TWO-DIMENSIONAL CROSS-CORRELATION ANALYSIS OF SPATIO-TEMPORAL VISUAL INFORMATION PROCESSING OF VERTEBRATE RETINA: APPLICATION TO CATFISH RETINAL NEURONS, AND TO GANGLION CELLS OF TADPOLE AND ITS ADULT FROG RETINAS

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ABSTRACT

A means was devised to visualize the retinal receptive field in time and space(i.e., spatio-temporal receptive field(STRF)) by using the noise on an unused television channel as spatio-temporal random noise stimulus and by performing cross-correlation between the input and output photographically. The methods were applied to characterize receptive fields of catfish retinal neurons(bipolar, horizontal, amacrine, and ganglion cells). TV snow noise stimuli revealed clear receptive field center with faint or undiscernible surround, suggesting that receptive field center predominantly concerns with the detection of local spatio-temporal changes of light. Spatio-temporal filtering property changed from simple to complex with the transition from distal to proximal neurons. Both on- and off-center ganglion cells were classified into two subtypes, small-, and large-field cells according to the STRF properties. Small-field cells had circular receptive-field shape whereas large-field cells elliptical configuration. Such receptive field profile was found in sustained amacrine cells. Large-field cells tended to respond better to changes of light than small-field cells. Receptive field surround of ganglion cells was often localized as hot spot.

Spatio-temporal regulation of the receptive field center by the surround was studied in catfish bipolar and ganglion cells by using micro-computer system which was newly developed for the analysis of STRFs. Response properties of the receptive field center of bipolar cells were predominantly affected by the mean

illuminance of surround whereas those of ganglion cells were largely influenced by the fluctuation of surround stimulation in addition to mean illuminance level. Temporal properties of ganglion cells significantly changed with the coarseness of center stimulation whereas those of bipolar cells were mainly affected by the coarseness of surround stimulus. The receptive field profile of bipolar and ganglion cells was little affected by surround stimulus pattern. Spatio-temporal interaction property as shown in human visual system was observed in ganglion cells but not in bipolar cells.

Effects of dopamine(DA) on catfish retinal neurons were examined by using a spot of light or spatio-temporal random noise. DA increased the response amplitude by about 50% and markedly narrowed spatial profile of the responses from the horizontal cell soma but not from the axon terminal. Without DA, the response property of bipolar and ganglion cells was similar to that induced by center stimulation alone. DA application recovered normal center-surround interaction in these cells, suggesting that DA plays an important role in center-surround interaction or light adaptation process in the retina.

STRFs of tadpole and of its adult frog were examined by use of TV snow noise and photographic cross-correlation methods. The time-course of STRF of frog ganglion cells was twice as fast as that of tadpole cells. STRF of tadpole ganglion cells was either a center-brightening or a center-dimming type whereas in the frog, there was another class of cells which had complex STRFs. Size of receptive fields of ganglion cells was similar in both

frog and tadpole retinas.

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CHAPTER 1

GENERAL INTRODUCTION

Vision is a primary source of information which provides us joy of life as well as imperative signals for survive. Visual information processing is so elaborate that one can hardly imagine that it is a series of processes performed in specific locations with close link each other. This processing owes greatly its primary performance to the retina that bears on the first stage of visual sensation. The purpose of this dissertation is to elucidate what visual information is extracted within the retina to be conveyed to the central nervous system. Furthermore, what sorts of parameters in incident light are concerned with the regulation of response properties of retinal neurons and how response regulation within the retina is related with its visual performance.

Visual information processing in the retina:

The vertebrate retina is a thin tissues of less than 0.4mm in thickness and is specialized to conduct the first stage of visual sensation. This small organ attached to the inner surface of the eye ball develops from neural tube of the ectoderm, to form a layered structure i.e., outer and inner nuclear layers, ganglion cell layer, outer and inner plexiform layers. One finds five types of neurons in the retina, i.e. photoreceptors, bipolar cells, horizontal cells, amacrine cells, and ganglion cells (Cajal, 1893; Polyak, 1941; Rodieck, 1973). The elaborate processing tasks are hierarchically achieved by the interactions among these neurons based on specific cellular connections.

Thus, photoreceptors catch photon signals to transduce the light energy to an electrical signal after a series of photochemical events that take place on the disk membrane located in the outer segment (Chabre, 1985). Light hyperpolarizes the membrane of every class of vertebrate photoreceptors without action potentials (Tomita et al., 1967; Toyoda et al., 1969; Tomita, 1970; Baylor et al., 1970; Baylor et al., 1974). This hyperpolarization results from the reduction of sodium conductance which in turn brought about by decrease of the phototransductive internal messenger recently identified to be cyclic GMP (Fesenko et al., 1985; Matthews et al, 1985; Yau and Nakatani, 1985a, b; Cobbs and Pugh, 1985; Kawamura and Murakami, 1986). Photoreceptor signals are transmitted to bipolar cells and horizontal cells via chemical synapses of rather special kinds, namely ribon synapses and basal junctions (Stell, 1967, 1972; Raviola and Gilula, 1975; Lasansky, 1978; Schaeffer et al., 1982; Saito et al, 1985; Hidaka et al, 1986).

Bipolar cells are non-spiking second-order neurons that constitute the principal retinal pathway from photoreceptors to ganglion cells. Bipolar cells fall into two distinct categories, namely on-center and off-center cells (Werblin and Dowling, 1969; Kaneko, 1970; Matsumoto and Naka, 1972; Schwartz, 1974; Naka and Ohtsuka, 1975; Richiter and Simon, 1975; Ashmore and Folk, 1980). On-center bipolar cells respond to a centered spot of light with depolarization and to an annulus with hyperpolarization, whereas off-center cells behave in the opposite fashion, hyperpolarizing in response to a spot and depolarizing in response to an annulus.

Receptive field center is driven by direct signals from photoreceptors and surround is mediated by the signals from horizontal cells (Werblin, 1977; Saito et al., 1979, 1981; Marchiafava, 1978; Toyoda and Kujiraoka, 1982; Saito et al., 1985; Sakuranaga and Naka, 1985; Saito, 1987). Bipolar cells detect local changes of light falling on the receptive field with the aid of center-surround interaction.

Horizontal cells are another type of non-spiking second-order neurons that are classified into luminosity(L-type) (Naka and Rushton, 1966b; Simon, 1973) and chromaticity(C-type) (MacNicol and Svaetichin, 1958; Naka and Rushton, 1966a) types according to the response properties to light. L-type cells are hyperpolarized independent of the wavelength of light whereas C-type cells are hyperpolarized or depolarized depending on the spectrum of light. These second-order retinal neurons are electrically coupled via gap junctions (Yamada and Ishikawa, 1965) to form a lamina, which is often referred to as S-space (Naka and Rushton, 1967; Kaneko, 1971; Simon, 1973; Mitarai et al, 1974; Lamb, 1976). Hence, horizontal cells have a large receptive field far exceeding their dendritic field and mediate first stage of lateral interactions in the retina. This feature enables the detection of mean illuminance by summating light signals over a large area. Horizontal cells participate in the regulation of response properties of bipolar and ganglion cells by forming the receptive field surround of these cells (Maksimova, 1970; Naka and Nye, 1971; Werblin, 1974; Thibos and Werblin, 1978).

Ganglion cells generate action potentials and provide the final output of the retina to be conveyed along the optic nerve to the brain. Physiological studies have shown that some vertebrate ganglion cells are relatively simple analysers of changes of light intensity within the receptive field (Kuffler, 1953; Hubel and Wiesel, 1960; Naka and Nye, 1970; Dowling and Ripps, 1970; Weinstein et al, 1971; DeMonasterio, 1978). However, there are many other species whose ganglion cells respond selectively to specific features of the visual stimulus such as the size, velocity, and moving direction of objects (Barlow, 1953; Lettvin et al, 1959; Maturana et al, 1960; Maturana and Frenk, 1963; Gaze and Jacobson, 1963; Barlow et al, 1964; Levick, 1967; Grusser and Grusser, 1976; Van Dongen et al., 1976; Semm, 1978; Bowling, 1980). That is, these retinas act as more than a simple transducers of light intensity. Such retinas possess thick inner plexiform layer rich with amacrine cell processes and show very complicated synaptic interactions involving bipolar, amacrine, and ganglion cells (Dowling, 1968; Dubin, 1970). Elucidation of true feature extracted by these highly pattern sensitive cells has been crucial problems of feature extraction analysis of receptive field (Rowe and Stone, 1980). However, basic functional units ubiquitous to vertebrate retinal ganglion cells are on- and off-center cells which subserve detection and transmission of local brightening and dimming of incident light with the antagonistic receptive field organization composed of the center and surround regions. Physiological (Naka, 1977) and morphological (Famiglietti and

Kolb, 1976; Famiglietti et al, 1977; Nelson et al., 1978) studies revealed that the connections from bipolar to ganglion cells form the segregation of on- and off-signal pathways. Namely, on-center bipolar cells make synapses exclusively onto on-center ganglion cells and off-center bipolars preferentially onto off-center ganglion cells. Thus, independent on and off systems are formed and no cross-transfer occurs between the two.

Amacrine cells are thought to mediate second stages of lateral interactions by extending their processes over the inner plexiform layer where connections among bipolar, ganglion, and other amacrine cells are formed with ribbon synapses (Kidd, 1962; Dowling and Boycott, 1966), conventional synapses (Dowling and Boycott, 1966) and gap junctions (Zimmerman, 1983). Despite the great diversity of morphological subtypes of amacrine cells (Kolb et al., 1981; Sterling, 1983), physiological subtypes reported so far are considerably limited. Amacrine cells are physiologically classified into three subtypes on the basis of response characteristics to light stimulation. On amacrine cells show sustained depolarization with occasional oscillation to step illumination whereas off amacrine cells hyperpolarize during illumination accompanied by occasional oscillatory activities at the termination of light (Kaneko and Hashimoto, 1969; Toyoda et al., 1973; Naka and Ohtsuka, 1975; Murakami and Shimoda, 1977; Marchiafava and Weiler, 1982). Unlike bipolar cells, the presence of surround antagonism is obscure in amacrine cells and the cause of oscillatory phenomena is not known. In any case, the functional role of either on or off amacrine cells remains to be

fully understood (Naka, 1977; Davis and Naka, 1980; Nelson, 1982) On-off amacrine cells respond with a transient depolarization to initiation and cessation of illumination (Werblin and Dowling, 1969; Kaneko, 1970; Matsumoto and Naka, 1972; Schwartz, 1973; Naka and Ohtsuka, 1975; Marchiafava and Torre, 1978). On-off amacrine cells show a sustained depolarization to spatial or temporal changing patterns of light (Werblin, 1972; Davis and Naka, 1980). Such behavior of on-off amacrine cells suggests that on-off amacrine cells regulate the sensitivity of ganglion cells by detecting changes of incident light in both spatial and temporal domain (Thibos and Werblin, 1978b; Werblin and Copenhagen, 1974; Wunk and Werblin, 1979). Moreover, on-off amacrine cells might represent a preparatory stage for motion-detecting ganglion cells found in several species (Barlow and Levick, 1965; Masland et al., 1984). However, the exact functional role of on-off amacrine cells remains speculative as is the case of on and off amacrine cells. Hence, the exploration of the amacrine cells' function is a quite important problem in the retinal physiology (Witkovsky, 1980).

High capacity and exquisiteness of the retina as a visual processing organ may be understood in considering its operational range. The retina can discriminate an enormous range of light intensity of up to 10^{10} fold (Rushton, 1965; Gregory, 1970; Rose, 1973). In comparison, the dynamic range of individual cells is surprisingly limited being no greater than 10^{4} fold. This aspect in ganglion cells is further restricted due to the use of spikes rather than analog potentials (Kuffler, 1953; Barlow, 1981).

Therefore, the retina cannot encode the light intensity over 10 Log unit without an appropriate mechanism for controlling the sensitivity of visual neurons according to photic environment. The retina circumvents this crucial problem by incorporating the mechanism of a sensitivity regulation or adaptation and by sharing different dynamic ranges of different cell types (Barlow, 1981; Shapley and Enroth-Cugell, 1984; Barlow, 1986). Photoreceptors cover a wide range of incident light by two types of cells called rods and cones. Rod and cone photoreceptors take different territories to cover more than 10 Log of intensity. In humans, rods handles the lower 3 Log units and cones deal with the upper 6 Log units (Riggs, 1965). Segregation of signals by on- and off-center cells may belong to the range fractionation to encode the brightening and dimming of incident light.

The retinal automatic change in sensitivity(adaptation) consists of two distinct mechanisms, dark adaptation and light adaptation. Dark adaptation refers to change in sensitivity associated with the regeneration of photopigment from bleaching (Dowling, 1960; Rushton, 1961a,b; Rushton and Westheimer, 1962; Kleinschmidt and Dowling, 1975). Hence, dark adaptation is often called as bleach adaptation. This adaptive process is characterized by a slow time course. Physiological (Lamb, 1981) and psychophysical (Rushton, 1961a, b) studies have shown that absolute sensitivity reduced by a strong bleaching light recovers to its extremes in about an hour, accompanied by diminution of the dark noise (Barlow, 1964; Baylor et al., 1979) in full darkness. Light adaptation occurs independently of any

alterations in visual pigment levels in the eye and is characterized by a relatively fast time course at both onset and cessation of illumination (Rushton, 1965; Enroth-Cugell and Shapley, 1973; Green et al, 1975; Cicerone and Green, 1980). The light adaptation mechanism induces reduction in the incremental sensitivity of vision in proportion to the background intensity. This is widely known as Weber-Fechner's law. According to this law, contrast detection depends on the reflectance of visual object without being influenced by any level of background illumination (Shapley and Enroth-Cugell, 1984). Actually, the incremental sensitivity of photoreceptors (Kleinschmidt and Dowling, 1975; Bastian and Fain, 1979), bipolar and ganglion cells (Enroth-Cugell and Shapley, 1973; Green et al., 1975; Naka et al., 1979) has been reported to obey this law. Furthermore, the retina can handle a wide range of illumination levels by decrementing the sensitivity with background intensity. In addition, contrast-dependent sensitivity regulation or contrast gain control (Shapley and Victor, 1978, 1979) is present in cat retinal ganglion cells. In amphibian (Werblin and Copenhagen, 1974; Thibos and Werblin, 1978b) and cat (Enroth-Cugell and Jakiela, 1980) retina, the sensitivity of ganglion cells is affected not only by the surround illuminance level but also by intensity changes of surround light in both space and time domain.

The foregoing line of evidence suggests that retinal sensitivity is regulated not only by mean illuminance level but also by other parameters such as contrast. In brief, the retinal

sensitivity is controlled initially by the state of adaptation of the photoreceptors (Dowling and Ripps, 1970; Normann and Werblin, 1974; Kleinschmidt and Dowling, 1975; Bastian and Fain, 1979; Lamb et al., 1981), then modified by the lateral interactions between horizontal cells at the outer plexiform layer (Werblin, 1974; Thibos and Werblin, 1978a) and finally influenced by lateral interactions between amacrine cells at the inner plexiform layer (Dowling, 1967; Thibos and Werblin, 1978b). Therefore, it is the final phase of retinal adaptation to adjust the spatio-temporal filtering property of ganglion cells. To this end, the retina needs to know parameters which characterize the property of incident light; mean illuminance, intensity distribution around mean illuminance, contrast, spatio-temporal frequency of stimulus light, and so on.

