Whatever the precise relationship of the substantia nigra to seizure-propagating circuits, inhibition of nigral outflow, as accomplished by GABA agonist drugs (*17, 19*), appears to deter seizure generalization. This proposal is supported by preliminary evidence from our laboratory that electrolytic or kainic acid lesions of the substantia nigra can attenuate bicuculline-induced convulsions (*20*). In addition, intranigral injections of GVG or muscimol do not preclude the animal's ability to exhibit the motor components of a seizure. A dose of convulsant, two to three times that normally required for inducing tonic seizures, elicits a full tonic seizure in an animal that had been given bilateral injections of GVG or muscimol (*21*). A similar shift in the dose-response for the convulsants is observed with nigral lesions.

Although we do not believe that a decrease in GABA-mediated transmission in substantia nigra is likely to generate seizures (*22*), such a process could facilitate the generalization of seizure activity emanating from more rostral loci. In this case, a loss of inhibitory tone in substantia nigra (or augmentation of excitatory transmission at this site) might enhance the probability of obtaining generalized seizures. Thus, the substantia nigra must be considered as a site at which pathology could alter the susceptibility to generalized convulsions. The appearance of overt clinical seizures may thus depend on both an epileptogenic focus (for example, in the forebrain) and a compromised inhibitory control mechanism at critical synapses in the substantia nigra.

MICHAEL J. IADAROLA*
KAREN GALE†
Department of Pharmacology, Georgetown University Schools of Medicine and Dentistry, Washington, D.C. 20007

