then be sufficiently extended for the bird to resolve its superior retinal image in a localised region.

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Cyclophosphamide delays 3-methylcholanthrene sarcoma induction in mice

THERE is increasing evidence to show that suppressor T lymphocytes facilitate the growth of neoplasms that have tumour-specific transplantation antigens[1–6]. Studies on suppressor cell activity with respect to various non-tumour antigens have shown that treatment of mice with cyclophosphamide depresses suppressor cell-mediated mechanisms to a greater extent than the effector arm of the immune response[7–9], provided the proper dose and timing for drug administration was used. Based on these observations we speculated that treatment of mice with cyclophosphamide during the latency period of tumour induction might prevent (or at least delay) the appearance of primary tumours. We show here that this hypothesis is correct. In BALB/c mice given 3-methylcholanthrene (MCA) and injected with cyclophosphamide (2 mg per mouse) every 10 days, the appearance of primary sarcomas was delayed. Because the effects were striking, and were obtained with one of the drugs most commonly used in cancer chemotherapy, we decided to report the data. We are, however, aware that explanations for the drug effect other than interference with suppressor cell activity are equally possible, including a direct effect of the drug on tumour cells.

BALB/c mice were bred by brother to sister mating at the Fred Hutchinson Cancer Research Center. Female mice, 6–8 weeks old, were randomised into six experimental groups, each group comprising 50 mice except group 6 which had 45 mice. All mice received an intramuscular injection into each thigh of 0.1 mg MCA dissolved in trioctanoin. The day of MCA injection is referred to as day 1 of the experiment. Two groups (1 and 4) were injected subcutaneously on 4 occasions (days −10, 20, 50, 80) with 10^6 heavily irradiated cells per mouse from tumour 1423. This tumour is an MuLV antigen negative MCA-induced BALB/c sarcoma; these tumour cells were pre-irradiated with 15,000 rad *in vitro*[6]. The tumour cells were injected to determine whether any immunisation to putative common TSTA could be obtained. Two other groups (2 and 5) were similarly injected with cells from normal BALB/c kidneys, while the remaining two groups (3 and 6) received phosphate-buffered saline (PBS) only. Cyclophosphamide was injected intraperitoneally at 10-day intervals in a dose of 2 mg per mouse (corresponding to approximately 100 mg per kg body weight at the onset of the experiment), starting 13 days before MCA and continuing throughout the experiment, in groups 4, 5 and 6. This dose of cyclophosphamide was chosen on the basis of experiments performed in an allograft system, which examined suppressor cell activity controlling the cell-mediated allograft response in BALB/c mice[10]. The time schedule was based on the evidence that suppressor T cells have a half life of less than 4 weeks[11]. Groups 1, 2 and 3 were injected with PBS instead of cyclophosphamide. The previously eartagged mice were observed at weekly intervals for tumour development; the treatment

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