The purpose of the present study:

The overall aim of this study is to know how the retinal ganglion cells adapt to the visual environment and what sorts of mechanisms reside in the retina to make the best of ganglion cells' capacity. As a first step for investigating these problems, how spatio-temporal visual images are seen by retinal neurons was examined. This was done by stimulating the retina with spatio-temporal random-noise pattern. The research then went on by asking what stimulus parameters affect spatio-temporal filtering properties of bipolar and ganglion cells. Third, the regulation of spatio-temporal dynamics of retinal neurons by endogenous chemicals(dopamine) was studied. Finally, changes of receptive field organization in ganglion cells during ontogenic

development were studied by comparing spatio-temporal receptive fields of ganglion cells in tadpole and adult frog retinas.

In this study, the retina of channel catfish(Ictalurus punctatus) was chosen because of several advantages over other retinas. First, the catfish retina shows a simple functional and morphological organization that appears to lack color vision. Second, all retinal neurons except for photoreceptors are easily accessible to intracellular and extracellular recordings. Third, a considerable wealth of knowledge has been accumulated over the years as regards both function and morphology of the retinal neurons by Naka and his collaborators (Naka and Nye, 1970, 1971; Marmarelis and Naka, 1973; Naka and Ohtsuka, 1975; Naka, 1977; Naka et al, 1979; Davis and Naka, 1980).

The first part of this thesis addresses to the problem of spatio-temporal filtering properties of the catfish retinal interneurons(bipolar cells, horizontal cell's somas, and amacrine cells) and ganglion cells. The method used to this end was a spatio-temporal cross-correlation analysis which allows us to characterize functional properties of retinal neurons in a unified realm of time and space (Hida and Naka, 1982, Hida et al., 1983). That is, it is possible to map out how the electrical response of a given retinal cell depends upon the retinal distance from and the time elapsed from the elementary stimulus, i. e., a small-spot flash of unit intensity. Thus, the outcomes of these measurements tell "sphere of influence" in the space-time domain and can be called "spatio-temporal receptive field" as opposed to the usual notion of "receptive field" which

often overlooks the time-varing aspect. These results indicate that the receptive field center predominantly contributes to the detection of spatio-temporal changes of incident light in bipolar, amacrine, and ganglion cells (Hida and Naka, 1982). The filtering properties in catfish retina became more complex from distal to proximal neurons. Furthermore, dynamical interactions in space-time domain were found in ganglion cells.

Based on these results, the second part deals with the regulation of the response properties of the receptive field center by surround mechanisms in bipolar and ganglion cells of catfish retina. In addition, spatio-temporal dynamical interactions of bipolar cells and of ganglion cells were studied by relating with surround mechanism. To analyze response properties of neurons more quantitatively than did in the first part, micro-computer system for the measurement of spatio-temporal receptive field was developed (Mizuno et al., 1985) and introduced for the analysis in the second part. The results showed that response properties of receptive field center of bipolar cells dominantly depended on the mean illuminance of light impinged on the surround. In ganglion cells, on the other hand, response properties of receptive field center were affected not only by the mean illuminance of surround stimulus but also of fluctuations of the surround illumination. Response properties of receptive field center in bipolar cells did not change with the spatial frequencies of center pattern whereas temporal kinetics of receptive field center of ganglion cells was altered by coarseness of random noise incoming on the center region.

The theme of the part three is the modifications of the sensitivity, receptive field profile, and response kinetics of retinal neurons by dopamine which is an important endogenous substance in the teleost retina. Dopamine is also considered to be a very important biogenic amines in the central nervous system. Physiological study (Negishi and Drujan, 1979; Teranishi et al, 1983; Piccolino et al., 1984; Lasater and Dowling, 1985) in the retina has indicated that dopamine regulates spatial properties of horizontal cells by modulating the conductance of gap junctions. The methodology employed in the part three was fundamentally identical with that of the part two. In addition, however, flashing and moving spots of light were also employed to explore the cellular spatial properties. The present study confirmed earlier findings (Negishi, 1979; Teranishi et al., 1984) concerning the effects of dopamine on horizontal cells. In addition, the difference in dopamine effects on the soma as well as axon terminal of horizontal cells was revealed (Hida et al., 1984). Moreover, dopamine effects on bipolar and ganglion cells strongly suggest that dopamine plays a crucial role in the center-surround interactions of bipolar and ganglion cells.

The final part of this dissertation deals with the growing retina with reference to changes in the spatio-temporal dynamical characteristics of ganglion cells. During its development, the vertebrate retina exhibits substantial changes of constituent neurons including appearance of new neurons and expansion of neural dendrites. In particular, the amphibian retina is known to undergo drastic functional as well as morphological changes

before and after metamorphosis (Gaze and Peters, 1961; Pomeranz and Chung, 1970; Fisher and Jacobson, 1970; Straznicky and Gaze, 1971; Cima and Grant, 1980) However, this interesting process is not fully elucidated. For instance, the functional transition of ganglion cells from larval to adult is understood only to a very limited extent. In this research, therefore, spatio-temporal receptive fields of ganglion cells were measured and the data from tadpole(Rana Catesbeiana) and its adult frog were compared. These results obtained by using TV snow noise and photographic cross-correlation method (Shingai et al., 1983) demonstrate qualitatively as well as quantitatively changes in the functional properties of ganglion cells that underly the developing retina.

CHAPTER 2

RECEPTIVE FIELD ANALYSIS OF VERTEBRATE RETINAL NEURONS: WITH SPECIAL REFERENCE TO GANGLION CELLS

-----HISTORICAL REVIEW-----

The study of receptive field has been a central problem in vision physiology. Receptive fields of retinal neurons need to be analysed thoroughly before their functional role can be really understood. The receptive-field analysis also permits comprehensive cellular classification that may stimulate comparative study to unveil the evolution of vertebrate retina (Tyner, 1975). The notion of receptive field was first proposed by Hartline in his analysis of light-induced responses of the ganglion cells in the frog retina (Hartline, 1938). He stimulated the retina with a small spot of light and became aware of a certain area "which must be illuminated in order to obtain a response in any given fiber." He referred to this region as receptive field. Further, he described three cell types with different responses; (1) on response, an initial burst of impulses followed by a maintained discharge lasting throughout illumination, (2) off response, spike activity in response to the cessation of stimulus, (3) on-off response, burst of impulses only to onset and cessation of light. Hartline subsequently showed that a ganglion cell's sensitivity to a spot of light is not uniform over its receptive field, but is maximal near the center of the receptive field and decreases in the peripheral retina (Hartline, 1940a). The size of receptive field depends on the stimulus intensity and size in such a way that the two

parameters are interchangeable over certain ranges in eliciting a threshold response(Riccow's law) (Hartline, 1940b).

Parametric analysis of receptive fields:

After thirteen years since Hartline's pioneering work, there was another substantial progress in the understanding of receptive field of retinal cells. This was made by Kuffler and Barlow. Kuffler studied cat retinal ganglion cells in the intact eye. He found that the receptive field of ganglion cells consists of two antagonistic regions; a center region where light illumination induces either on- or off- discharges and concentric surround where stimulation elicits the opposite response (Kuffler, 1953). Hence, the surround mechanism can be thought to inhibit the center response as shown in the lateral inhibition of limulus eye (Hartline et al., 1952; Hartline and Ratliff, 1957). More recently, the functional role of surround mechanism was intensively investigated by intracellular analysis of amphibian retinal bipolar and ganglion cells (Werblin, 1974; Werblin and Copenhagen, 1974; Thibos and Werblin, 1978a,b) and by extracellular recording of ganglion cells in the cat retina (Maffei, 1968; Kruger and Fischer, 1973; Enroth-Cugell and Lennie, 1975; Enroth-Cugell et al., 1975).

Also, Barlow examined area/threshold property of ganglion cells in the excised retina of the frog, and found an inhibitory surround region of on-off cells as has been shown in cat retinal ganglion cells (Barlow, 1953). Furthermore, he provided evidence that the organization of receptive fields changes with dark adaptation and that the surround influence diminishes as the

retina adapts to low ambient illumination (Barlow et al., 1957). Hubel and Wiesel reported that monkey retinal ganglion cells possess a center-surround antagonistic receptive field of smaller sizes than that of cat retinal ganglion cells (Hubel and Wiesel, 1960). Rodieck and Stone quantitatively analysed the receptive field profile of cat retinal ganglion cells from spike discharges elicited by various sizes of slit or of spot of light, and reported two principal findings. First, they showed that responses of cat retinal ganglion cells to stationary and moving visual stimuli are synthesized through a single receptive field mechanism with a sensitivity profile shaped like "Mexican hat" (Rodieck and Stone, 1965a). In fact, the cellular responses to various moving stimuli are predictable from the knowledge of such receptive-field patterns together with the transient kinetics of responses to flashing stationary spots of light (Rodieck, 1965). Second, they concluded that a population of ganglion cells with a concentrically organized receptive field can signal far more information to the central visual system than any single ganglion cells (Rodieck and Stone, 1965b). For instance, velocity and direction of a moving object can be encoded by an array of on-center cells and/or off-center cells, to the effect that the cell is a motion detecting unit. The receptive field analyses cited above are usually referred to as parametric analysis (Rowe and Stone, 1980).

An important result from this type of work was a contrast-sensitivity analysis of cat retinal ganglion cells by the use of sinusoidal gratings (Enth-Cugell and Robson, 1966). Sinusoidal

gratings whose intensity distribution in space is changed sinusoidally, have often been used in psychophysical studies of the human vision, for example, to characterize contrast-sensitivity function. Cat retinal ganglion cells respond with sinusoidal variations of spike frequencies to sinusoidal gratings moving at a constant speed. However, the magnitude of the response to stationary sinusoidal patterns changes with the position or phase of sinusoidal gratings. Thus, in both on-center and off-center units, they found two-distinct types of cells which differ in spatial summation properties. The cells which have linear spatial summation property, did not show the change of spike frequencies in spite of introduction and withdrawal of grating when grating was presented in certain position within the receptive field. On the other hand, the ganglion cells which possess nonlinear spatial summation property showed the increase of impulses at both introduction and withdrawal of the grating patterns wherever the grating was projected within the receptive field. These cells with linear and nonlinear spatial summation properties are referred to as X-cells and Y-cells, respectively (Enroth-Cugell and Robson, 1966). X-cells and Y-cells differ in the following other aspects as well. Receptive field centers of Y-cells are generally larger than those of X-cells. X-cells are encountered more frequently than Y-cells, if the comparison is made near the area centralis of the cat retina. These findings have been widely confirmed (Cleland et al., 1973; Stone and Fukuda, 1974; Cleland and Levick, 1974; Rowe and Stone, 1976; Derrington et al., 1979; Stone and Keens, 1980) and have been

interpreted as evidence that X-cells subserve high-resolution pattern vision, while Y-cells facilitate low-resolution spatial vision or movement vision. The conduction velocity of Y-cells is faster than that of X-cells, (Fukada, 1971; Cleland et al., 1971) correlating with the somatic size and axon diameter (Boycott and Wassle, 1974). In general, Y-cells respond more transiently than X-cells to step illumination, supporting the notion of temporal vision subserved by Y-cells (Ikeda and Wright, 1972; Cleland et al., 1971, 1973). X- and Y-cells are also found in monkey retina (DeMonasterio, 1978). These functional distinctions between X- and Y-cells seem to suggest that the two ganglion cell types represent cellular substrates of temporal and spatial channels (Stone et al., 1979; Lennie, 1980). Human psychophysical experiments support the validity of this thought (Tolhurst, 1973; Kulikowski and Tolhurst, 1973). Whether X- and Y-cells dichotomy or spatial- and temporal-channel separation has come into existence in an early stage of vertebrate evolution remains to be fully understood (Shapley and Gordon, 1978; Tuttle and Scott, 1979). The investigations described above did not employ cell specific stimuli nor invoked any preposition on receptive field properties.

Feature extraction analysis:

The second major stream of work on receptive field analysis is an attempt to establish a new experimental paradigm by using more natural stimuli instead of artificial spots and moving geometrical figures. The operational trait of a cell can be characterized by some feature of the visual world to which the

cell is uniquely sensitive; for example, a small object moving in a particular direction. Such stimuli are called the cell's trigger feature (Barlow, 1961). In general, the ultimate function of visual neurons is to detect the occurrence of that feature in a certain part of the animal's visual field and to signal that occurrence to the brain. The works along this line are called a feature extraction approach and were made in the frog (Lettvin et al. 1959; Maturana et al. 1960; Lettvin et al., 1961; Barlow, 1961), pigeon (Maturana and Frenk, 1963), and rabbit (Barlow et al. 1964; Levick, 1967; Wyatt and Daw, 1975), and have added greatly to the knowledge about ganglion cells. These workers reported several "natural groups" among retinal ganglion cells, concluding that cells of each group carry out a discrete and invariant analysis of the visual image and encode a particular feature of the image. Each cellular operation is defined in terms of the effective stimulus for activating the cell. Maturana et al., proposed five operations in this regard; sustained edge detection, convex edge detection, changing contrast detection, dimming detection, and dark detection (Maturana et al., 1960). Subsequently, however, Lettvin et al. regrouped the ganglion cells: boundary detectors, movement-gated units, dark convex boundary detectors, movement or changing contrast detectors, dimming detectors, and unclassified units (Lettvin et al., 1961). These workers emphasized that once true operations the cell type in question performs have been identified, meaningful questions can be asked about it and may be answered. However, the problem is how the true operation could be reliably identified by using

test stimuli that are as natural as possible. A premise underlying the feature extraction approach is that a distinction is always present between features considered important (often referred as a natural invariant (Maturana et al., 1960) or trigger feature (Barlow, 1961; Barlow et al., 1964) or key feature (Levick, 1975)) and features presumably unimportant, accidental (Maturana et al., 1960) or secondary (Hughes, 1979).

Receptive field analysis using random noise or sum of sine waves:

In the parametric analysis, the receptive field is usually treated as static rather than time-varing. In the on-center ganglion cells with a simple center-surround organization, a centered flash of light initially increases spike discharges and then acts to decrease the firing rate. Therefore, the receptive field center may function as on unit or off unit depending on the time elapsed from the flashing stimulus. Thus, the spatial organization of receptive field may change with time. This aspect can never be overlooked, especially when one studies ganglion cells that bear complex spatio-temporal operations as described in the feature extraction analysis.