References and Notes

1. D. B. Tower, in *GABA in Nervous System Function*, E. Roberts, T. N. Chase, D. B. Tower, Eds. (Raven, New York, 1976), p. 461; B. S. Meldrum, *Int. Rev. Neurobiol.* **17**, 1 (1975).
2. B. S. Meldrum, *Clin. Neuropharmacol.* **6**, 293 (1982).
3. K. Gale and M. J. Iadarola, *Science* **208**, 288 (1980). In contrast to systemic administration, direct intracerebral injection of GVG rapidly increases GABA in nerve terminals, reaching a maximum by 6 hours [M. Casu and K. Gale, *Life Sci.* **29**, 681 (1981)]. We therefore tested for anticonvulsant activity starting at 6 hours after microinjection of GVG.
4. M. J. Iadarola, A. Raines, K. Gale, *J. Neurochem.* **33**, 1119 (1979); K. Gale and M. J. Iadarola, *Eur. J. Pharmacol.* **68**, 233 (1980).
5. P. J. Schechter, Y. Tranier, M. J. Jung, A. Sjoerdsma, *J. Pharmacol. Exp. Ther.* **201**, 606 (1977); W. Loscher, *Naunyn Schmiedebergs Arch. Pharmakol.* **315**, 119 (1980).
6. Stimulus parameters were 200 mA, 0.2 second, 60 Hz; corneal electrodes were used. Electroshock apparatus was described by L. A. Woodbury and V. D. Davenport [*Arch. Int. Pharmacodyn. Ther.* **92**, 97 (1952)]. A preliminary electroshock was administered to all rats at least 24 hours before microinjection; rats with durations of tonic hindlimb extension of 4 seconds or less were eliminated (this represented less than 15 percent of rats tested).
7. At 6 hours, GABA elevation was less than maximum at distances beyond 3 mm and was not significant beyond 6 mm from the injection site. In all groups, the volume of tissue in which GABA elevation was observed at 24 hours was three to four times greater than that affected at 6 hours; this may account for partial anticonvulsant effects seen 24 hours after thalamic and pontine injections of GVG.
8. The anticonvulsant effect of intracerebral injections of GVG is associated with increases in GABA in the midbrain comparable to those observed when GVG is administered systemically in anticonvulsant doses (*3*).
9. The injections of muscimol produced a characteristic behavioral stereotypy consisting of repetitive, compulsive sniffing and gnawing. The time course of seizure protection and stereotypy closely coincided.
10. D. Jinnai, T. Yoshida, T. Souji, F. Kosaka, *Acta Med. Okayama* **8**, 26 (1954); T. Hayashi, *Jpn. J. Physiol.* **3**, 46 (1953); *ibid.* p. 306.
11. The presence of stereotypy itself does not, however, influence the seizure response; we have found that the dopamine agonist apomorphine (1 to 5 mg/kg subcutaneously), which induces strong sniffing and gnawing stereotypies, does not attenuate bicuculline-induced convulsions (unpublished observations).
12. M. J. Iadarola and K. Gale, *Brain Res. Bull.* **5** (Suppl. 2), 13 (1980); ———, in *Advances in Epileptology: XIth Epilepsy International Symposium*, R. Conger, F. Angeleri, K. J. Penry, Eds. (Raven, New York, 1980), p. 449.
13. See for example, discussion by W. Loscher [*J. Neurochem.* **36**, 1521 (1981)].
14. W. H. Faeth, A. E. Walker, O. J. Andy, *Epilepsia* **3**, 37 (1954).
15. R. G. Heath, *J. Neurol. Neurosurg. Psychiatry* **39**, 1037 (1976).
16. It is unlikely that the anticonvulsant effects are mediated by the dopamine neurons in pars compacta since neither dopamine agonists nor antagonists produce significant anticonvulsant activity in the tests employed (K. Gale and M. Iadarola, unpublished observations; H. Kupferberg, personal communication).
17. A large proportion of zona reticulata efferents are inhibitory GABA neurons, which are themselves GABA-receptive [I. C. Kilpatrick, M. S. Starr, A. Fletcher, T. A. James, N. K. MacLeod, *Exp. Brain Res.* **40**, 55 (1980); G. Di Chiara, M. L. Porceddu, M. Morelli, M. L. Mulas, G. L. Gessa, *Brain Res.* **176**, 273 (1979); M. Anderson and M. Yoshida, *ibid.* **137**, 361 (1977); J. A. Childs and K. Gale, *Soc. Neurosci. Abstr.* **7**, 196 (1981)].
18. A disinhibitory effect upon the reticular formation may act, by ascending reticular connections with the cortex, to suppress focal or diffuse cortical seizure activity. Such an effect has been demonstrated in primates receiving intravertebral injections of Metrazol [P. Gloor, *Epilepsia* **9**, 249 (1968)].
19. A. A. Grace and B. S. Bunney, *Eur. J. Pharmacol.* **59**, 211 (1979); B. Waszczak, N. Eng, J. R. Walters, *Brain Res.* **188**, 185 (1980).
20. D. Garant, M. J. Iadarola, K. Gale, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **41**, 1064 (1982).
21. This may be because structures other than those in the preferred circuit are recruited by the higher doses of convulsant drug.
22. Neither intranigral injections of bicuculline (up to 0.5 μg) nor isoniazid (up to 70 μg) elicited seizure activity in rats (unpublished data). Bilateral intranigral application of picrotoxin did not provoke seizures, but elicited a cataleptic state in rats [M. C. Olianas, G. M. DeMontis, G. Mulas, A. Tagliamonte, *Eur. J. Pharmacol.* **49**, 233 (1978)]. Electrical stimulation of nigra does not produce seizures, although stimulation of the adjacent reticular formation may do so [F. A. Gibbs and E. L. Gibbs, *Arch. Neurol. Psychiat.* **35**, 109 (1936); A. Kreindler *et al.*, *J. Neurophysiol.* **21**, 430 (1958); F. Bergmann, K. A. Costin, J. Gutman, *Electroenceph. Clin. Neurophysiol.* **15**, 683 (1963)]. Cobalt injections confined to the substantia nigra do not provoke overt convulsions [R. G. Fariello and O. Hornykiewicz, *Exp. Neurol.* **65**, 202 (1979)].
23. PTZ or bicuculline produced a tonic seizure in 1 to 3 seconds; the maximum response observed was tonic extension of forelimbs. Seizure intensity was rated as follows: 0, no seizure; 0.5, mild clonic with forepaw clonus; 1.0, moderate clonic with twisting of body; 2.0, severe clonic with explosive motor activity; 3.0, tonic forelimb extension. With few exceptions, PTZ was fatal to controls; bicuculline seizures rarely caused death.
24. R. W. Olsen, M. Ban, T. Miller, *Brain Res.* **102**, 283 (1976).
25. Supported by HHS grants DA 02206 and MH32359. We thank Centre de Recherche, Merrell International, for their gift of GVG. These results were presented in preliminary form at the Society for Neuroscience meeting, November 1981.
* Present address: Laboratory of Preclinical Pharmacology, St. Elizabeths Hospital, Washington, D.C. 20032.
† Send requests for reprints to Department of Pharmacology, Georgetown University School of Medicine, Washington, D.C. 20007.

