INTERNATIONAL ATOMIC ENERGY AGENCY
UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION

INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
34100 TRIESTE (ITALY) - P.O.B. 586 - MIRAMARE - STRADA COSTIERA 11 - TELEPHONE: 2240-1
CABLE: CENTRATOM - TELEX 460392-1

SMR/302-55

COLLEGE ON NEUROPHYSICS:
"DEVELOPMENT AND ORGANIZATION OF THE BRAIN"
7 November - 2 December 1988

"Development of the Visual System"

Maureen K. POWERS
Department of Psychology
Vanderbilt University
Nashville, TN
USA

Please note: These are preliminary notes intended for internal distribution only.

In press

Chapter 11 in The Visual System of Fish, Douglas and Djamgoz, eds., Croom Helm, London.

DEVELOPMENT OF THE VISUAL SYSTEM

Maureen K. Powers

Department of Psychology
Vanderbilt University
Nashville, Tennessee
U.S.A. 37240

Pamela A. Raymond
Department of Anatomy and Cell Biology
University of Michigan
Ann Arbor, Michigan
U.S.A. 48109

CONTENTS

Introduction

Development of the optics of the eye

Development of the retina

Early development

Adult development

Effects of environmental lighting

Regenerating retina

Development of the optic tectum

INTRODUCTION

Many aspects of the retinal structure and visual function of fishes are typical of all vertebrates. Trichromatic color vision, based on the presence of three primary cone pigments (Marks, 1965) and on the color-opponent organization of retinal ganglion cells (Wagner, MacNichol and Wolbarsht, 1965) is perhaps the best known example. While research on such typical properties has contributed greatly to our understanding of the neural basis of vertebrate vision, ~~there are~~ other properties ~~that~~ deserve equal interest because they are not typical. The development of the visual system is an example of this kind of property.

Unlike most other vertebrates, neurogenesis continues to occur in adult teleost fishes. This continued "development" must occur while the fish is performing its usual daily repertoire of visual tasks: finding food, participating in reproductive or aggressive behavior patterns, and so forth. The puzzle of how this can be done -- and, as will become clear below, there are some very serious puzzles -- has yet to be solved, but attempts to do so have provided ~~many~~ important clues about the rules by which synaptic connections are made (see Easter, 1983).

This chapter reviews the current literature on the development of the visual system in teleost fishes, with an emphasis on those aspects that seem most relevant for behavior. Space limitations preclude an exhaustive review; instead we have attempted to highlight selected topics which to us are the most interesting or have the most potential for future progress. The first topic is optics, because the amount and geometry of ocular growth is obviously relevant to the quality of the image received by the retina and thus to the visual process. Next the development of the neural retina itself will be

considered, followed by development of the primary visual projection area in fish, the optic tectum. There is unfortunately almost no information about the development of any of the other brain targets of retinal axons; we suggest at the outset that this is an area where more research is badly needed. Finally, visual functions will be considered separately under each heading because we still know more about the anatomy and the physiology in isolation than we do about how they subserve the mechanisms that allow the fish to see.

THE OPTICS OF THE EYE

The eyes continue to grow even in adulthood in many teleost species, but the growth of the ocular components is generally balanced so that optical properties do not change dramatically. In fact, ~~as we will see~~, in many areas of visual development the teleost nervous system is exquisitely engineered for continued growth. One example is the constancy of visual field size (Easter, Johns and Baumann, 1977): goldfish between 6 and 20 cm sbl (lens diameters of about 2 to 4 mm) all ~~had~~ have visual fields that subtended about 185 deg, despite a nearly 9-fold ~~increase~~ difference in retinal area. This property results from the precise scaling of all ocular components with body size: the lens diameter, pupil diameter, axial length etc. all increase, but they do so in proportion to one another.

The mechanisms that control ocular growth are not well understood, but several lines of evidence suggest that the size of the eye is regulated autonomously, at least in part. For example, in several mutant strains of goldfish the eyes grow excessively large; of these, the Black Moor has received the most attention. In Black Moors, the posterior chamber is enlarged but the

lens is of normal size, and the eye is therefore myopic (Easter and Hitchcock,

The defect can be expressed to a variable degree in the two eyes of a g al, such that one eye may grow larger than the other (Raymond, et al., 1988). The reason for the excessive ocular growth is not certain, but it may be a result of abnormalities in fluid dynamics in the eye because the intraocular pressure in Black Moor eyes tends to be elevated compared to normal, size-matched goldfish (Raymond et al., 1984). This interpretation is reasonable since intraocular pressure is thought to play a role in determining vertebrate eye size: in classic experiments by Coulombre and associates (50's and 60's) early embryonic chick eyes were cannulated to release pressure before the stage at which intraocular pressure began to rise, and the cannulated eyes failed to grow. Intraocular pressure may also be one of the factors that regulate ocular growth in young mammals and birds ( ).