It is important, therefore, to conceptualize the receptive field including its temporal factor as well as spatial factor. With this spirit in mind, a new notion of receptive field was put forward by Yasui, Fender, and Sutter in mid-1970 (Yasui and Fender, 1975, Sutter, 1975). They added the new dimension of time to the classical receptive field so that the filtering characteristics of visual neurons can be described in a unified realm of time and space, and this was referred to as spatio-

temporal receptive field (Yasui et al., 1979). This notion had its origin in the multi-dimensional extension of white-noise analysis by Marmarelis and his associates (Marmarelis and McCann, 1973; Marmarelis and Naka, 1974). The extended version of white-noise analysis was applied by using a stimulus configuration that consisted of a centered spot with a concentric annulus of light each modulated by an independent white-noise signal, and catfish retinal neurons were extensively investigated this way (Marmarelis and Naka, 1973, 1974). A further extension would be to increase the number of white-noise inputs from two to n. By cross-correlating the n test inputs with a single output, spatially distributed impulse response functions or spatio-temporal receptive field kernels can be calculated (Yasui et al., 1979). The method described above is a spatio-temporal extension of the Wiener-Lee-Schetzen theory (Wiener, 1938, 1958; Lee and Schetzen, 1965). Such n-inputs white-noise stimuli are scintillation of light modulated in both time and space. In fact, the ensemble of these signals forms a spatio-temporal random noise or spatio-temporal white noise.

So far, two methods have been proposed to determine the spatio-temporal receptive field: one employs the spatio-temporal random noise (Powers and Arnett, 1981; Citron et al., 1981; Hida and Naka, 1982) and the other makes use of a flashing spot of light (Stevens and Gerstein, 1976; Stein, et al., 1983). The latter approach presents two difficulties: (1) it requires a long and stable recording to complete the receptive field measurement. This restricts the application to intracellular

recordings. (2) In the normal environment, neurons in the visual systems function as an interconnected neural network. It is doubtful, therefore, whether a flashing spot of light which stimulates only a small number of neurons is adequate for testing such a system. In contrast, the receptive field analysis by use of spatio-temporal random noise provides a highly potent strategy for investigating retinal neurons in several respects. First, the spatio-temporal random noise stimulates a large number of neurons simultaneously in order to mimic the "natural input" to the visual system. The stimulation of this type has two additional advantages:(1) the state of adaptation can be kept constant and (2) a short experiment time for the receptive field measurement because the stimulus tests the cells en mass (Powers and Arnett, 1981; Hida and Naka, 1982; Hida et al., 1983). Furthermore, the method extracts visual images which the cell detects, without any assumption of its receptive field properties. Thus, the spatio-temporal receptive field measurement provides a reliable link between the parametric analysis and the feature extraction analysis (Hida and Naka, 1982).

Another approach to the spatio-temporal receptive field measurement was proposed, by Victor and Shapley, which resorts to Fourier analysis of the response to a random grating pattern (Victor and Shapley, 1980). The input they used composed of a sum of sinusoids of various frequencies, rather than stochastic signals. This method was applied to the analysis of X- and Y-types of cat retinal ganglion cells (Victor and Shapley, 1979; Shapley and Victor, 1978, 1979). As is the case of white-noise

analysis, this method allows one to determine linear and nonlinear components of cellular response separately. Based on this procedure, Victor and Shapley obtained a receptive field model of Y-cells that can account for the nonlinear spatial summation property of these cells(Victor and Shapley, 1979).

CHAPTER 3

SPATIO-TEMPORAL RECEPTIVE FIELDS OF CATFISH RETINAL NEURONS AS REVEALED BY TV SNOW NOISE

Introduction:

The vertebrate retina is a two-dimensional array processor which filters visual stimuli in time and space. Spike trains from retinal ganglion cells encode the spatio-temporal visual message to be conveyed to the central nervous system. The signal processing carried out in the retina is based on the elaborate mutual interactions among several types of neurons packed in layers (Dowling and Werblin, 1969; Werblin and Dowling, 1969; Rodieck, 1973). Two approaches have been advanced for quantitatively analysing the function of retinal neurons. In one, the temporal and spatial properties are analysed independently. Flashing spot or annulus and sinusoidal grating are the favorable probes in this line of research (Kuffler, 1953; Enroth-Cugell and Robson, 1966; Kaneko, 1970). In the other approach, the filtering properties of retinal neurons are defined in a unified realm of time and space. Two kinds of test stimuli have been devised in this respect; stimulation of various retinal areas by a small flashing spot (Stevens and Gerstein, 1976; Stein et al., 1983) and illumination of a broad retinal region by a spatio-temporal random noise (Citron et al., 1981; Powers and Arnett, 1981).

The latter type of test inputs was used in this study, and catfish retinal neurons were analysed by measuring the spatio-temporal receptive field(STRF). STRF is an extended concept of the classical receptive field in which the dimension of time is

added to the two-dimensional space of retinal surface (Yasui et al., 1979). Thus, TV snow noise as a physical realization of spatio-temporal random noise and photographic cross-correlation were used to estimate the spatio-temporal receptive field in two spatial and one temporal coordinates. The primary aim of this section is to characterize spatio-temporal properties of visual neurons in the intact retina of catfish.

Materials and Methods:

Theoretical formulation of spatio-temporal receptive field(STRF):

Visual stimuli the retina experiences in daily life fluctuates in time and space. In the idealized case, the spatio-temporal signal is characterized as follows.

$$\overline{s(x_1,y_1,t_1)s(x_2,y_2,t_2)}=P\delta(x_1-x_2,y_1-y_2,t_1-t_2) \qquad (1)$$

The bar denotes the average over time t. P is a constant corresponding to the power spectral density defined in the joint-frequency domain of time and space. $\delta(.,.,.)$ stands for a three-dimensional Dirac delta function in which the function has zero value unless all three arguments are zero. The equation (1) shows that spatially or temporally separated picture elements of the stimulus light fluctuate independently in time and space.

Suppose that the system under study behaves linearly in both time and space. Then, the cell's response R(t) to the spatio-temporal random noise which stimulates a large area encompassing the receptive field can be completely expressed as (2).

$$R(t)=R_0+\iiint h(x,y,\tau)s(x,y,t-\tau)dxdyd\tau \qquad (2)$$

where x,y are the spatial coordinate variables on the retinal surface and R_0 is the DC or steady component of the response. Even if the input-output relation of the cell is not linear, the integral term of equation (2) represents the best linear approximation to the response to spatio-temporal random noise (Yasui et al., 1979). $h(x,y,\tau)$ is referred to as the first-order spatio-temporal Wiener kernel or STRF. $h(x,y,\tau)$ describes the influence of past stimuli presented at the various parts of the retina on the present response. As being analogous to the impulse response interpretation of usual first-order Wiener kernel, $h(x,y,\tau)$ describes the AC response waveform caused by an infinitesimally small spot of flashing light presented at retinal position (x,y) and at time $t=\tau$ ago. Namely, STRF defines the AC dynamic property of the visual neuron in response to spatially and temporally changing light.

From equations (1) and (2), $h(x,y,\tau)$ can be computed by cross-correlating the stimulus(spatio-temporal random noise) and resulting response.

$$h(x,y,\tau)=\frac{1}{P}\overline{R(t)s(x,y,t-\tau)} \qquad (3)$$

Equation (3) is a spatio-temporal extension of the well-known stochastic identification algorithm based on input-output cross-correlation (Yasui et al. 1979; Sakuranaga et al, 1986).

Stimulation and recording:

Eyes were excised from the channel catfish(Ictarulus punctatus) and the anterior portion and excess vitreous humor were carefully removed. The opened eyecup was maintained in a

chamber where a moisted oxygen of 100% was continuously supplied at room temperature. Intracellular recordings were made from horizontal cell somata, bipolar cells, and amacrine cells with glass capillary microelectrodes filled with 2M potassium citrate having the resistance of 50-100MΩ. Intracellular responses to photic stimuli(TV snow noise) were amplified with a preamplifier(WPI-MZ01; WPI) and a main amplifier(AM502; Sony Tectronix). The records were VF(voltage-frequency)-converted to store on the audio channel of a video tape recorder(VTR, CR-8500L; Victor). Spike discharges of ganglion cells were recorded extracellularly with tangsten electrodes whose tip was gold-plated and platinized to form a platinum-black contact. Amplified spike signals were recorded on the audio channel of the VTR.

As shown in Fig. 3.1, the photic stimulus pattern used in this study was the television(TV) snow noise seen on an unused channel of a TV set. Prior to the experiment, the TV snow noise was prerecorded on the video channel of a video tape by means of a TV camera (PT105; Ikegami). Distortion of TV snow noise was assessed by accumulating the prerecorded noise on the film during 1-4min. The resulting films showed quasi-uniform bright pictures without recognizable distortion. The TV snow noise was played back on the TV monitor screen(PM-52T; Ikegami) and was imaged on the retinal surface with a focusing lens. The noise pattern encompassed about two-thirds of the retinal area. The grain size of the TV snow noise on the retinal surface was adjusted by changing the distance from the picture monitor to the retinal surface. The mean illuminance of this noise stimulus was 1.0

$\mu W/cm^2$ on the retina. The responses to the TV snow noise were recorded on an audio channel of the stimulus-source video tape. Thus, the TV snow noise and the evoked responses were recorded on the same video tape, and were subsequently processed to obtain STRF by cross-correlating the stimulus(TV snow noise) and the neural response.

Cross-correlation:

Cross-correlation function of a pair of data, x(t) and y(t) can be obtained by taking the average product of the values, x(t) at time t and $y(t+\tau)$ at time $t+\tau$ over the observation time T(Lee, 1960). In the case of ganglion cells, cross-correlation must be performed between the input(TV frames) and digital output(spikes).

The reverse trigger correlation method (de Boer and Kuyper, 1968; Eggermont et al., 1983) was applied for this purpose after being modified to suit the present spatio-temporal analysis (Hida and Naka, 1982; Hida et al., 1983). This scheme is illustrated in Fig. 3.2. In output time series, a spike event can be approximated as '1' and absence of spikes as '0'. Therefore, cross-correlation between input frames and output spikes can be approximated to summate the TV frames that elicited the spikes(Fig. 3.2A). In other words, the spike signal triggers the summation of the TV frames that elicited the spikes. First, we played backward the stimulus-source tape and the signals of the audio channel (evoked spikes) were delayed through the delay circuit(Fig. 3.1). This procedure permitted us to arrange the TV frames which produced the spike discharge and the resulting

spikes in parallel(Fig. 3.2B). Then the video signals were fed into the video sample-and-hold circuit to display the TV frames for 30msec immediately the spike occurred(Fig. 3.1). The long exposure of a 35-mm camera in front of the picture monitor(PM52-T; Ikegami) accumulates the television frames which produced spike discharges after a given delay(Fig. 3.2A). Owing to the wide latitude and improved gradation, H&W monochrome films(H&W Control; H$W) were used for the accumulation of the TV frames. In most cases, the duration of the playback needed to last for 5-6min to obtain a STRF with a good fidelity. The cross-correlation procedure was repeated for several delays(0 to 240 msec of 30 msec steps) to form a three-dimensional STRF. The data from changing the steps of delays showed that delays of 30 msec steps up to 240 msec were sufficient to cover the entire STRF properties of catfish retinal neurons.

In the case of non-spiking neurons such as horizontal, bipolar, and amacrine cells, the audio channel of the reversed stimulus source tape was FV-converted and then was delayed through analog delay circuit. Brightness of the TV monitor screen in front of the camera was modulated according to the analog excursion of membrane potentials from the dark level. As was the case of ganglion cells, a map of STRF was obtainable through the accumulation of the TV frames for a period of 2-4min.

A STRF thus obtained was composed of the pictures of different delay times(0 to 240 msec of 30 msec steps). These pictures were digitized by a computer(VAX 11/780)-controlled image digitizer (Oscon) to assess quantitatively the magnitude

and size of STRFs at different delay times.

Results:

Horizontal cell soma:

Horizontal cells showed a sustained hyperpolarizing response with small fluctuation in response to the TV snow noise stimulation (Fig. 3.3). Enlargement of the grain size of TV snow noise resulted in increase of fluctuation. In contrast, the sustained hyperpolarization(DC-response component in itself) did not significantly change with the grain size, provided that the mean illuminance level of TV snow noise was kept constant. This indicates that the major signal coded by horizontal cells is the mean illuminance of incident light.

STRFs were obtained with best fidelity when the mean grain size was 300 μm. The reduction of the mean grain size to less than 300 μm caused the deterioration of the measured STRF. Fig. 3.4 shows a STRF of horizontal cell's soma demonstrating that the soma detects radially symmetric patterns of light regardless of the delay. As shown in Fig. 3.5, spatial and temporal filtering properties of horizontal cell somata can be characterized by STRF profiles that were monophasic and nearly circular. The receptive field profile had its maximal value at a delay of 60 msec and then vanished at a delay of 180 msec. No polarity change was seen in the time-varying profile. Half-width of the receptive field profile at a delay of 60 msec was about 400 μm(Table 3.1), a value similar to the receptive field profile delineated from the response to a single bar of light moving in one direction (Davis and Naka, 1980). The shapes of receptive

field profile at different delays were similar, indicating that the spatial filtering property does not change with time.

In contrast to the soma, horizontal cell axons failed to yield good-quality STRF, at least with the mean grain size employed in this experiment(maximum of mean grain size was about 500μm). The fluctuation responding to the TV snow noise was considerably smaller in axon than in soma, probably reflecting larger spatial summation area of axon compared with soma. On the other hand, the sustained deviation from the dark level was no much different between soma and axon.

Bipolar cells:

Whereas on-center bipolar cells depolarize and off-center ones hyperpolarize in response to the full field illumination (Naka and Ohtsuka, 1975), the responses of both types to the TV snow stimulation were random swings between hyperpolarization and depolarization around the resting dark potential level(Fig. 3.3). Unlike horizontal cells, the membrane voltage fluctuation of bipolar cells in response to the TV snow noise dominated that to the TV snow noise, indicating that bipolar cells predominantly encode the information about spatio-temporal changes of incident light. In off-center bipolar cells, the response waveform to the TV snow noise was quite binary like. In both on-center and off-center units, the peak-to-peak amplitude of membrane fluctuation did not change when the mean grain size of the TV noise was increased from 200 μm to 400 μm. In addition, the mean membrane potential was not affected by the mean grain size.

For both on-center and off-center bipolar cells, high-

fidelity STRF data were obtainable from records of 2-3min long with a mean grain size of 200 μm. The necessary recording duration seemed minimal in bipolar cells. Examples of STRF from on-center and off-center bipolar cells are shown in Fig. 3.6. The photograph in each frame represents the spatial pattern cell extracts from various spatial images impinged on the retina at each delay time. In the case of on-center bipolar cells, a center-brightening spatial pattern emerged at the delays of 60, 90, and 120 msec. On the other hand, off-center cells produced a set of center-dimming STRF patterns at the delays of 60, 90, and 120 msec. Thus, on-center cells are thought to detect center-brightening spatio-temporal patterns of light whereas off-center units extract center-dimming visual scenes. Although receptive field surround is not clearly recognized in the STRF data of Fig. 3.6, the classical test clearly indicated the presence of an antagonistic surround; cells which showed a center-brightening STRF depolarized in response to the field illumination whereas those with a center-dimming STRF hyperpolarized in response to the field light.