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Fish Vision and the Detection of Planktonic Prey

Abstract. *Planktivorous sunfish of various sizes were studied to ascertain whether growth-related changes in the retina are related to the ability to capture small planktonic crustaceans. Behaviorally, the larger fish detected and captured crustaceans that subtended smaller visual angles. Histological examination of the retinas revealed that the distance between cones, measured in minutes of visual angle, decreased as the animals grew, suggesting that the larger retinas could resolve smaller objects. These correlated behavioral and anatomical results suggest that improved visual resolution contributes to improved predation. This finding provides a selective advantage for the continuous retinal growth noted in many fish.*

Predation by fish is an important factor in the structure of freshwater zooplankton communities, because the fish feed selectively on certain sizes and species of the zooplankters (*1*). The capture of the prey often depends on visual detection; therefore, efforts have been directed toward discovering what makes some prey more visible than others (*2*). In these studies it was assumed that the predator's visual system did not vary. This assumption warrants examination in that the retinas of some fish acquire a higher acuity as the fish grow (*3*). Such a change might affect visual detection and recognition of prey (*4*) and therefore make the zooplankton community's structure dependent on the size distribution of the predators.

In our behavioral and anatomical

study (conducted in the laboratory) of predation, several sizes of the prey (a crustacean, *Daphnia magna*) and the predator (the bluegill sunfish, *Lepomis macrochirus*) were used. The visual angle subtended by the *Daphnia* at the fish's eye at the moment of detection was compared with the spacing of cells in the fish's retina. Bigger fish capture prey that subtend smaller visual angles, and this improvement in visual detection is accompanied by a reduction in the distance (measured in visual angle) between cones.

Predation experiments were conducted in an aquarium (75 by 30 cm), with water 6 cm deep; the bottom was marked off in a grid of 1 cm squares. The fish (standard lengths, 3.7 to 5.8 cm) were caught in a Rhode Island pond and maintained in stock tanks for a year. In any one set of observations, three fish of matched size were used because single fish became skittish and would not feed. Laboratory-grown *Daphnia* were sieved into four size classes (the mean lengths were 1.1, 1.6, 2.0, and 2.4 mm); individuals were introduced into the aquarium, one at a time, by a pipet, at the end opposite to the one occupied by the fish (*5*). At this time, the fish were too far away to see the *Daphnia*, but eventually, the prey were encountered and caught. The capture was clear-cut in that a fish would turn, swim directly toward the *Daphnia*, and snap it up. Sham introductions of prey (with an empty pipet), never evoked similar behavior by the fish. From overhead video records of these events we obtained the x,y coordinates of two points: the positions of the attacker's head (i) at the moment before the attack began and (ii) when it snapped. The distance between these two points was d, the reaction distance and the diameter of the *Daphnia* was h (*6*). The reaction angle was calculated as $2 \tan^{-1} (h/2d)$.

Reaction angles (361) were measured with 12 fish (Fig. 1); the result led to two conclusions. (i) For fish of a given size, the reaction angles to all four sizes of *Daphnia* did not differ statistically; this suggests that the true diameter of the prey, h, was unimportant to detection by the fish. (ii) The reaction angle dropped from a mean of 27.8 minutes of arc in the small fish to a mean of 14.2 in the large ones. These results are consistent with the idea that visual detection limits predation under these experimental conditions.

The retinas of conspecific sunfish were examined microscopically, both immediately after removal from the eye of a freshly killed fish, and in sections of fixed and embedded tissue (*7*). The cones are the photoreceptors used in daylight vision. Their rectangular arrangement (Fig. 2) was similar throughout the retina, although the sizes of the repeating units and of the cells varied slightly with retinal region and with the size of the fish. Radial sections through the centers of the eyes of 14 fish were examined quantitatively. The numbers of all cones and the diameters of a randomly selected subset of them were determined over measured sample lengths. These numbers were then corrected for histological artifacts (*7*) to yield the retinal planimetric density, the number of cones per square millimeter of retinal surface as viewed from the lens (*8*). The average distance between cells was computed as the reciprocal of the square root of the retinal planimetric density. For fish of the range of sizes used in the behavioral experiments, the intercone distance was relatively constant, at 6.3 ± 0.5 μm (mean ± standard deviation). This constancy is somewhat misleading, as it masks the changing relation of the retina to the outside world. As the fish grows, its eye receives light from the same portion of the outside world, but the retina enlarges and recedes from the lens center (*3*). Thus, the retinal magnification factor, defined as the number of micrometers on the retinal surface per degree of visual angle, must increase, with the result that a given object at a fixed distance casts a larger image in the larger eye. The constant number of micrometers between cones corresponds to a steadily shrinking number of minutes of visual angle (Fig. 1). The intercone angles are the same order of magnitude as the reaction angles of Fig. 1, but smaller. Both angles decreased in the larger fish; the relative slopes of the two regression lines can be compared by noting that an increase of fish size from 3.5 to 6.0 cm corresponds to decreases in visual angle of approximately 50 percent along both regression lines. Thus, in relative terms, the two angles depended similarly on body size (*9*).