Fernald and Wright have studied the postembryonic development of the lens (Fernald and Wright, 1985a) and of accommodation (Fernald and Wright, 1985b) in the African cichlid, Haplochromis burtoni (see Chapter 12, this volume). They found that for fish between 0.5 and 20 g (lens diameters of about 2 to 3 mm), chromatic aberration was constant at about 1.9% of focal length ~~between~~ from 656 ~~and~~ to 486 nm. In addition, the limit of resolution by the lens was always about 10 times better than the retinal limit. As will be discussed below, retinal acuity increases with fish size, and Fernald and Wright found that optical resolution seems to increase in parallel, and resolution approaches diffraction-limited values for all sizes of fish they tested. This interesting observation--that the lens is many times better optically than the retina can resolve--implies that the phenomenon of aliasing (Williams, 1985) should occur under ordinary viewing conditions in small and large fishes where

the cone mosaic is regular enough (Yellott, 1982) and enough high frequency components are present in the visual world.

DEVELOPMENT OF THE RETINA

One of the unique features of the visual system of fishes is that its structure changes throughout life, even into adulthood. This property means that the functioning visual system must somehow recruit new neurons on a daily basis and integrate them into existing circuitry. The dynamics of these changes and how they relate to the ability to function visually have been the subject of a growing number of studies aimed at understanding the neurobiological principles of visual development.

Three general categories or stages of neural development can be identified in teleost fishes, and this section of the chapter will be organized accordingly. The first could be called Early Development, and includes the initial formation of the retina and brain. The end of this phase is somewhat arbitrary, but for our purposes we will use the appearance of an "adult-like" morphology as the mark of the end of early development. This phase would include embryonic, larval and early juvenile stages. The second stage will be referred to as Adult Development, to indicate that the changes observed are characteristic of animals that are approaching or have reached sexual maturity. Finally, the remarkable property of neural Regeneration, which has allowed scientists to study pathway formation and the factors that control cell-to-cell contacts, will be considered as a separate category because examination of the similarities and differences it shares with the other two categories may provide important clues to the regulation of developmental events.

Early development

To a first approximation, the retina develops from inner to outer layers, with the photoreceptors last. The presumptive neural retina in the embryo is a sheet of dividing, undifferentiated neuroepithelial cells. Ganglion cells are the earliest neurons formed, and as soon as they cease mitotic division they segregate from the mass of immature, still mitotic cells and establish a separate layer on the vitreal surface (Hollyfield, 1972; Grun, 1975; Sharma and Ungar, 1980). As development proceeds, other retinal cells become morphologically distinguishable and segregate into their appropriate layers.

In most species of teleost fish, formation and differentiation of the photoreceptors follows a similar pattern (Ali, 1959; Blaxter and Jones, 1967; Blaxter, 1968; Sandy and Blaxter, 1980; Sharma and Ungar, 1980; Branchek and BreMiller, 1984; Raymond, 1985). One of the most striking features is that rod development lags behind that of cones, and production of new rods continues long after cones are mature.

Until recently the general belief was that teleost fish with duplex retinas acquired rods very late in development--at metamorphosis--and that during larval stages there were only cones (reviewed by Blaxter, 1975). This idea was based on light microscopy of developing retinas from several species of mostly marine teleosts. As a result of recent observations with electron microscopy, this idea has been revised somewhat. Larval stages of, for example, guppy (Poecilia reticulata), zebrafish (Brachydanio rerio), and goldfish (Carassius auratus) do have rods (Kunz, et al., 1983; Branchek and BreMiller, 1984; Raymond, 1985), but not very many. Rods are added continuously in the larval animal, and they slowly accumulate by a mechanism to be discussed below.

Thus, it is more accurate to say that the retinas of larval teleost fish are cone-dominated than to say they contain only cones.

Just before hatching in zebrafish and goldfish, a layer of immature cone nuclei appears along the outer surface (external limiting membrane) of the neural retina (Branchek and BreMiller, 1984; Raymond, 1985). Outer segments of cones are discernible in electron micrographs at or slightly before hatching, and synaptic components are apparent within the next day. The several morphological types of cone, including double and single cones, can be recognized from early on (Kunz, et al., 1983; Branchek and BreMiller, 1984; Raymond, 1985). As stated above, in general, rod nuclei begin to appear after cone differentiation has commenced, but there are some exceptions. In guppies both cones and a few rods are evident at the earliest stages (Kunz, et al., 1983). Furthermore, Kljavin (1987) has described a specialized region in the ventral retina of zebrafish embryos, where photoreceptor differentiation is precocious and rods develop early compared to other retinal regions. In the adult retina this area has a higher density of rods. The functional significance of this specialized region is not clear, except that presumably visual sensitivity would be higher here (cf Powers et al., 1988a, 1988b).