Fig. 3.7 shows some receptive field profiles of an off-center bipolar cell at different delays. The magnitude of receptive field center reached its maximal value at a delay of 60 msec and then monotonically decayed to the zero level. A similar time course was seen in on-center cells. In average, the delay time to the maximum STRF magnitude was about 65 msec in on-center cells and 50 msec in off-center cells. As shown in A3 and B3 of Fig. 3.7, the normalized receptive field profiles at

different delays had an almost identical spatial configuration, indicating that spatial filtering property of bipolar cells did not alter with the stimulus-referenced time. Fig. 3.8 is given to show that the receptive field shape of both bipolar cell types was circular at any delay time. The mean half width of the receptive field profile at a delay of 60 msec was 227±40 μm in on-center cells(N=15) and 183±24 μm in off-center cells (N=27)(Table 3.1). In each types of bipolar cells, the size and shape of receptive field were considerably similar.

Amacrine cells:

Amacrine cells of the catfish retina are classified into N(sustained) and C(transient) types according to their response patterns to a flash of light (Naka and Ohtsuka, 1975). Sustained amacrine cells fall into two sub-categories: TYPE NA cells (which show a sustained depolarization with initial oscillations to a step illumination) and TYPE NB cells (a sustained hyperpolarizing response to a step illumination and an oscillatory off-response). As shown in Fig. 3.3, TYPE NA cells responded noisily with a sustained depolarization to the TV snow noise stimulation. The fluctuating response contained oscillations and spike-like depolarizations. TYPE NB cells showed a sustained hyperpolarization with noisy fluctuation accompanied by spike-like oscillatory behavior similar to TYPE NA cells. In both TYPE NA and TYPE NB cells, the amplitude of fluctuation was enhanced by increasing the grain size of TV snow noise.

A mean grain size of 300 μm produced well-repeatable STRFs from both TYPE NA and NB cells. TV snow noise with a mean grain

size of less than 300 μm failed to yield good-fidelity STRF from TYPE N cells. Fig. 3.9 exemplifies the STRF of a TYPE NA cell (top rows) and that of a TYPE NB cell (middle row), demonstrating that the NA cell sees center-brightening spatio-temporal changes of light whereas the NB cell is tuned to center-dimming visual patterns. As was the case of bipolar cells, the surround was not, however, discernible in either type. The receptive fields of each type reached its maximal magnitude at a delay of 60 msec and then monotonically decayed to the zero level. STRF profiles of different TYPE NA and TYPE NB cells are shown in Fig. 3.10. In each of these cells, the horizontal profile was larger and more diversified compared with the vertical profile, indicating that the receptive field of sustained amacrine cells is somewhat elongated horizontally(Table 3.1). A vertically elongated receptive field was never found in either cell type. The mean delay time to the maximum STRF value was about 60msec in both types of amacrine cell. The temporal property of sustained amacrine cells of both types was similar to that of the horizontal cell soma.

Transient amacrine cells(TYPE C cells), which respond with a transient depolarization to the initiation and cessation of field illumination, responded to the TV snow noise with a normally distributed fluctuation superposed on a sustained depolarization(Fig. 3.3). When grain size of TV snow noise increased, the amplitude of fluctuating response increased without changing the sustained level of depolarization. The sustained depolarization disappeared when the TV frame was

frozen, suggesting that the sustained depolarization was caused by temporal changes of stimulus light. The fluctuating component was composed of a transient depolarization as observed in on-off response to step illumination. As shown in Fig. 3.9(bottom row), the cell showed a center-dimming receptive field at a delay of 60 msec. The STRF yielded its maximal value at 60 msec and then changed its polarity due to the appearance of a noisy center-brightening spatial pattern at delays of 120 and 150 msec. The half width of the receptive field profile at 60msec delay was about 200 μm(Table 3.1).

On-center ganglion cells:

Ganglion cells of the catfish retina are classified into on-center, off-center, and on-off cells (Naka and Ohtsuka, 1975). STRFs of on-center and off-center cells were examined here. On-center ganglion cells, which produce a burst of impulses followed by a maintained discharge during a field illmination, are classified into large-field and small-field cells on the basis of the spatial configurations of STRF.

Typically, each of these two types of on-center ganglion cells yielded the STRF as shown in Fig. 3.11; a small-field cell(upper row) and a large-field cell(lower row). At a delay of 60 msec(A1), the small-field cell 'sees' or most likely to responds to a center-brightening pattern against the background. At 120 and 150 msec delays, the receptive field was weaker than that of 60 msec delay. The STRF of the large-field cell is shown in Fig. 3.11(B1-B4), indicating that the STRF is elliptical with the long axis parallel to the naso-temporal axis of catfish. At

120 and 150 msec delays, clear receptive field was not discernible.

STRF profiles of on-center cells are shown in Fig. 3.12. The size of vertical profiles of receptive field of small-field cells was nearly the same as the large-field case whereas the average horizontal profile of large-field cells was about two times larger than that of small-field units(Table 3.2). Furthermore, polarity reversal of receptive field center was observed at a delay of 180msec. This observation indicates that the cell type in question is specialized in detecting a center-brightening or center-dimming pattern depending on the delay. In other words, spatial filtering characteristics seem to change as a function of the stimulus-referenced time. STRF results obtained by analog cross-correlation method(brighteness of TV monitor screen was modulated by the magnitude of the output of a spike counter with 30msec bin) were similar to those obtained by the trigger cross-correlation method. Consequently, the polarity change was not due to a methodological artifact. Moreover, it seemed that omission of the spikes that occurred successively within 30 msec after a triggered spike, did not have much effect on STRF measurements. In fact, both on- and off-center ganglion cells responded with an intermittent burst of discharges to TV snow noise.

Off-center ganglion cells:

Off-center ganglion cells can also be classified into two subtypes; small-field and large-field cells according to the receptive field properties. Fig. 3.13 shows STRF of a small-field cell(upper row) and that of a large-field cell(lower row). These

figures are thought to be most efficient in producing a spike discharge at each delay time. The small-field cell had a radially symmetrical dimming center at delays of 60, 90, 120 msec (A1-A3). At a delay of 150 msec, however, the cell showed center-brightening receptive field pattern. In contrast with the small-field cell, the large-field cell yielded an elliptical center-dimming pattern at delays of 60 and 90 msec. The receptive field of this unit changed its polarity at a delay of 120 msec before the decay to the dark level.

Fig. 3.14 shows STRF profiles of a small-field off-center cell. The receptive field had its maximal magnitude at a delay of 60 msec and then monotonically decayed. The receptive field reversed its polarity at a delay of 180msec. The normalized receptive field profiles at different delays were not as similar as in the case of bipolar cells.

Fig. 3.15 shows STRF profiles of five off-center small-field cells (A,B) and five large-field cells (C,D) at delays of 60,120, and 180 msec. Small-field cells showed a receptive field of circular or radially symmetrical shape, whereas large-field ones had an elliptical receptive field(Table 3.2). In either subtypes, however, the antagonistic surround was not discernible. At a delay of 120 msec, five small-field cells did not show reversed receptive field profiles(A, B) whereas two out of five large-field cells showed reversed receptive field profiles(C, D). At a delay of 180 msec, two small-field and four large-field cells showed reversed profiles. Such slight differences in temporal properties of two subtypes of off-center ganglion cells were

quantified in Fig. 3.16 by plotting the time-dependent receptive fields. Before the polarity reversal, the receptive field reached its maximum magnitude at about 40-60 msec delay in both subtypes. The polarity change took place around a delay of 110msec in large- field cells and 150 msec in small-field cells. The zero level was arrived at a delay of 200 msec in large-field cells whereas about 240 msec in small-field cells. These observations seem to indicate that large-field cells tend to respond better to the changing light than small-field cells.

Localized surround of ganglion cells:

The TV noise method revealed that about 10% out of the ganglion cells had localized spots of the antagonistic receptive field surround(Table 3.2). No such localized surround was found in bipolar cells and amacrine cells. Three examples of such receptive fields are shown in Fig. 3.17; two off-center cells(A and B) and one on-center cell(C). As these figures show, surrounds are not uniformly distributed but localized. Size of localized spots of surround was similar or smaller than center size. In each case, the center and localized surrounds reached their peak magnitude at the same value of delay time and the surrounds never reversed the polarity. Also, the position of each localized surround did not change.

Spatio-temporal coupling properties of horizontal cells and ganglion cells:

Whether retinal neurons interact or behave independently in time and space is a important problem to understand the visual information mechanism including central visual system (Burbeck

and Kelly, 1980; Enroth-Cugell et al. 1983; Dawis, et al. 1984). Spatio-temporal interactions within the receptive field were assessed by examining the STRF as a function of the spatial parameter(grain size) of the TV noise. If the temporal property changes with this parameter, then the cell is thought to have a space-time coupling property. The experiments were carried out on horizontal cell somata and ganglion cells. Coarse and fine random noise were used with the same mean intensity. The coarse random noise was magnification of the fine one by a factor of four(Fig. 3.1).

Fig. 3.18 shows some results from horizontal cells delineated by plotting the peak amplitude of the receptive field profile at successive delay times. Twenty somata examined showed a nearly identical temporal pattern for the coarse and fine tests, indicating that spatial and temporal properties behaved independently. On the other hand, the spatio-temporal coupling was found in five cells out of fourteen off-center ganglion cells. Fig. 3.19 shows temporal properties of a large-field(A) and a small-field cell(B). In A, the delay to the initial peak was about 35 msec with the coarse noise and 55 msec with the fine noise. Furthermore, the delay to the polarity change with the coarse noise was 20 msec shorter than in the fine case. Such differences were also found in B where the temporal property obeyed a monophasic time course for fine noise, and it was biphasic with a faster time course when the coarse noise was given. In contrast, on-center ganglion cells did not show such space-time coupling as apparent from Fig. 3.19C.

Discussion:

Comparison of spatio-temporal receptive field in catfish retinal neurons:

Spatio-temporal filtering properties of catfish retinal neurons changed from distal to proximal neurons in time and space. First of all, the STRF structures of neurons are more diversified than STRFs of distal neurons; receptive fields of horizontal and bipolar cells are fairly stereotyped being radially symmetric whereas those of amacrine and ganglion cells tend to be diversified in size and shape. This aspect also has been reported in the receptive field analysis using a moving slit of light or one-dimensional random grating (Davis and Naka, 1980; Powers and Arnett, 1981; Lasater, 1982). The less stereotyped STRF profiles of proximal cells may reflect that these cells engage in more complex and sophisticated information processing than do distal neurons. Perhaps, the complexity of proximal cells in spatial organization is due to the convergence of signal pathways from bipolar to amacrine cells and also to ganglion cells. The sustained amacrine cells with the horizontally elongated STRF pattern(Fig. 3.9, Fig. 3.10) may correspond to the TYPE NB amacrine cells which respond preferentially to a vertically moving object (Naka, 1980).

The temporal feature also changes along the retinal pathway from interneurons to ganglion cells. In this regard, only ganglion cells unequivocally showed the time-dependent polarity reversal of receptive field(Fig. 3.12, Fig. 3.13). The polarity reversal in ganglion cells may well arise from the signal

transmission from bipolar to ganglion cells. This synaptic transfer presumably involves amacrine cells as well and this aspect may very well play a crucial role in giving rise to the polarity reversal in the temporal STRF pattern of ganglion cells (Wunk and Werblin, 1979; Belgum et al., 1982). It is interesting to note that the temporal property was different in amacrine cells and ganglion cells though both receive signals from bipolar cells.

Antagonistic receptive field surrounds of bipolar and ganglion cells were very small or not discernible according to the present method based on TV snow noise stimulation. This negative result does not necessarily mean the absence of surround mechanisms in bipolar and ganglion cells in catfish retina. As already mentioned in the Materials and Methods, mean illuminance level of TV snow noise is identical everywhere within the stimulus area. Horizontal cells are thought to form the receptive field surround of bipolar and ganglion cells (Dowling and Werblin, 1969; Kaneko, 1970; Naka and Nye, 1970). To TV snow noise, horizontal cells showed a large hyperpolarizing response with small fluctuation presumably by large spatial summation property(Fig. 3.3). Therefore, surround signals in bipolar and ganglion cells are thought to contain very small response component to the changes of light. Thus, very faint surrounds seem to be revealed by TV snow noise.

Two types of ganglion cells:

On-center and off-center ganglion cells of the catfish retina are each divided into two subtypes; small-field and

large-field cells (Davis and Naka, 1980; Lasater, 1982). Small-field cells had a circular-shaped receptive field whereas large-field units had a horizontally-elongated receptive field whose size in the horizontal direction was about twice that of small-field cells(Table 3.2). This observation appears to be consistent with the earlier analysis using a moving slit of light (Davis and Naka, 1980) or one-dimensional random grating (Lasater, 1982).

Ganglion cells of mammalian retina are classified into X-, Y-, and W-cells according to their functional properties (Enroth-Cugell and Robson, 1966; DeMonasterio, 1978; Stone et al., 1979). It was reported that the receptive field size of X-cells was smaller than that of Y-cells(Enroth-Cugell and Robson, 1966; Cleland and Levick, 1974; Stone and Fukada, 1974), and that X-cells showed a sustained response whereas Y-cells transient response to a step change of illumination(Cleland et al., 1971; Fukada, 1971). In addition, Y-cells show a nonlinear spatio-temporal property but X-cells do not (Enroth-Cugell and Robson, 1966; Hochstein and Shapley, 1976; Victor and Shapley, 1979). In retinas of non-mammalian species(e. g., eel, goldfish, and mudpuppy) X-like and Y-like cells have been described with the linear(X) and nonlinear(Y) spatial summation properties (Shapley and Gordon, 1978; Levine and Shefner; 1979, Tuttle and Scott; 1979). The distinctions in spatio-temporal properties of catfish ganglion cells may be analogous to the well-established functional distinctions of X- and Y-cells in mammalian retinas.
The localization of receptive field surround:

In catfish retina, about 10% of ganglion cells showed

conspicuous localized surround or "hot spot". Localization of receptive field surrounds was first reported in cat retinal ganglion cells(Rodieck and Stone, 1965b). The spatially inhomogeneous receptive field surround of X-cells in the lateral geniculate nucleus of cat is thought to cause spatio-temporal interactions in the cellular processing of visual signal(Dawis et al., 1984). It is important to note that localized surrounds were found in this study in both large-field and small-field cells(Table 3.2).

Spatio-temporal coupling properties of ganglion cells:

One striking property in catfish ganglion cells was that the temporal property of STRF depended on the grain size of TV snow noise. This observation indicates the presence of space-time signal interactions in ganglion cells. In contrast, the horizontal cells never showed such dependence on the noise size. The space-time signal interaction of cat retinal ganglion cells has been analysed elsewhere by the use of sine-wave grating (Derrington and Lennie, 1982; Enroth-Cugell et al., 1983; Dawis et al., 1984). Derrington and Lennie reported that the spatial contrast sensitivity of both X-cells and Y-cells changed from a bandpass characteristics to a lowpass characteristics with increase of the temporal frequency of the sinusoidal gratings. Enroth-Cugell et al. showed that the spatial frequency responsivity function of X-cells depended on the temporal frequency of the grating and that the temporal phase of their response measured at every constant temporal frequency depended on the spatial frequency of the stimulus. Furthermore, they

explained the spatio-temporal interactions by the mechanism in which the surround signal was delayed relative to the center signal by a few millisecond. In the present study, whether the spatio-temporal interaction of catfish ganglion cells was caused by the delayed mechanism suggested by Enroth-Cugell et al.,is not certain because of the poor temporal resolution as well as of the difficulty in finding clear surround mechanism. However, the spatio-temporal interaction of teleost ganglion cells found in this study may suggest the existence of a common mechanism underlying spatio-temporal interactions in retinas of different species.