Why did the larger fish attack smaller visual prey? We suggest that they attacked what they could recognize as prey, and the growth-related changes in retinal structure were responsible for this improved resolution. Visual resolution may depend on factors other than the mosaic of photoreceptors, including aberrations caused by the dioptric apparatus and by diffraction through a small pupil. But the fish lens has little spherical and chromatic aberration (*10*). The pupils would have produced blur circles

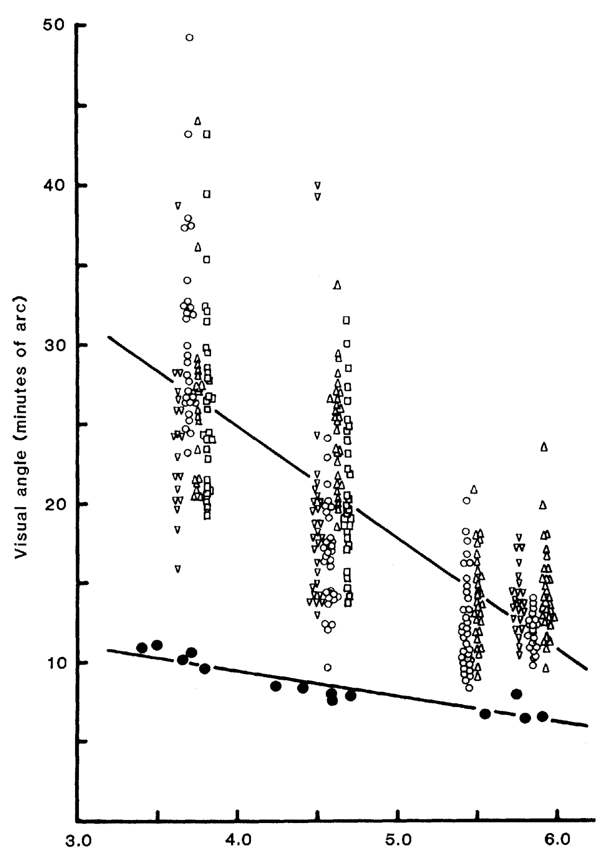

Fig. 1. Two independent measures of bluegill sunfish vision as a function of fish standard length. The open symbols are behaviorally measured reaction angles of four sizes of fish (3.7, 4.6, 5.5, and 5.8 cm) to four sizes of *Daphnia* (▽, 1.1; ○, 1.6; △, 2.0; and □, 2.4 mm). The data should fall directly above one of the four fish sizes, but are spread out horizontally to facilitate illustration. Linear regression of reaction angle, θ, in minutes of arc, on fish size, standard length, in centimeters: $\theta = 52.9 - 7.0$ SL (standard error of slope = 0.0014, $N = 361$, $F = 483.4$, $P < .0001$). The filled circles show the intercone spacing, measured from histological sections. Linear regression of intercone spacing on fish size: $\theta = 15.9 - 1.6$ SL (standard error of slope = 0.19, $N = 14$; $F = 68.16$, $P < .0001$).