Although the precise details of timing and the rate of development of photoreceptors differ among species, the rule seems to be that by the time a fish becomes free-swimming and begins to feed, differentiation of cones (and some rods) has been completed. However there have been only a few attempts to examine specifically the visual capacities of larval fish. Branchek (1984) recorded electroretinograms (ERG's) of zebrafish from day 2 through adulthood, to determine the relative sensitivity of zebrafish to lights flickering at different rates. Cones can resolve higher temporal frequencies than rods, so

this test can determine which classes of photoreceptor are functional. The correlation between Branchek's functional results and the structural changes during development was strong. Until outer segments were present (about day 3 after fertilization) no ERG responses could be recorded. Between days 4 and 12 the ERG could be elicited, but it was smaller in amplitude and less sensitive overall than in adulthood. Up to 12 days the flicker fusion curves were approximately cone-like. Adult ERG amplitudes were approached but not reached by 15-24 days, when the flicker fusion curves became 2-branched, indicating that duplex vision had been attained. These times correlate with the initial appearance of cone-related synapses (by 4 days) and with the clear presence of both rods and cones (after 12 days) (values from Branchek and BreMiller, 1984). Blaxter and Jones (1967) have also demonstrated that retinomotor movements, as assessed by the position of the melanin granules within pigment epithelial cells (Ali, 1959), do not occur until rods appear in the photoreceptor sheet.

Behavioral studies of visual function in larval fish are also rare, but those that exist suggest that the developing retinal structure and physiological connections are rapidly available to the young fish to aid it in visual tasks. This is especially true for spectral sensitivity, where the Purkinje shift is absent initially and threshold is generally high, but at about the same time as the rods appear in the retina threshold drops and spectral sensitivity changes between dark- and light-adapted states (Blaxter, 1968, 1969). However, in terms of spatial vision, function seems to lag behind structural maturity, insofar as maturity is indicated by the presence of certain cell types. Specifically, in the zebrafish, acuity for following striped fields in an optomotor task develops more slowly than would be predicted if the intercone

spacing were the sole limiting factor in detection (Clark, 1981). Whether this is due to the necessity for the wiring to be more complete after the receptors appear awaits further experimentation, but the phenomenon brings to mind the question of whether more complex tasks in the color vision domain (i.e., ones that would presumably invoke interactions between separate cone mechanisms, like wavelength discrimination) also lag behind.

The recent psychophysical demonstration of ultraviolet sensitivity in the adult goldfish (Hawryshyn and Beauchamp, 1985) led Hawryshyn et al (1987) to investigate the development of the cone mosaic and of UV sensitivity in trout. They found a correlation between the presence during early development of presumptive UV cones and high UV sensitivity; the disappearance of this cone type, the so-called additional single cone at the corners of the square cone mosaic (Lyall, 1957a, b), was accompanied by a decline in sensitivity to very short wavelengths (Hawryshyn et al., 1987). Why young trout should be selectively more sensitive to UV wavelengths remains a mystery, as does the mechanism by which a certain class of cone drops out of the mosaic as the animal approaches maturity.

The mechanism whereby rods continue to be generated during larval retinal development (and also in adults, see below) is less mysterious, having first been suggested by Scholes (1976) and Sandy and Blaxter (1980). Their results were confirmed and extended by Johns and Fernald (1981) and Johns (1982) (see also the chapter by Fernald, this volume). By using the technique of thymidine autoradiography to label mitotic cells and follow their differentiated progeny, it was discovered that scattered mitotic cells persist in differentiated regions of retina, long after cones and other retinal neurons are no longer being produced in those regions. These mitotic cells (called rod

precursors), give rise to rods, which are inserted into the photoreceptor mosaic. This results in a continuous accumulation of rods and a gradual shift in the ratio of rods to cones in favor of the former. In the early larval retina of goldfish, before rods first appear, rod precursors are located in the inner nuclear layer in association with Muller glia; they later migrate along the radial processes of the glial cells to the outer nuclear layer, where they persist in the adult retina (Raymond and Rivlin, 1987). The functional consequences of continued production of rods in adulthood will be addressed below.