According to human psychophysical studies, the contrast sensitivity measurement by sinusoidal gratings shows a spatio-temporal interaction (Robson, 1966; Van Nes et al., 1967; Kelly, 1972, 1979). In this regard, Kelly's spatio-temporal resolution limit diagram demonstrates that the spatial resolution of the visual system deteriorates with increase of the temporal frequencies and vice versa. Suppose that the spatio-temporal properties of catfish ganglion cells obey the foregoing diagram, then the result shown in Fig. 3.19 can be interpreted as follows. If the grain size of TV snow noise is decreased, the response component that reduces the time resolution will be enhanced. Therefore, the temporal property showed slower lowpass filtering characteristics with the fine TV snow-noise stimulation whereas the ganglion cells act as a temporal bandpass filter with a coarse noise(Fig. 3.19). It is not, however, possible to explain why some off-center and on-center ganglion cells have the

same temporal property irrespective of the grain size of TV snow noise. It may result from the poor temporal resolution of TV snow noise(about 30 msec). Also, it is conceivable that a certain group of ganglion cells have a spatio-temporal coupling property, and another class have a space-time separating property as is the case of horizontal cells. A more elaborate analysis is required in this respect.

Advantages underlying the measurement of spatio-temporal receptive field by spatio-temporal random noise:

Spatio-temporal random noise used in this study stimulates a retinal area far broader than the receptive field area of the neuron under study. The cross-correlation between the spatio-temporal random noise and the resulting response allows one to estimate the STRF of single cells without having any a priori knowledge about the receptive field property. Another approach to the STRF measurement is to map out each location-dependent response time course to a flashing small spot of light which successively illuminates various point over the retinal surface (Stevens and Gerstein, 1976; Stein et al., 1983).

In the former approach one can manage to obtain STRF with a shorter time of recording. This property permits quick STRF identification without being interfered with by visual adaptation. Therefore, the cross-correlation approach is particularly suitable for cells such as bipolar and amacrine cells which rarely withstand long stable recording. Through the process of cross-correlation, spatio-temporal patterns are selected which are most effective in producing the cellular

response. We used TV snow noise as stimulus light and the photographic procedure for the two-dimensional cross-correlation. Thus, no computer system was required in this entire project although photographs representing STRF spatial patterns were often processed for quantitative analysis.

Figure Legends:

Fig. 3.1: Schematic diagram of the system to measure spatio-temporal receptive fields(STRF) of ganglion cells. A sample of spatio-temporal random noise was stored on the video channel of a video tape by recording through a TV camera "snow noise" on an unused TV channel. The tape was played back to display the TV snow noise on a picture monitor. The spatio-temporal random pattern of TV noise was then imaged on the retina of the eye cup preparation. Insets, A and B are examples of TV snow noise pattern; pattern A was a magnification of pattern B by a factor of four. Spike discharges of the ganglion cell responding to this stimulus were recorded on the audio channel of the tape where TV snow noise had been prerecorded. The grain size of the TV snow noise was adjusted by changing the distance between the picture monitor and the mirror. STRF patterns were obtained by cross-correlating the TV snow noise stimulus and the response spikes. To cross-correlate TV frames with spike events, the video tape was played backward. Then, the video signal(TV snow noise) and the audio signal(spikes) were fed into a video sample-and-hold circuit and a digital-delay circuit, respectively. A spike event held a TV frame for 30msec. A long-exposure film(H & W Control; H & W) in the camera in front of the monitor screen accumulated those TV frames which had elicited the spikes.

Fig. 3.2: Schematic illustration of the trigger cross-correlation method. Trigger cross-correlation operated to summate the input signal(TV snow noise frames) by the triggering signal of output(spikes), so that a long-exposure film in front of a

picture monitor accumulated the TV frames that were brightened during 30 msec soon after the spike occurred(A). Followed by the experiment, the video singals(TV snow noise) and the audio signals(elicited spikes) were recorded in the video tape like the left scheme of B. (1)-(7) indicate the sequential numbers assigned to the successive frames. After playing backward the video tape and concurrently passing the spikes through the delay circuit, the stimulus(TV frames) and the resulting response(spikes) were arranged in parallel(B, right).

Fig. 3.3: Responses of catfish retinal interneurons(horizontal cell's somata, bipolar cells, and amacrine cells) to the TV snow noise of two kinds of the grain size(fine and coarse noises). The mean grain size of the fine noise was about 200 μm and the coarse noise was magnification of the fine noise by a factor of four. Horizontal cell soma showed a large sustained hyperpolarization with small fluctuations which became more prominent when the grain size of TV snow noise was enlarged. In contrast with horizontal cells, both on-center and off-center bipolar cells responded with binary-noise-like fashion around the dark level. The response amplitude did not change with increase of the grain size. Note that response waveforms were considerably similar in on-center and off-center cells. Amacrine cells showed complex response waveforms to the TV snow noise stimulation. TYPE NA cells showed a sustained depolarization with occasional oscillations and spike-like waveforms. With enlargement of the grain size, oscillations and spike like responses prominently appeared. TYPE NB cells hyperpolarized accompanied by small

oscillations and spike like activities. Unlike TYPE NA cells, the amplitude and frequency of occurrence of oscillations were smaller than TYPE NA cells. In both TYPE NA and TYPE NB cells, the sustained polarization level from the dark resting level did not change with the grain size of TV snow noise. TYPE C cells showed a sustained depolarization with a fluctuating component. With enlargement of the grain size, the amplitude of fluctuation increased without changing the sustaining depolarization level. Response-amplitude distribution is shown on right hand of each response trace. Scale of 10 mV is for the horizontal cell soma.

Fig. 3.4: A photographically obtained STRF of a horizontal cell soma. 1-4 show the receptive field at delays of 60, 90, 120, and 150 msec, respectively. Calibration: 1.0 mm.

Fig. 3.5: A digitized representation of the STRF of a horizontal cell soma showing its time-varing receptive field profile. A1-A4 are the horizontal profiles at delays of 60, 90, 120, and 150msec, respectively. Downward deflection corresponds to dimming of the receptive field. The horizontal axis coincides with the naso-temporal axis of the catfish. B1-B4 are the vertical profiles of the same set of delays. The results from three units are superposed.

Fig. 3.6: STRFs of two bipolar cells photographically obtained by the TV noise stimulation; an on-center cell(upper row) and an off-center cell(lower row). (A1,B1)-(A4,B4) were taken at delays of 60, 90, 120, and 150msec, respectively. Calibration: 0.5mm.

Fig. 3.7: STRF profiles of an off-center bipolar cell; horizontal(A1) and vertical(B1) profiles at delay times from

30msec to 210msec of 30msec steps. Downward deflection corresponds to dimming of the receptive field. The horizontal(A2) and vertical(B2) profiles at five different delays(30-150msec) are superposed. Also, the horizontal(A3) and vertical(B3) patterns were each normalized and superposed at four different delays.

Fig. 3.8: STRF profiles of bipolar cells. Horizontal(A) and vertical(B) profiles from five on-center bipolar cells. Horizontal(C) and vertical(D) profiles from five off-center cells. 1-3 denote delays of 60,120, and 180msec respectively. Both on-center and off-center cells show receptive field profiles of similar size. The antagonistic surround is not discernible in any of these profiles.

Fig. 3.9: STRFs of amacrine cells photographically obtained through the TV noise stimulation; TYPE NA(A), TYPE NB(B), and TYPE C(C) amacrine cells. 1-4 indicate delays of 60, 90, 120,and 150 msec, respectively. In the TYPE NA and TYPE NB cells, the magnitude of the receptive field reached its peak at a delay of 60msec and then monotonically decayed to the dark level without polarity change. The receptive field of the TYPE NB cell had horizontally elongated shape as was the case of large-field ganglion cells(cf. Fig. 3.13). The TYPE C cell showed an irregular receptive field accompanied by a polarity change(C4). Calibration: 1mm.

Fig. 3.10: Receptive field profiles of four TYPE NA(A1-A3,B1-B3) and four TYPE NB(C1-C3,D1-D3)amacrine cells. Horizontal and vertical profiles are shown in (A1-A3, C1-C3) and in (B1-B3, D1-

D3), respectively. 1-3 indicate delays of 60,120, and 180msec, respectively. No antagonistic surround was clearly found in either TYPE NA or TYPE NB cells at any delay. These profiles of both TYPE NA and TYPA NB cells were very similar in size and in shape to those of large-field ganglion cells(cf. Fig. 3.13).

Fig. 3.11: STRFs from on-center ganglion cells; small-field cell(A) and from large-field cell(B). 1-4 denote delays 60,90,120, and 150msec, respectively. These pictures demonstrate visual patterns the cell is likely to produce spikes after a given delay. Calibration: 0.5mm.

Fig. 3.12: STRF profiles of on-center ganglion cells; horizontal(A) and vertical(B) profiles of five cells composed of small-field and large-field cells. 1-3 signifies delays of 60, 120, and 180msec, respectively.

Fig. 3.13: STRFs of off-center ganglion cells; a small-field(upper row) and a large-field cell(lower row). 1-4 indicate delay times of 60, 90, 120, and 150msec, respectively. Small-field and large-field cells seem to extract circular and elliptical spatial configurations, respectively. A polarity change occurred at a delay of 120msec in the large-field cell at 150msec in the small-field cell. Calibration: 0.5mm.

Fig. 3.14: STRF profiles of a small-field off-center ganglion cell; horizontal(A1) and vertical(B1) profiles at delay times of 30msec to 210msec of 30msec steps. The STRF magnitude took its maximal value at a delay of 60msec and then monotonically decayed. A polarity change occurred at a delay of 180msec. A2 and B2 are superpositions of the profiles of A1 and of B1,

respectively. The normalized receptive fields at delays of 60, 90, 120, and 180msec are superposed in A3(horizontal profiles) and B3(vertical profiles).

Fig. 3.15: STRF profiles of small-field and large-field off-center ganglion cells. The profiles of five cells are superposed at delays of 60,120, and 180msec(1,2,3). (A1,A2,A3) and (B1,B2,B3) are horizontal and vertical profiles of small-field cells, respectively. (C1,C2,C3) and (D1,D2,D3) are horizontal and vertical profiles of large-field cells, respectively. The receptive fields of small-field cells were radially symmetrical (A, B) whereas those of large-field cells were elongated horizontally(C, D). No small-field cell underwent a polarity change before a delay of 120msec(A2,B2), whereas two large-field cells, made a polarity reversal in the receptive field center(C2,D2).

Fig. 3.16: Temporal properties of large-field(A) and small-field(B) off-center ganglion cells. These graphs were obtained by averaging the response time course delineated by plotting the peak magnitude of receptive fields at successive delays(fifteen large-field cells; twenty-one small-field cells). The latency to the peak of the graph was about 40msec in large-field cells and was about 55msec in small-field units. A polarity change of the graph appeared around a delay of 110msec in large-field cells and 150msec in small-field cells.

Fig. 3.17: Three examples of STRF with non-concentrically localized surrounds or hot spots; two off-center cells(A, B) and an on-center cell(C). A dark center and bright islands(A, B), and

a bright center surrounded by a dark region(C). In all cases the surrounds were smaller in size than the receptive field center. These three patterns are thought to be most efficient in producing a spike discharge 60 msec later. Calibration: 0.5 mm.

Fig. 3.18: Temporal properties of horizontal cell somata(A, B, C) ;coarse(●) and fine(o) TV snow noise with the relative grain size being ● :o =4:1. Unlike off-center ganglion cells(Fig. 3.19), horizontal cells' temporal property did not depend on the grain size of TV snow noise.

Fig. 3.19: Dependence of temporal properties of ganglion cells on the grain size of TV snow noise; two off-center cells(A, B) and one on-center cell(C). The size ratio of coarse(●) and fine noise(o) is 4:1. Temporal properties of the off-center ganglion cells to coarse noise is more band-passed with coarse noise than fine noise(A). In B, the polarity change occurred with coarse noise but not with fine noise. In on-center ganglion cells, such dependence of temporal properties on the grain zise of TV snow noise was not found(e.g., C).