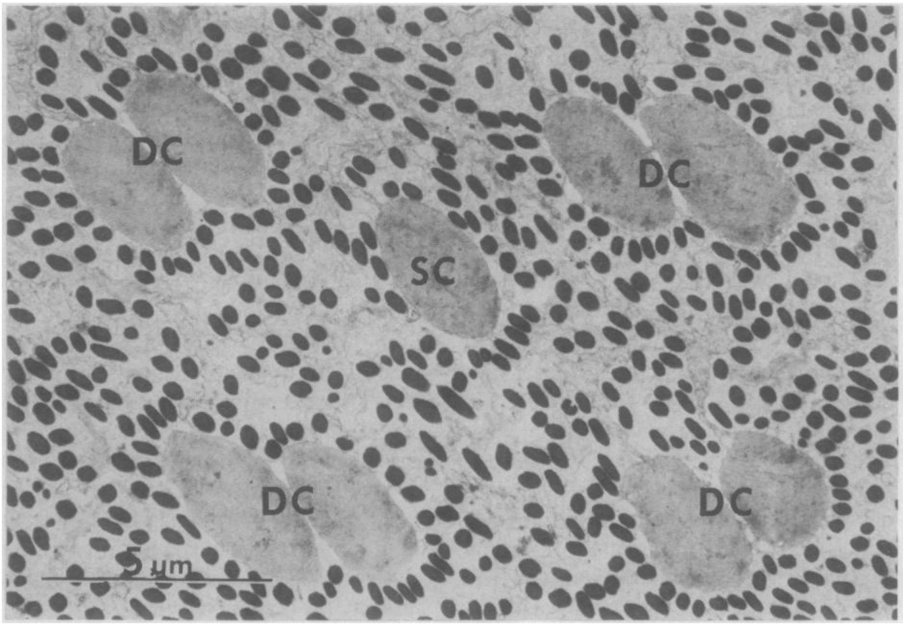

Fig. 2. Electron micrograph of bluegill retina. The plane of section is parallel to the outer limiting membrane. The quadratic photoreceptor mosaic consists of four double cones (*DC*) and one single cone (*SC*). The spaces between the cones are filled by processes of glial cells, pigmented epithelial cells, and the myoid portions of the rod cells. The rod outer segments lay sclerad to the cones in this light-adapted retina. At the light intensities used in the behavioral experiments, the rods were saturated, and nonfunctional.

with diameters of, at most, 2.2 minutes of arc, which is much smaller than the intercone spacing, and therefore not an important limiting factor (*11*). Brindley analyzed the factors limiting visual acuity and concluded: "An obvious idea that will not be very far from the truth is that the least resolvable distance between retinal images corresponds to the distance between adjacent cones" (*12*). Comparative studies are generally in accord with this notion (*13*). We accept it, and suggest that it accounts for the correlated changes in behavior and anatomy reported above.

Factors other than visual may enter into the decision to attack. For example, in fish larger than 6 cm, intercone visual angle leveled off at a mean of 7.4 minutes of arc (*14*). Since this is still a low value, these fish must have seen the *Daphnia* but, in our laboratory experiment, they did not feed on them. It is a common observation that sunfish become less planktivorous as they grow larger (*15*). Apparently, other determinants of fish diet that change with fish size, such as metabolic rate and prey-handling time, are also involved (*4*).

These observations suggest two possibilities. First, the ability to detect prey which subtend smaller visual angles confers an advantage on the larger fish, since they will be able to detect prey at a greater distance. Thus, they have visual access to a larger volume of space from which they may obtain food. This may be one selective advantage associated with continued retinal growth. Second, large fish can see more prey than small fish in the same environment. Prey abundance is an important parameter in the theory of optimal foraging, and there is disagreement about whether bluegill feeding conforms to the predicted pattern (*16*). Thus the variation of fish size could provide a useful experimental means of altering fish perception of prey abundance without altering the true distribution of prey sizes.

NELSON G. HAIRSTON, JR.
KAO T. LI
Department of Zoology, University of Rhode Island, Kingston 02881
STEPHEN S. EASTER, JR.
Division of Biological Sciences, University of Michigan, Ann Arbor 48109