Adult Development

The adult fish retina increases in area by two mechanisms. The first is a simple stretching, as in the skin of a balloon being inflated (Ali, 1964; Johns and Easter, 1977); the second is by adding rings of new cells at the margin (Muller, 1952; Blaxter and Jones, 1967; Johns and Easter, 1977; Johns, 1977; Meyer, 1978; Rusoff and Easter, 1980; Johns and Fernald, 1981; Negishi, et al., 1982). Most of the new cells soon differentiate and become integrated into the existing retina, immediately flanking an annular cohort of cells born slightly earlier and therefore only slightly more mature than the most recently added ones. The peripheral growth zone in adult animals has all the features of a larval retina, including a paucity of mature rods and an active population of mitotic rod precursors (Johns, 1982). In the center of the retina, rod precursors are more scarce, but present nonetheless.

The effect of the addition of rods to the central, mature retina is two-fold. First, the planimetric density of the rods (# per mm^2 retinal surface) remains approximately constant or even increases slightly with growth, whereas the density of other retinal neurons, including cones, decreases due to

stretching of the eye (Muller, 1952; Ali, 1964; Johns and Easter, 1977; Kock, 1982; Powers, et al., 1988b). Second, as a consequence of the lack of cone addition, the ratio of rods to cones increases dramatically with growth (Johns and Easter, 1977). With regard to the first point, we have recently shown that the pattern of development of dark-adapted sensitivity, as measured psychophysically in adult goldfish, reflects the relative constancy of rod density in that larger fish are approximately as sensitive as smaller fish (Powers et al., 1988b). Interestingly, this pattern is also observed in OFF-type retinal ganglion cells in extracellular recordings (Falzett et al., 1988). Results from ERG studies on goldfish of different sizes also indicate that the changing rod:cone ratio is visually functional because spectral sensitivity reflects an increasing influence of rods in larger fish (Chen and Powers, 1988).

Whereas the density of rods remains nearly constant with adult growth, as mentioned above, the density of all other retinal neurons declines. For ganglion cells, the lower density is compensated by increased dendritic field size (Kock and Reuter, 1978; Hitchcock and Easter, 1986; Hitchcock,), which has the effect of maintaining a constant overlap factor throughout life. This compensation is apparently reflected in the relatively constant receptive field size of light-adapted retinal ganglion cells with growth (Macy and Easter, 1981).

Other changes occur in the retina as well: examples are that synaptic densities in the inner plexiform layer increase (Fisher and Easter, 1979; Marotte, 1980) and the number of synapses between rods and rod bipolar cells increases (Kock and Stell, 1985). The functional consequences of these changes are unknown, although we have postulated that in the dark adapted

retina the changing rod:bipolar cell synaptic ratio may be an important determinant of the signal-to-noise ratio at threshold (Powers et al., 1988).

Another consequence of continued retinal growth is that the density of cone photoreceptors per degree visual angle increases (Easter, Johns and Baumann, 1977; Johns and Easter, 1977; Fernald, 1985). In bluegill sunfish this increase correlates with the ability to detect smaller prey with growth (Hariston, et al., 1982). These observations suggest that intercone spacing is a primary limit for acuity, as several authors have suggested (Tamura, 1957; O'Connell, 1963; Brindley, 1970; Schwassmann, 1975; Johns and Easter, 1977; Hariston, et al., 1982). Taken together with the apparent lack of change in receptive field size of goldfish retinal ganglion cells (Macy and Easter, 1981), the results would also suggest that the role of ganglion cells in regulating spatial vision at its limits should be re-examined.

Effects of Environmental Lighting

Regenerating Retina

Retinal regeneration has been extensively studied in amphibians, but it is not widely known that teleost fish can also, regenerate retinal tissue. Most of the studies of teleost retinal regeneration have used goldfish and have employed neurotoxins to destroy the retina. When the Na^+-K^+ pump inhibitor, ouabain, is injected intravitreally in micromolar doses, the neural retina degenerations from inner to outer layers and over the following several weeks the neural retina regenerates (Maier and Wolburg, 1979; Raymond, et al., 1988). The source of regenerating retina appears to be the mitotic rod precursor population, which in the normal retina gives rise only to rods (Raymond, et al.,

1988). Regeneration is initiated at multiple foci scattered across the retina, and therefore, in marked contrast to normal development, maturation takes place in a dysnchronous pattern. On the other hand, the sequence of steps in retinal differentiation during regenerating at any given locus mimics larval development, with rods formed last. Kastner and Wolburg (1982) have shown that the regenerated retina is functional as measured by return of the optokinetic nystagmus reflex. For reasons unknown, retinal regeneration in adult trout following intraocular ouabain injections is not as vigorous as in goldfish (Kurz-Isler and Wolburg, 1982). Regeneration of retinal neurons in goldfish has also been observed following administration of other neurotoxins such as 6-hydroxydopamine or 5, 7-dihydroyxtryptamine (which preferentially destroy catecholaminergic neurons) and kainate (a glutamate analogue), provided these drugs are given at dosages high enough to produce a large amount of retinal destruction (Negishi, et al., 1987, 1988). In these experiments, only the regeneration of dopaminergic cells are monitored using a histofluorescent. Although to our knowledge there are no published studies of visual function during or after retinal regeneration, we submit that the ability of the adult teleost retina to regenerate offers a unique opportunity for the experimentalist to study retinal development and maturation of visual function in a robust adult animal.