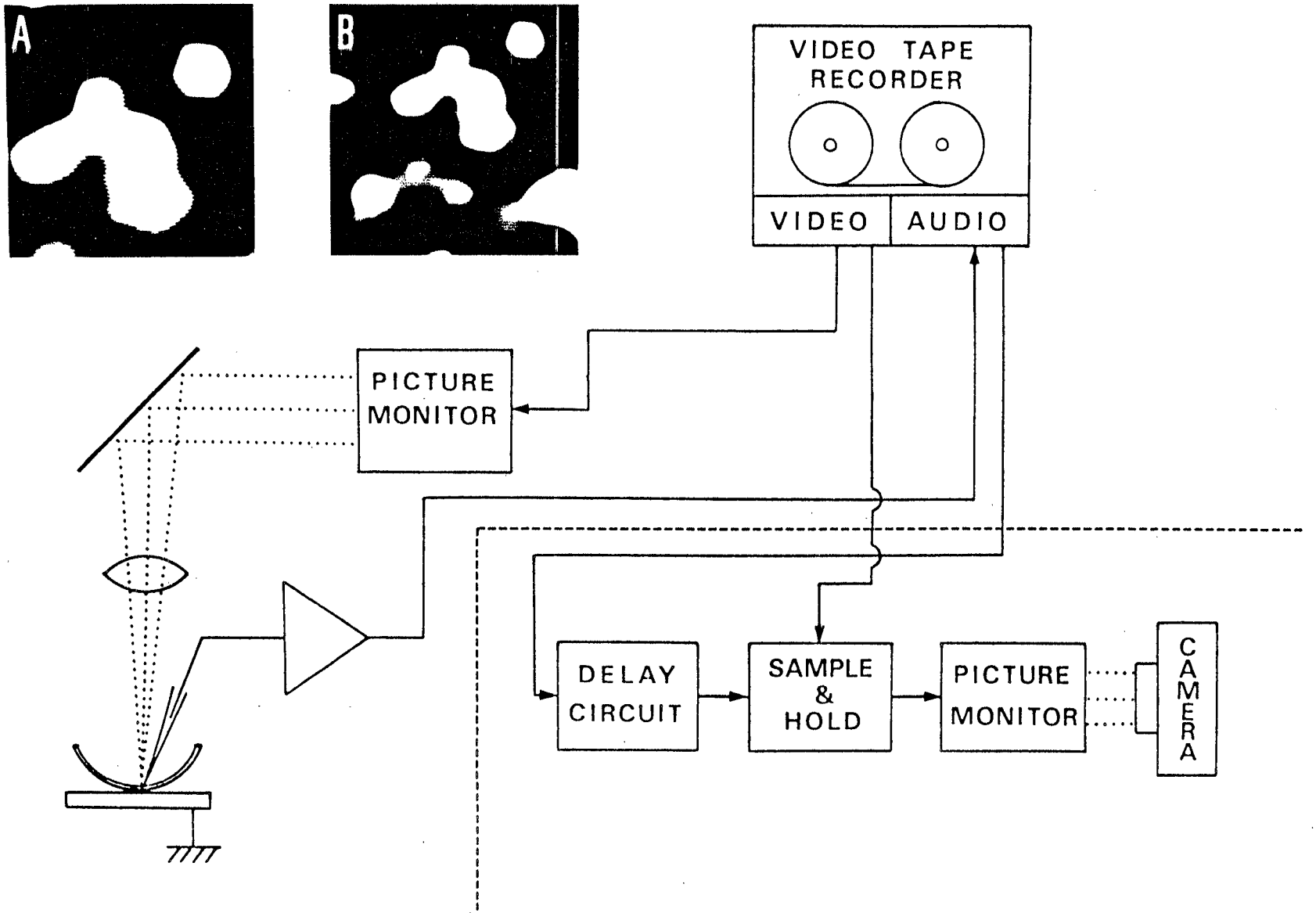
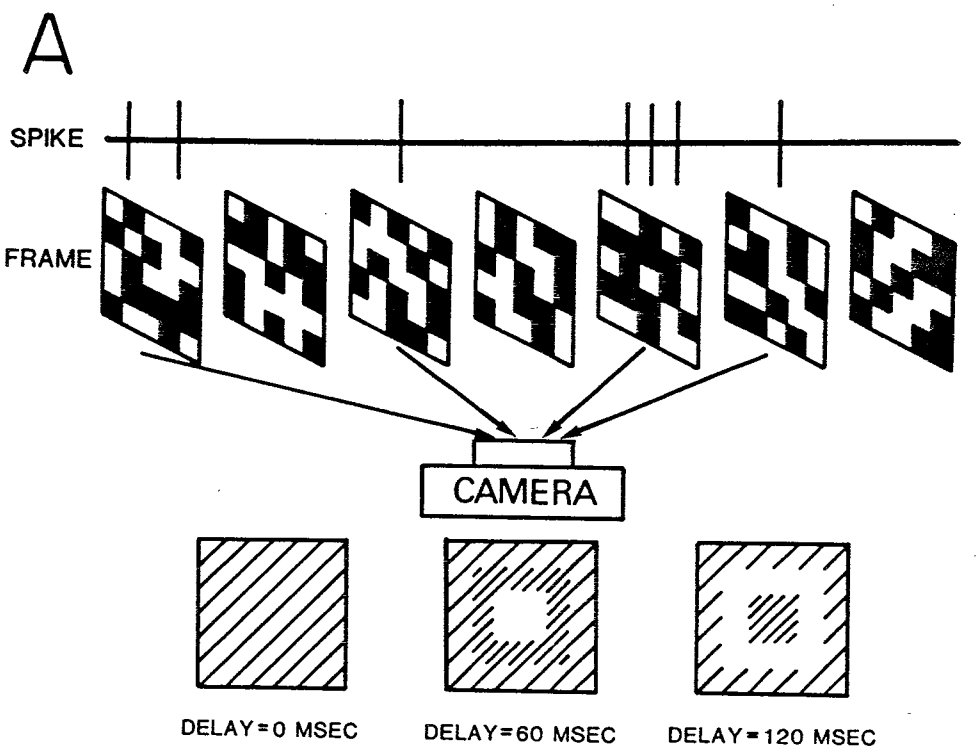

A
B
VIDEO TAPE RECORDER
VIDEO
AUDIO
PICTURE MONITOR
DELAY CIRCUIT
SAMPLE & HOLD
PICTURE MONITOR
CAMERA

Fig. 3.1


A
SPIKE
FRAME
CAMERA
DELAY=0 MSEC
DELAY=60 MSEC
DELAY=120 MSEC

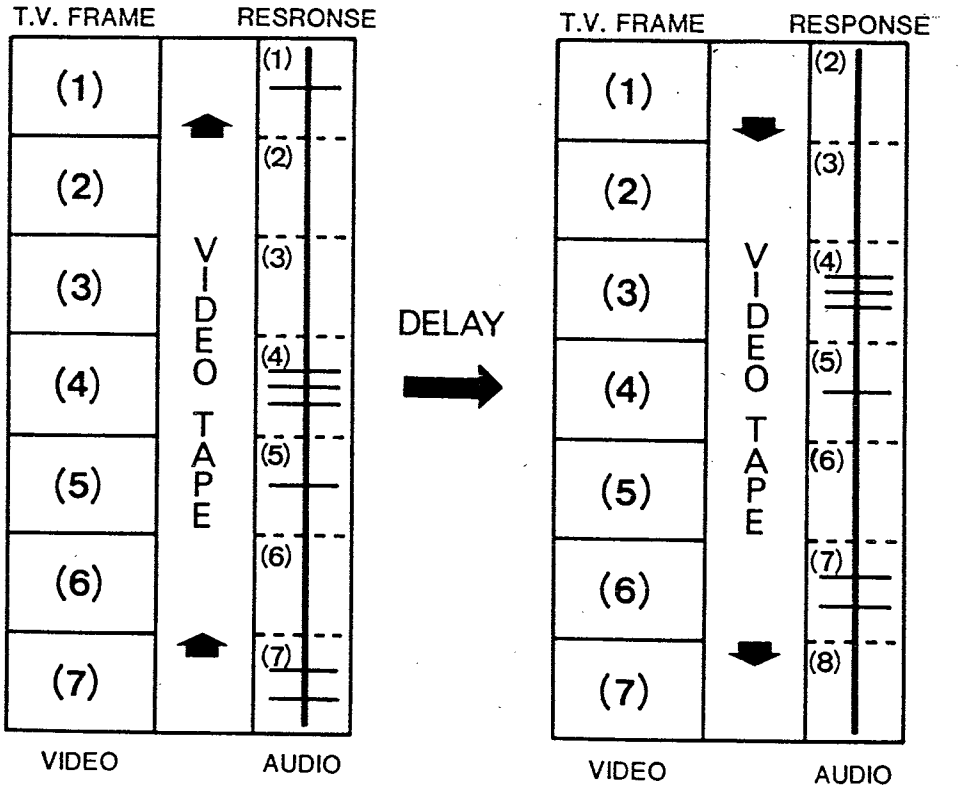

B
T.V. FRAME
RESRONSE
(1)
(2)
(3)
(4)
(5)
(6)
(7)
VIDEO TAPE
VIDEO
AUDIO
DELAY
T.V. FRAME
RESPONSE
(1)
(2)
(3)
(4)
(5)
(6)
(7)
(8)
VIDEO TAPE
VIDEO
AUDIO

Fig. 3.2

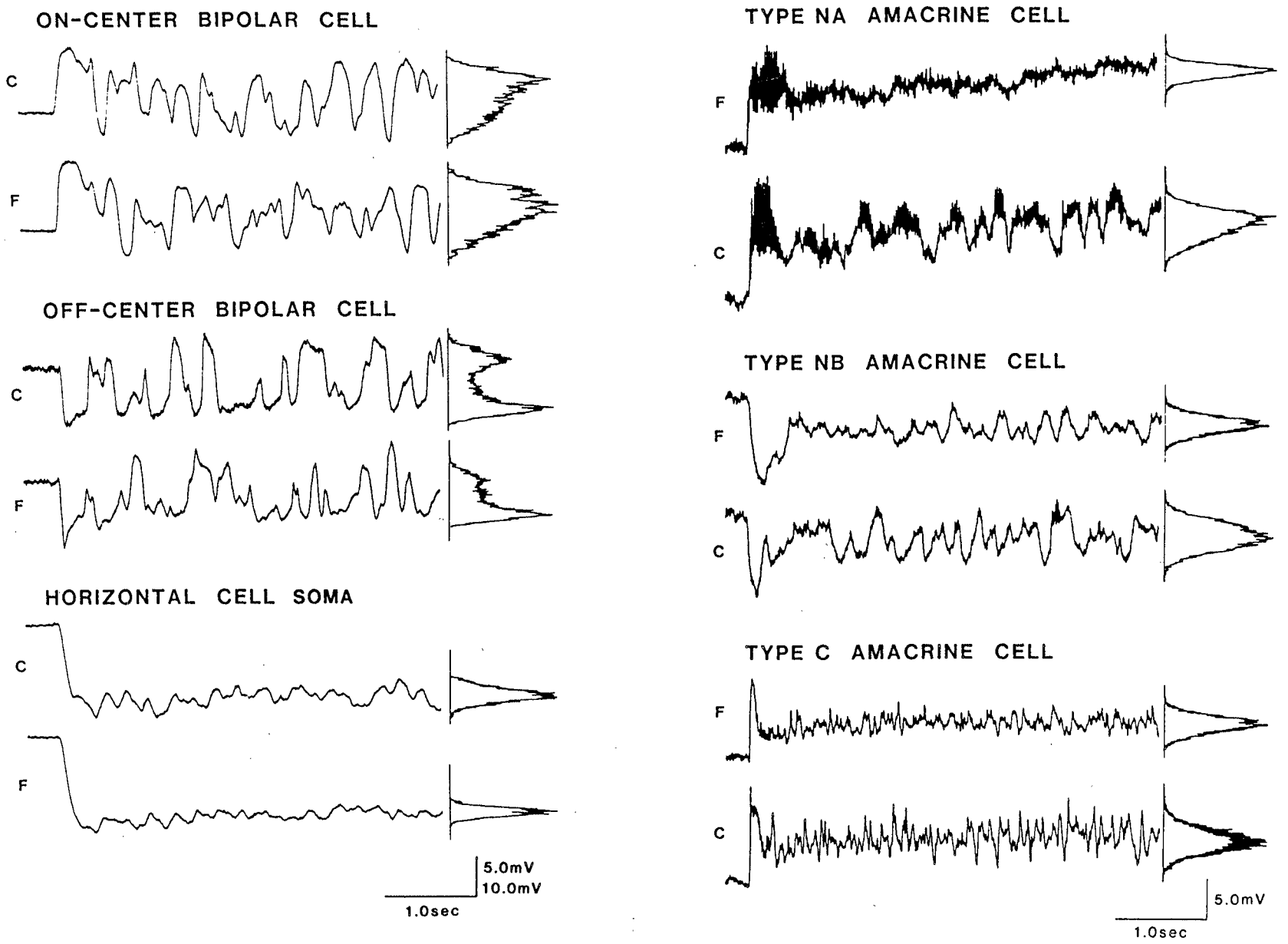

ON-CENTER BIPOLAR CELL
C
F
OFF-CENTER BIPOLAR CELL
C
F
HORIZONTAL CELL SOMA
C
F
5.0mV
10.0mV
1.0sec
TYPE NA AMACRINE CELL
F
C
TYPE NB AMACRINE CELL
F
C
TYPE C AMACRINE CELL
F
C
5.0mV
1.0sec

Fig. 3.3

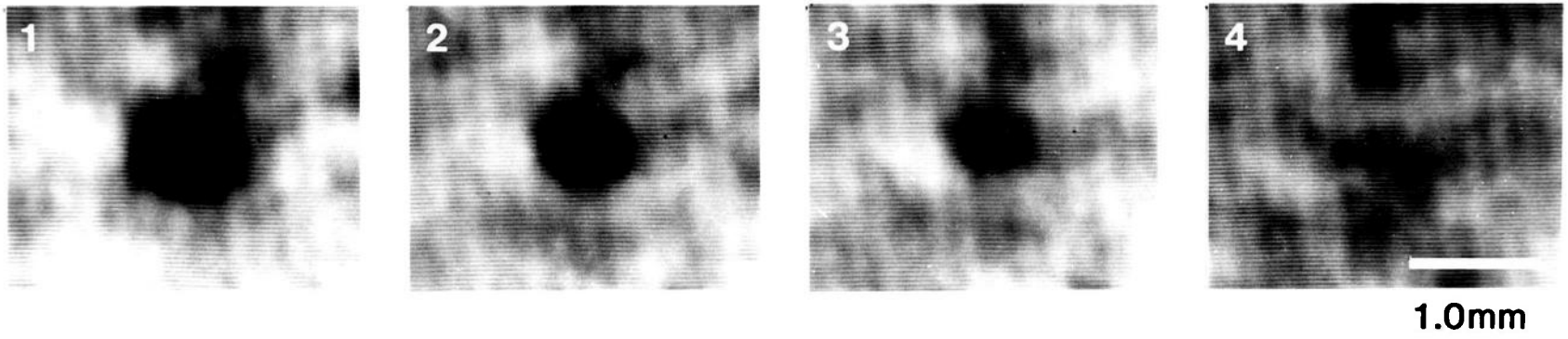

HORIZONTAL CELL SOMA
1
2
3
4
1.0mm
DELAY TIME
60msec
90msec
120msec
150msec

Fig. 3.4

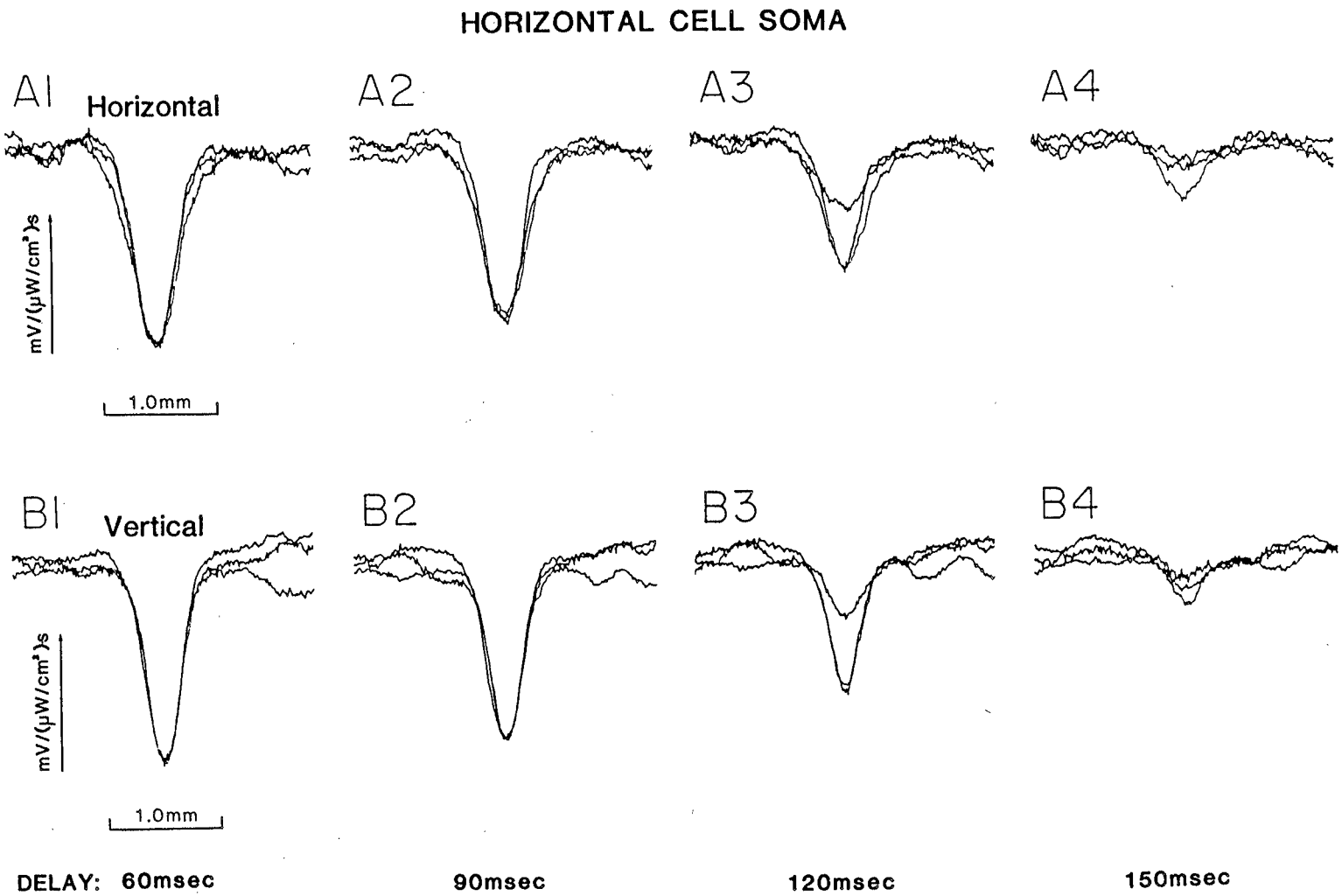

HORIZONTAL CELL SOMA
A1
Horizontal
A2
A3
A4
mV/(μW/cm²)s
1.0mm
B1
Vertical
B2
B3
B4
mV/(μW/cm²)s
1.0mm
DELAY: 60msec
90msec
120msec
150msec