References and Notes

1. J. Hrbáček, *Cesk. Akad. Ved. Rada Mat. Prirod. Ved.* **72**, 1 (1962); J. L. Brooks and S. I. Dodson, *Science* **150**, 28 (1965); T. M. Zaret, *Predation and Freshwater Communities* (Yale Univ. Press, New Haven, 1980).
2. J. L. Confer and P. I. Blades, *Limnol. Oceanogr.* **20**, 571 (1975); W. J. O'Brien, N. A. Slade, G. L. Vineyard, *Ecology* **57**, 1304 (1976); D. M. Ware, *J. Fish. Res. Board Can.* **30**, 787 (1973).
3. H. Muller, *Zool. Jahrb. Abt. Allg. Zool. Physiol. Tiere* **63**, 275 (1952); G. P. Baerends, B. E. Bennema, A. A. Vogelsang, *Zool. Jahrb. Abt. Syst. Oekol. Geogr. Tiere* **88**, 67 (1960); S. S. Easter, P. R. Johns, L. R. Baumann, *Vision Res.* **17**, 469 (1977); P. R. Johns and S. S. Easter, *J. Comp. Neurol.* **176**, 331 (1977).
4. G. G. Mittelbach, *Ecology* **62**, 1370 (1981); D. Schmidt and W. J. O'Brien, *Can. J. Fish. Aquat. Sci.* **39**, 475 (1982).
5. The aquarium was wrapped with white paper to give the fish a uniform visual background, and the observer sat behind a cardboard screen to avoid disturbing them. Illumination came from four warm white fluorescent lamps (λ_{max}, 550 nm) giving 0.45 W $\cdot$ m^{-2} at the water's surface. Fish were allowed to acclimate to the experimental aquarium for at least 48 hours and were fed frozen brine shrimp 1 day before a feeding trial. They had not been previously exposed to these experimental conditions.
6. Average *Daphnia* diameter was calculated as the diameter of a sphere having the same volume as an oblate spheroid with its major axis being the mean of the *Daphnia* length and width, and its minor axis, the *Daphnia* thickness. The video camera was suspended 200 cm above the aquarium; errors of parallax in determining the position of the fish would have introduced at most a 3 percent error in the measured reaction distance.
7. For electron microscopy retinas were first fixed in buffered aldehydes, and then postfixed in similarly buffered OsO_4, dehydrated with ethanol, and embedded in Epon. For light microscopy the retinas were fixed in Bouin's solution, dehydrated in ethanol, and embedded in paraffin. Sections (10 µm thick) were mounted and stained with hematoxylin and eosin. One radial section through the center of the eye was examined quantitatively under a 50× oil immersion lens at five to ten sample sites. The maximum diameters of the cone ellipsoids (parallel to the outer limiting membrane) were measured under a 100× oil immersion lens. The Abercrombie correction was used to obtain the number of ellipsoid centers per sample length of 10 µm thick section, and thence, numbers of cone centers per square millimeter of retinal surface in the embedded tissue. These, multiplied by 0.49 [$(0.7)^2$] to correct for 30 percent linear shrinkage, were checked against tangential sections and whole mounted fresh retinas. The intercone distances estimated from radial sections were too low by a factor of 1.6, and all were corrected accordingly.
8. L. J. Fisher and S. S. Easter, *J. Comp. Neurol.* **185**, 373 (1979).
9. It is probably unwise, given the uncertainty associated with the measurement of both reaction angle and intercone spacing, to assign much significance to the small differences between them. Among these uncertainties are (i) the part of the *Daphnia* that was detected may well have been smaller than *h*, the average diameter. If so, the reaction angle would be reduced to a value closer to the intercone spacing. (ii) The intercone spacing is subject to several approximations given in (*7*). In addition, there are slight intraretinal regional differences. If the fish were using one part of its retina in the detection, the intercone spacing there might be systematically different from the average figure we have used.
10. R. J. Pumphrey, in *The Cell and the Organism*, J. A. Ramsay, Ed. (Cambridge Univ. Press, London, 1961), pp. 193–208; however, see J. H. Scholes, *Phil. Trans. R. Soc. Ser. B* **270**, 61 (1975).
11. The diameter of the blur circle (Airy's disk) is the distance from the central maximum to the first dark ring of a diffraction pattern from a circular pupil. This distance in radians is 1.22 λ/D, in which λ is the wavelength of the light, and D, the diameter of the pupil. For the worst case of a small pupil (1.2 mm, for our smallest fish) and long wavelengths (assume λ = 650 nm), the distance is 2.2 minutes of arc.
12. G. S. Brindley, *Physiology of the Retina and Visual Pathway* (Williams and Wilkins, Baltimore, ed. 2, 1970), p. 167.
13. W. R. A. Muntz, in *The Eye, Comparative Physiology*, H. Davson and L. T. Graham, Jr. Eds. (Academic Press, New York, 1974), vol. 6, p. 155.
14. The eyes of six fish between 6.8 and 12.0 cm in length were sectioned. Intercone separation increased from 6.9 to 9.0 µm, while retinal magnification factors increased from 53.3 to 82 µm per degree. These compensating trends caused the intercone distance, measured as visual angle, to remain relatively constant.
15. A. Keast, *J. Fish. Res. Board Can.* **35**, 12 (1978); E. E. Werner, personal communication.
16. E. E. Werner and D. J. Hall, *Ecology* **55**, 1042 (1974); W. J. O'Brien, N. A. Slade, G. L. Vinyard, *ibid.* **57**, 1304 (1976); G. G. Mittelbach, *ibid.* **62**, 1370 (1981).
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