DEVELOPMENT OF THE OPTIC TECTUM

In teleost fish, the major target of optic nerve fibers from retinal ganglion cells is the midbrain optic tectum (for reviews of tectal anatomy?? and physiology, see N???, 1983; Vanega, 1983; also chapter by Gu??? and ???, this volume). In contrast to the relatively recent discovery that the entire retina can regenerate, it has been known for some time that teleost optic

nerve fibers will regenerate following axotomy and that functional vision is restored as a result. The classic experiments of Sperry and colleagues in the 1940's introduced the regenerating retinotectal projection in fish (and amphibians) as a model system in which to study the mechanisms underlying the establishment of specific neuronal connections (reviewed by Easter, 1985). Sperry's work stimulated four decades of intense and profitable experiments that have had a significant influence on general theories of neuronal specificity. Other important and unique aspects of the teleost retinotectal projection in addition to its capacity for regeneration that make it an appealing system for study are: 1) the high degree of topographic order in the projection, 2) continuous proliferation of retinal and tectal neurons, and 3) continuous remodeling of the terminal arbors of optic fibers as a consequence of growth (Easter, 1985).

The optic tectum is a hemispheric structure, and new neurons are added from a peripheral germinal zone, topologically equivalent to the retinal germinal zone, except that the germinal zone in tectum is an incomplete annulus, with a gap at the rostral tectal pole where the optic nerve fibers enter (Meyer, 1978; Raymond and Easter, 1983). Because the topography of the optic projection remains constant during growth, whereas the sites of cell addition in retina and tectum are not completely equivalent, the terminal arbors of the optic fibers are constantly shifting (Easter, 1985) at a rate of several micrometers per day (Raymond, 1986). The remarkable anatomical fluidity of this neuronal circuit is of great theoretical interest in light of the fact that most theories of development, learning and memory invoke synaptic alterations to explain persistent changes in neural activity.

Another interesting phenomenon, the significance of which is not entirely understood, is the modulation of cell proliferation in the optic tectum by ingrowing retinal afferents. When regenerating optic fibers begin growing into the tectum following axotomy, the rate of cell proliferation increases in the tectal germinal zone, which supplies new tectal neurons (Raymond, et al., 1983). Cell proliferation is also stimulated in the periventricular zone underlying the tectal neurons, from which an important type of tectal glial cell arises (Stevenson and Yoon, 1978; 1981). It is possible that the regulation of tectal cell proliferation by optic fibers is important in coordinating retinal and tectal growth during normal development.

The development of the tectum and the retinotectal projection in teleost fish has received less attention than regeneration of optic fibers in the adult. Two recent studies (Stuermer, 1988; Stuermer and Raymond, 1988) have examined the early stages in the development of the retinotectal projection in zebrafish and goldfish. In embryonic zebrafish, growing optic fibers leave the eye at 34-36 hours after fertilization, and reach the synaptic layers of tectum by 70-72 hours (Stuermer, 1988). From the earliest stages, the projection is topographically ordered. Although it is not known in this species when the first synaptic connections are made, the earliest opportunity is when the fibers first arrive, at about 3 days after fertilization. Zebrafish hatch at about 3 days and become free-swimming at 4 days. Note that in the development retina the first outer segments are seen on photoreceptors and ERG responses can be recorded at about 3 days (Branchek, 1984; Branchek and BreMiller, 1984). Thus, optic fibers traverse the optic nerve and arrive at their target before photoreceptors are capable of responding to light stimuli; the final stages of maturation of retina and tectum occur simultaneously and

synchronously with the achievement of coordinated swimming behavior, the ability to feed, and the achievement of duplex retinal function. A similar synchrony of retinal and tectal development is seen in larval goldfish (Stuermer and Raymond, 1988).

Rahmann and Jeserich (1977) combined a morphometric study of synaptogenesis in the optic tectum of the rainbow trout (Salmo gairdneri) with a behavioral analysis of acuity measured with an optomotor/optokinetic task. They showed that the main period of synaptogenesis begins about one week after hatching and continues to one month, when the larval trout start swimming freely. During this period, visual acuity improves steadily from 30 to 10 degrees of arc. A further period of slow improvement follows until the adult value of about 14 to 18 min of arc is reached.