Fig. 3.5

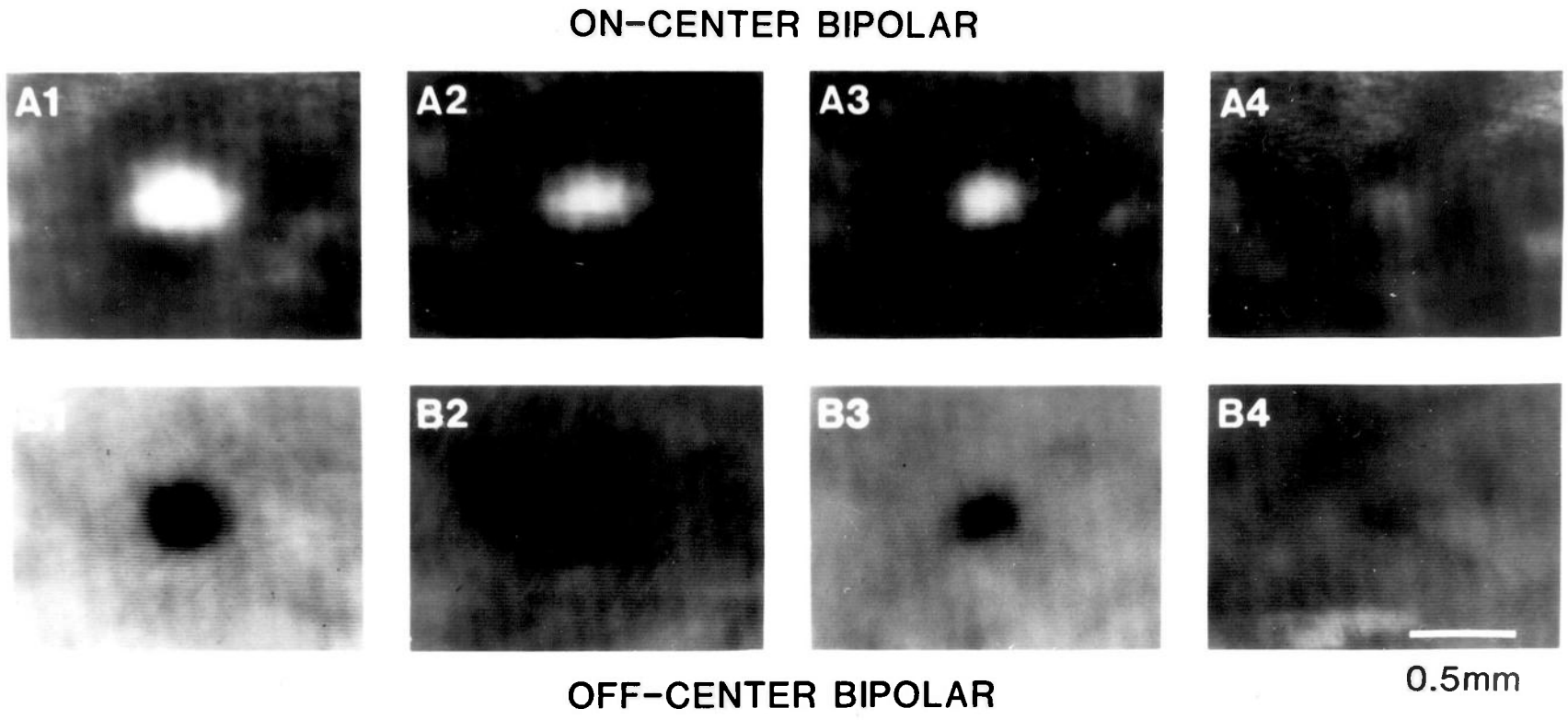

ON-CENTER BIPOLAR
A1
A2
A3
A4
B2
B3
B4
0.5mm
OFF-CENTER BIPOLAR
DELAY TIME
60msec
90msec
120msec
150msec

Fig. 3.6

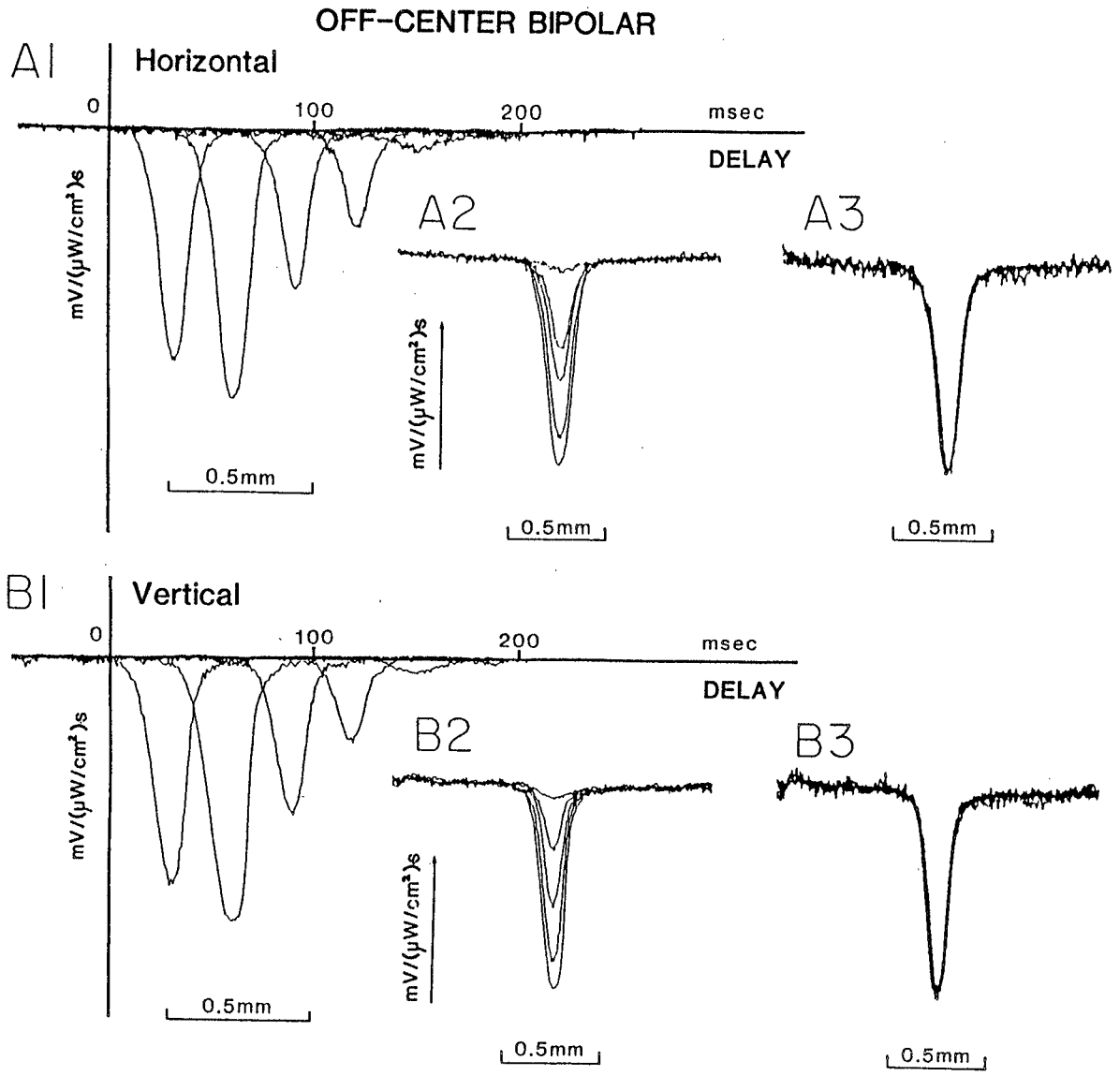

OFF-CENTER BIPOLAR
A1
Horizontal
0
100
200
msec
DELAY
mV/(μW/cm²)s
0.5mm
A2
mV/(μW/cm²)s
0.5mm
A3
0.5mm
B1
Vertical
0
100
200
msec
DELAY
mV/(μW/cm²)s
0.5mm
B2
mV/(μW/cm²)s
0.5mm
B3
0.5mm

Fig. 3.7

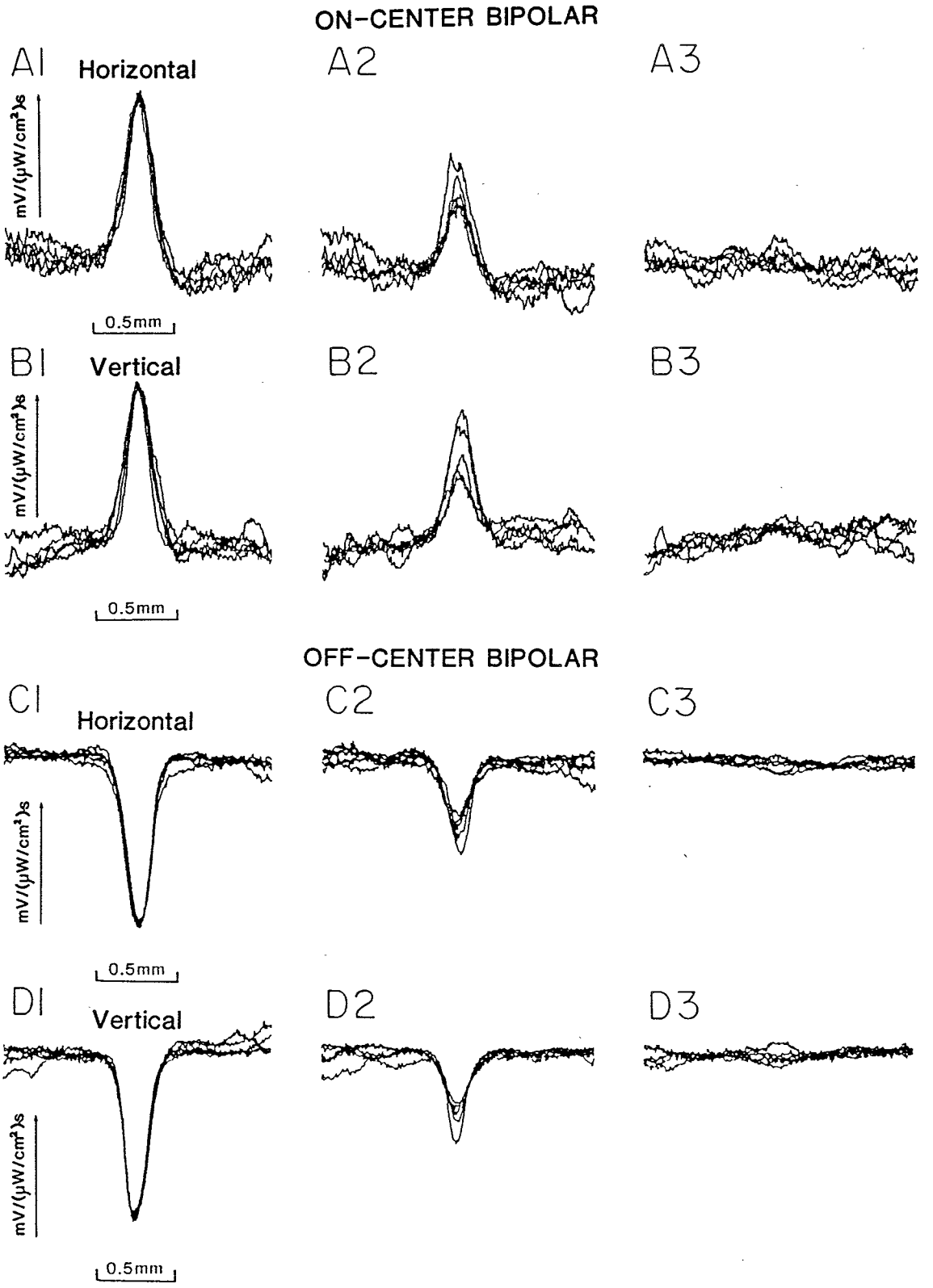

ON-CENTER BIPOLAR
A1
Horizontal
A2
A3
mV/(μW/cm²)s
0.5mm
B1
Vertical
B2
B3
mV/(μW/cm²)s
0.5mm
OFF-CENTER BIPOLAR
C1
Horizontal
C2
C3
mV/(μW/cm²)s
0.5mm
D1
Vertical
D2
D3
mV/(μW/cm²)s
0.5mm
DELAY: 60msec
120msec
180msec