Since the tectum, like the retina, adds neurons continuously in the growing adult fish, it is not surprising that the tectum is capable of regeneration following wounding or partial extirpation, provided that the germinal zone survives (Kirsche and Kirsche, 1960; Richter and Kranz, 1977). We are not aware of any behavioral studies to assess the functional visual capacity of the regenerated optic tectum, although Segaar (1965) has investigated the neuronal regeneration and recovery of aggressive, sexual and parental behaviors in the three-spined stickleback (Gasterosteus aculeatus) following lesions of the forebrain. To the extent such behaviors require visual input, the functional capacity to see must be restored.

REFERENCES

Ali, M. A. (1959) The ocular structure, retinomotor and photobehavioral responses of juvenile Pacific salmon. Can. J. Zool., 37: 965-996.

Ali, M. A. (1964) Stretching of the retina during growth of salmon (Salmo salar). Growth, 28: 83-98.

Blaxter, J. H. S.(1968) Visual thresholds and spectral sensitivity of herring larvae. J. Exp. Biol., 48: 39-53.

Blaxter, J. H. S. (1969) Visual thresholds and spectral sensitivity of flatfish larvae. J. Exp. Biol., 51: 221-230.

Blaxter, J. H. S. and Jones, M. P. (1967) The development of the retina and retinomotor responses in the herring. J. Mar. Biol. Assoc. U. K., 47: 677-697.

Blaxter, J. H. S. (1975) The eyes of larval fish. In, M. A. Ali (ed.), Vision in Fishes: New approaches in research, Plenum Press, New York, pp. 427-444.

Branchek, T. (1984) The development of photoreceptors in the zebrafish, Brachydanio rerio. II. Function. J. Comp. Neurol., 224: 116-122.

Branchek, T. and BreMiller, R. (1984) The development of photoreceptors in the zebrafish, Brachydanio rerio. I. Structure. J. Comp. Neurol., 224: 107-115.

Brindley, G. S. (1970) Physiology of the retina and visual pathway. Williams and Wilkins, Baltimore.

Chen, D.-M. and Powers, M. K. (1988) Development of spectral sensitivity in goldfish. Soc. Neurosci. Abst., 14: in press.

Clark, D. (1981) Visual responses in developing zebrafish. Ph.D. thesis, University of Oregon.

Coulombre, A. J. (1956) The role of intraocular pressure in the development of the chick eye. I. Control of eye size. J. Exp. Biol., 133: 211-225.

Easter, S. S., Jr. (1983) TINS.

Easter, S. S., Jr. (1985) The continuous formation of the retinotectal map in goldfish, with special attention to the role of axonal pathway. In, G. M. Edelman, W. E. Gall and W. M. Cowan, (eds.), Molecular Bases of Neural Development, Neurosciences Research Foundation, Inc., Boston, pp. 429-452.

Easter, S. S., Jr., Johns, P. R. and Baumann, L. R. (1977) Growth of the adult goldfish eye. I. Optics. Vision Res., 17: 469-476.

Easter, S. S., Jr. and Hitchcock, P. F. (1986) The myopic eye of the Black Moor goldfish. Vision Res., 26: 1831-1833.

Falzett, M., Nussdorf, J. D. and Powers, M. K. (1988) Responsivity and absolute sensitivity of retinal ganglion cells in goldfish of different sizes, when measured under "psychophysical" conditions. Vision Res., 28: 223-237.

Fernald, R. D. (1985) Growth of the teleost eye: Novel solutions to complex constraints. Env. Biol. Fish., 13: 113-123.

Fernald, R. D. and Wright, S. E. (1985) growth of the visual system of the African cichlid fish, H. burtoni: Optics. Vision Res., 25: 155-161.

Fisher, L. J. and Easter, S. S., Jr. (1979) Retinal synaptic arrays: Continuing development in the adult goldfish. J. Comp. Neurol., 185: 373-380.

Grun, G. (1975) Structural basis of the functional development of the retina in the cichlid tilapia leucostica. J. Embryol. Exp. Morph., 33: 243-257.

Hariston, N. G., Li, K. T. and Easter, S. S., Jr. (1982) Fish vision and the detection of planktonic prey. Science, 218: 1240-1242.

Hawryshyn, C. W. and Beauchamp, R. D. (1985) Ultraviolet photosensitivity in goldfish: an independent U. V. retinal mechanism. Vision Res., 25: 11-20.

Hawryshyn, C. W., Arnold, M. G., Chiasson, D. J. and Martin, P. C. (1987) Developmental changes in ultraviolet photosensitivity in rainbow trout. Soc. Neurosci. Abst., 13: 1298.

Hitchcock, P. F. (1987) Constant dendritic coverage by ganglion cells with growth of the goldfish's retina. Vision Res., 27: 17-22.

Hitchcock, P. F. and Easter, S. S., Jr. (1986) Retinal ganglion cells in goldfish: a qualitative classification into four morphological types, and a quantitative study of the development of one of them. J. Neurosci., 6: 1037-1050.

Johns, P. R. (1977) Growth of the adult goldfish eye. III. Source of the new retinal cells. J. Comp. Neurol., 176: 343-358.

Johns, P. R. and Easter, S. S., Jr. (1977) Growth of the adult goldfish eye. II. Increase in retinal cell number. J. Comp. Neurol., 176: 331-342.

Johns, P. R. and Fernald, R. D. (1981) Genesis of rods in teleost fish retina. Nature, 293: 141-142.

Johns, P. R. (1982)

Kirsche, W. and Kirsche, K. (1961) Experimentelle Untersuchungen zur Frage der regeneration und funktion des tectum opticum von carassius carassius L. Z. Mikroskop. Anat. Forsch., 67: 140-182.

Kljavin, I. J. (1987) Early development of the photoreceptors in the ventral retina of the zebrafish embryo. J. Comp. Neurol., 260: 461-471.

Kock, J.-H. (1982) Neuronal addition and retinal expansion during growth of the crucian carp eye. J. Comp. Neurol., 209: 275-286.

Kock, J.-H. and Reuter, T. (1978) Retinal ganglion cells in the crucian carp (Carassius carassius). I. Size and number of somata in eyes of different size. J. Comp. Neurol., 179: 535-548.

Kock, J. H. and Stell, W. K. (1985) Formation of new rod photoreceptor synapses onto differentiated bipolar cells in goldfish retina. Anat. Rec., 211: 69-74.

Kunz, Y. W., Ennis, S. and Wise, C. (1983) Ontogeny of the photoreceptors in the embryonic retina of the viviparous guppy, Poecilia retinculata P. (Teleostei). Cell Tiss. Res., 230: 469-486.

Kurz-Isler, G. and Wolburg, H. (1982). Morphological study on the regeneration of the retina in the rainbow trout after ouabain-induced damage: Evidence of dedifferation of photoreceptor cells. Cell Tiss. Res., 225: 165-178.

Lombardo -- get ref from Pamela. In her regen paper.

Lyall, A. H. (1957) The growth of the trout retina. Q. J. Microsc. Sci., 98: 101-110.

Macy, A. and Easter, S. S., Jr. (1981) Growth-related changes in the size of receptive field centers of retinal ganglion cells in goldfish. Vision Res., 21: 1497-1504.

Maier, M. and Wolburg, H. (1979) Regeneration of the goldfish retina after exposure to different doses of ouabain. Cell Tiss. Res., 202: 99-118.

Marks, W. B. (1965) Visual pigments of single goldfish cones. J. Physiol., 178: 14-32.

Marotte, L. R. (1980) Goldfish retinotectal system: Continuing development and synaptogenesis. J. Comp. Neurol., 193: 319-334.

Meyer, R. L. (1978) Evidence from thymidine labeling for continuing growth of retina and tectum in juvenile goldfish. Exper. Neurol., 59: 99-111.

Muller, H. (1952) Bau und Wachtstum der Netzhaut des Guppy (Lebistes reticulatus). Zool. Jb., 63: 275-324.

Negishi, K., Teranishi, T., and Kato, S. (1982) Growth zone of the juvenile goldfish retina revealed by fluorescent flat mounts. J. Neurosci. Res., 7: 321-330.

Negishi, K., Teranishi, T., Kato, S., and Nakamura, Y. (1987) Paradoxical induction of dopaminergic cells following intravitreal injection of high doses of 6-hydroxydopamine in juvenile carp retina. Dev. Brain Res., 33: 67-69.

Negishi, K., Teranishi, T., Kato, S., and Nakamura, Y. (1988) Immunohistochemical and autoradiographic studies on retinal regeneration in teleost fish. Neurosci. Res., (in press).

O'Connell (1963) in Johns and Easter

Pickett-Seltner, R. L., Sivah, J. G., and Pasternak, J. J. (1988) Experimentally induced myopia in chicks: Morphometric and biochemical analysis during the first 14 days after hatching. Vision Res., 28: 323-328.

Powers, M. K., Bassi, C. J., Rone, L. A. and Raymond, P. A. (1988b) Visual detection by the rod system in goldfish of different sizes. Vision Res., 28: 211-221.

Powers, M. K., Bassi, C. J., and Raymond, P. A. (1988a). Lighting conditions and retinal development in goldfish: ~~???~~ visual ~~security???~~. Invest. Ophthalmol. Vis. Sci., 29: 37-43. Absolute Sensitivity

Rahmann, H. and Jeserich, G. (1978) Quantitative morphogenetic investigation on fine structural changes in the optic tectum of the rainbow trout (Salmo gairdneri) during ontogenesis. Wilhelm Roux's Archives., 184: 83-94.

Raymond, P. A. (1985) Cytodifferentiation of photoreceptors in larval goldfish: Delayed maturation of rods. J. Comp. Neurol., 236: 90-105.

Raymond, P. A. (1986) Movement of retinal terminals in goldfish optic tectum predicted by analysis of neuronal proliferation. J. Neurosci., 6: 2479-2488.

Raymond, P. A., Spilman, D., Hill, R., and Bahn, C. (1984) The telescopic eyes of Black Moor goldfish: Elevated intraocular pressure and altered aqueous outflow pathways. Invest. Ophthal. Vis. Sci. Suppl., 25: 282.

Raymond, P. A. and Easter, S. S., Jr. (1983) Postembryonic growth of the optic tectum. I. Location of germinal cells and numbers of neurons produced. J. Neurosci., 3: 1077-1091.

Raymond, P. A., Easter, S. S., Jr., Burnham, J. A., and Powers, M. K. (1983). Postembryonic growth of the optic tectum in goldfish. II. Modulation of cell proliferation by retinal fiber input. J. Neurosci., 3: 1092-1099.

Raymond, P. A. and Rivlin, P. K. (1985) A germinal cell specific for rod photoreceptors in the goldfish retina. Devel. Biol.

Raymond, P. A., Reifler, M. J. and Rivlin, P. K. (1988) Goldfish retin aregenerates from precursor cells that produce only rods during normal growth.

Raymond, P. A., Hitchcock, P. F., and Palopoli, M. J. (1988) Neuronal cell proliferation and ocular enlargement in Black Moor goldfish. J. Comp. Neurol., 275 (in press).

Richter, W. and Kranz, D. (1977). Ueber die Bedeutung der Zellproliferation fuer die Hirnregeneration bei niederen Vertebraten. Autoradiographische Untersuchungen. Verh. Anat. Ges., 71: 439-445.

Rusoff, A. C. and Easter, S. S., Jr. (1980) Order in the optic nerve of goldfish. Science, 208: 311-312.

Sandy, J. M. and Blaxter, J. H. S. (1980) A study of retinal development in larval herring and sole. J. Mar. Biol. Assoc. U. K. 60: 59-71.

Schwassmann, H. O. (1975) Refractive state, accommodation, and resolving power of the fish eye. In, M. A. Ali, ed. Vision in Fishes, Plenum, New York, pp. 279-288.

Segaar, J. (1965) Behavioral aspects of degeneration and regeneration in fish brain: A comparison with higher vertebrates. In, M. Singer and J. P. Schade, (eds.), Degeneration Patterns in the Nervous System, Progress in Brain Research, Vol. 14, pp. 143-231.

Sharma, S. C. and Ungar, F. (1980) Histogenesis of the goldfish retina. J. Comp. Neurol., 191: 373-382.

Stephenson, J. A. and Yoon, M. G. (1978) Regeneration of optic nerve fibers enhances cell proliferation in the goldfish optic tectum. Brain Res., 153: 345-351.

Stephenson, J. A. and Yoon, M. G. (1981) Mitosis of radial glial cells in the optic tectum of adult goldfish. J. Neurosci., 1: 862-875.

Stuermer, C. A. O. (1988) Retinotopic organization of the developing retinotectal projection in the zebrafish embryo. J. Neurosci., (in press).

Stuermer, C. A. O., and Raymond, P. A. (1988) The developing retinotectal projection in larval goldfish. J. Comp. Neurol., (in press).

Tamura, T. (1957) A study of visual perception in fish, especially on resolving power and accommodation. Bull. Jpn. Soc. Sci. Fish, 22: 536-557.

Wagner, H. G., MacNichol, E. F., Jr. and Wolbarsht, M. L. (1960) The response properties of single ganglion cells in the goldfish retina. J. Gen. Physiol., 43: 45-62.

Williams, D. R. (1985) Aliasing in human foveal vision. Vision Res., 25: 195-205.

Yellott, J. I., Jr. (1982) Spectral analysis of spatial sampling by photoreceptors: Topological disorder prevents aliasing. Vision Res., 22: 1205-1210.