Fig. 3.8

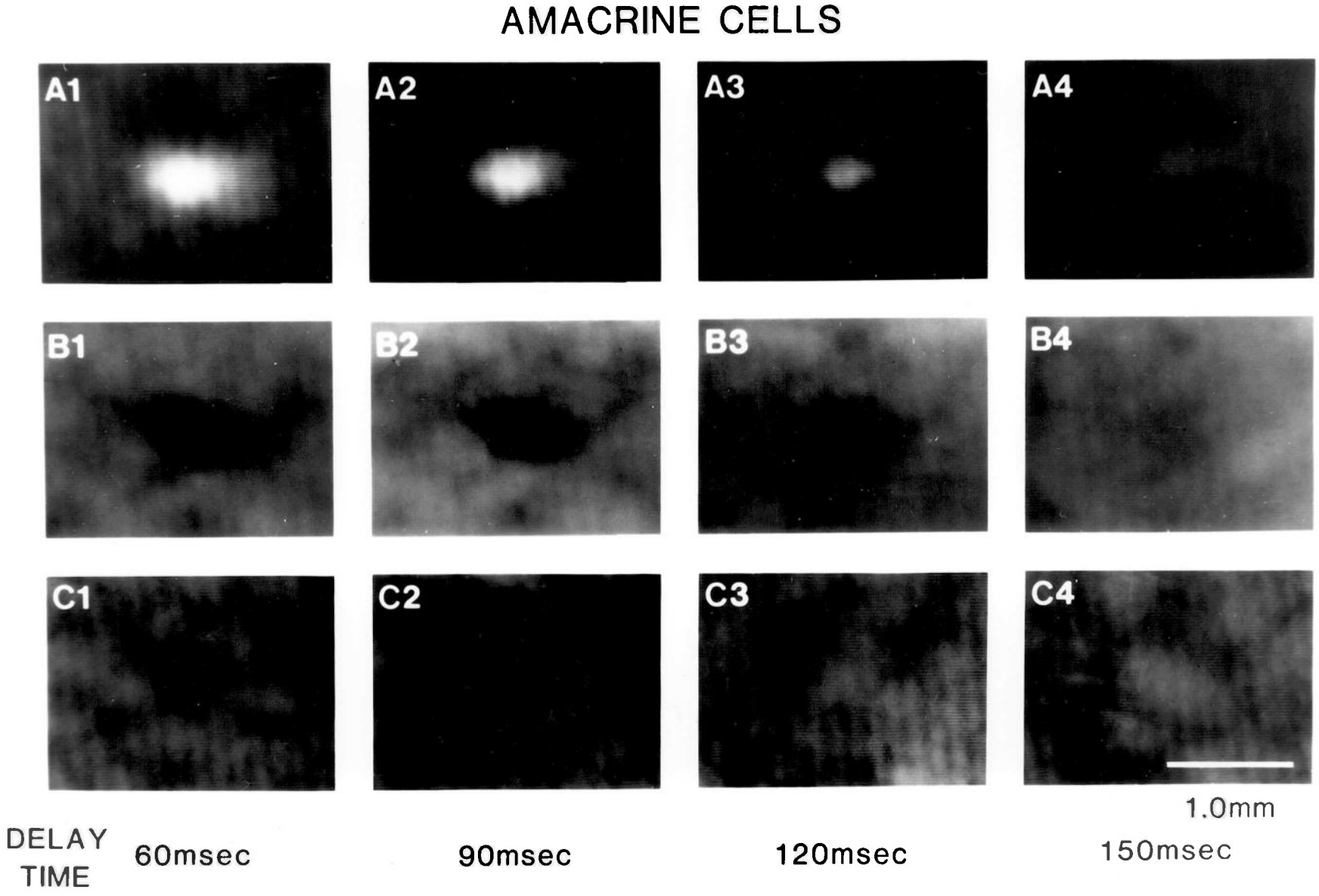

AMACRINE CELLS
A1
A2
A3
A4
B1
B2
B3
B4
C1
C2
C3
C4
1.0mm
DELAY TIME
60msec
90msec
120msec
150msec

Fig. 3.9

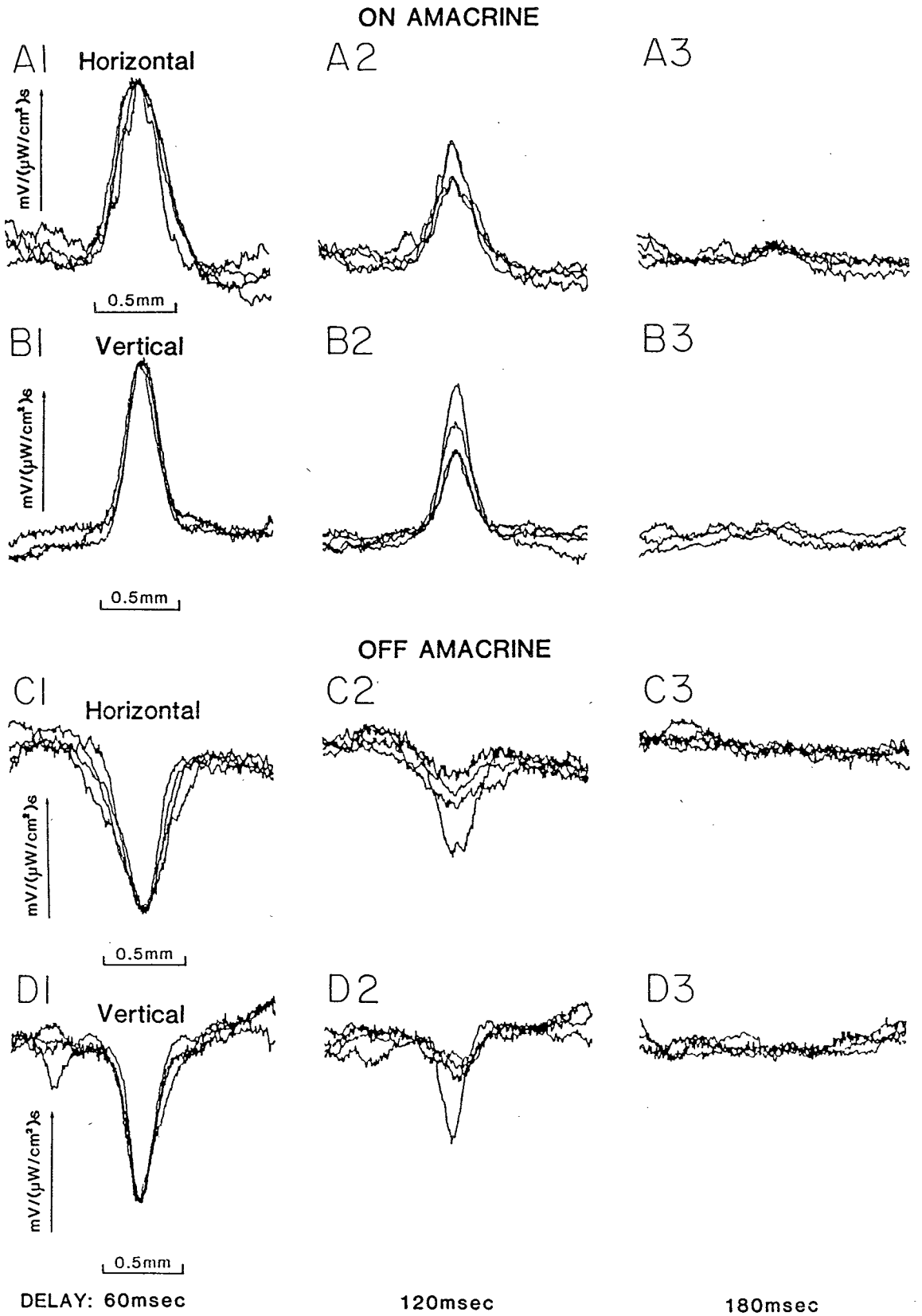

ON AMACRINE
A1
Horizontal
A2
A3
mV/(μW/cm²)s
0.5mm
B1
Vertical
B2
B3
mV/(μW/cm²)s
0.5mm
OFF AMACRINE
C1
Horizontal
C2
C3
mV/(μW/cm²)s
0.5mm
D1
Vertical
D2
D3
mV/(μW/cm²)s
0.5mm
DELAY: 60msec
120msec
180msec

Fig. 3.10

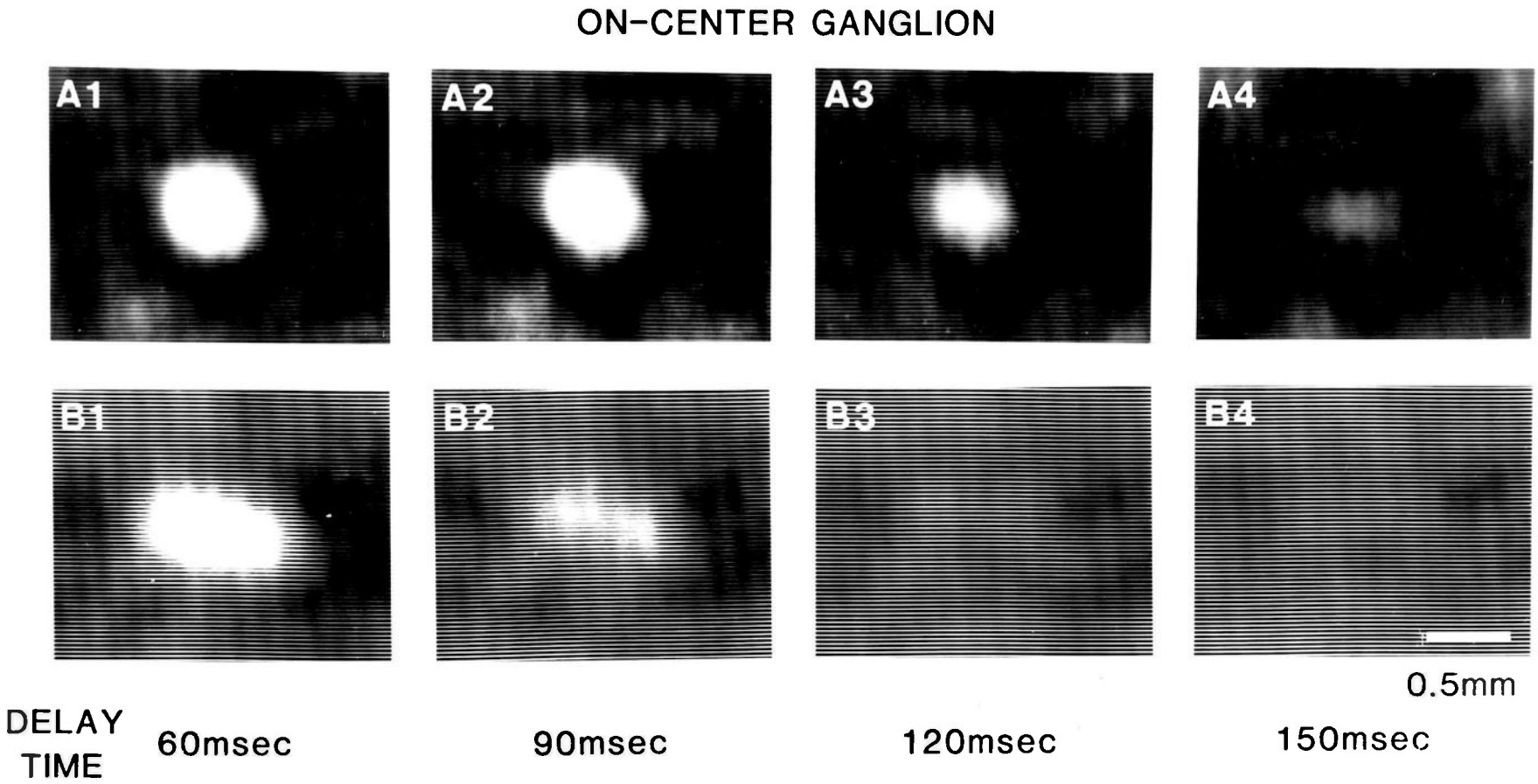

ON-CENTER GANGLION
A1
A2
A3
A4
B1
B2
B3
B4
0.5mm
DELAY TIME
60msec
90msec
120msec
150msec

Fig. 3.11

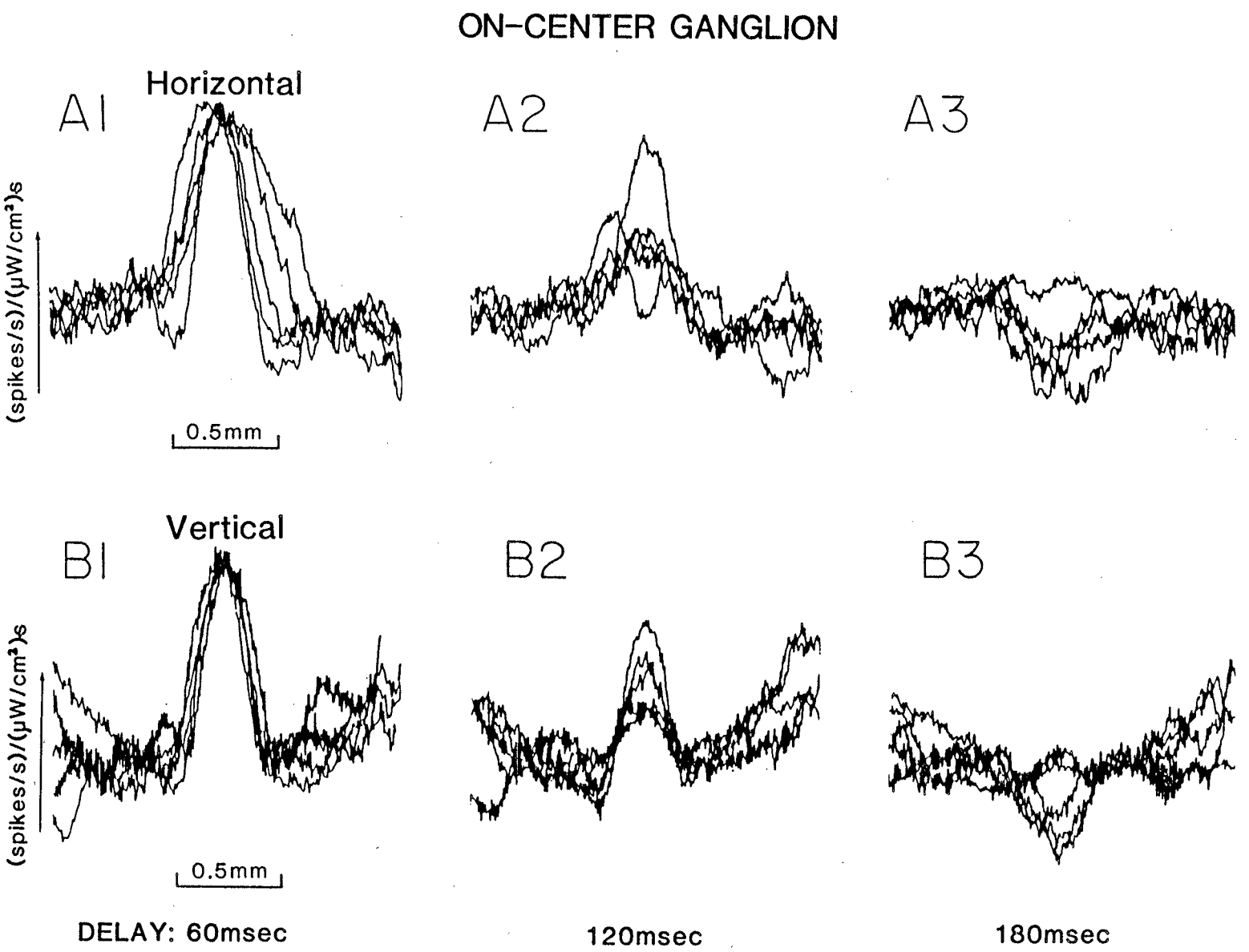

ON-CENTER GANGLION
Horizontal
A1
A2
A3
(spikes/s)/(μW/cm²)s
0.5mm
Vertical
B1
B2
B3
(spikes/s)/(μW/cm²)s
0.5mm
DELAY: 60msec
120msec
180msec

Fig. 3.12

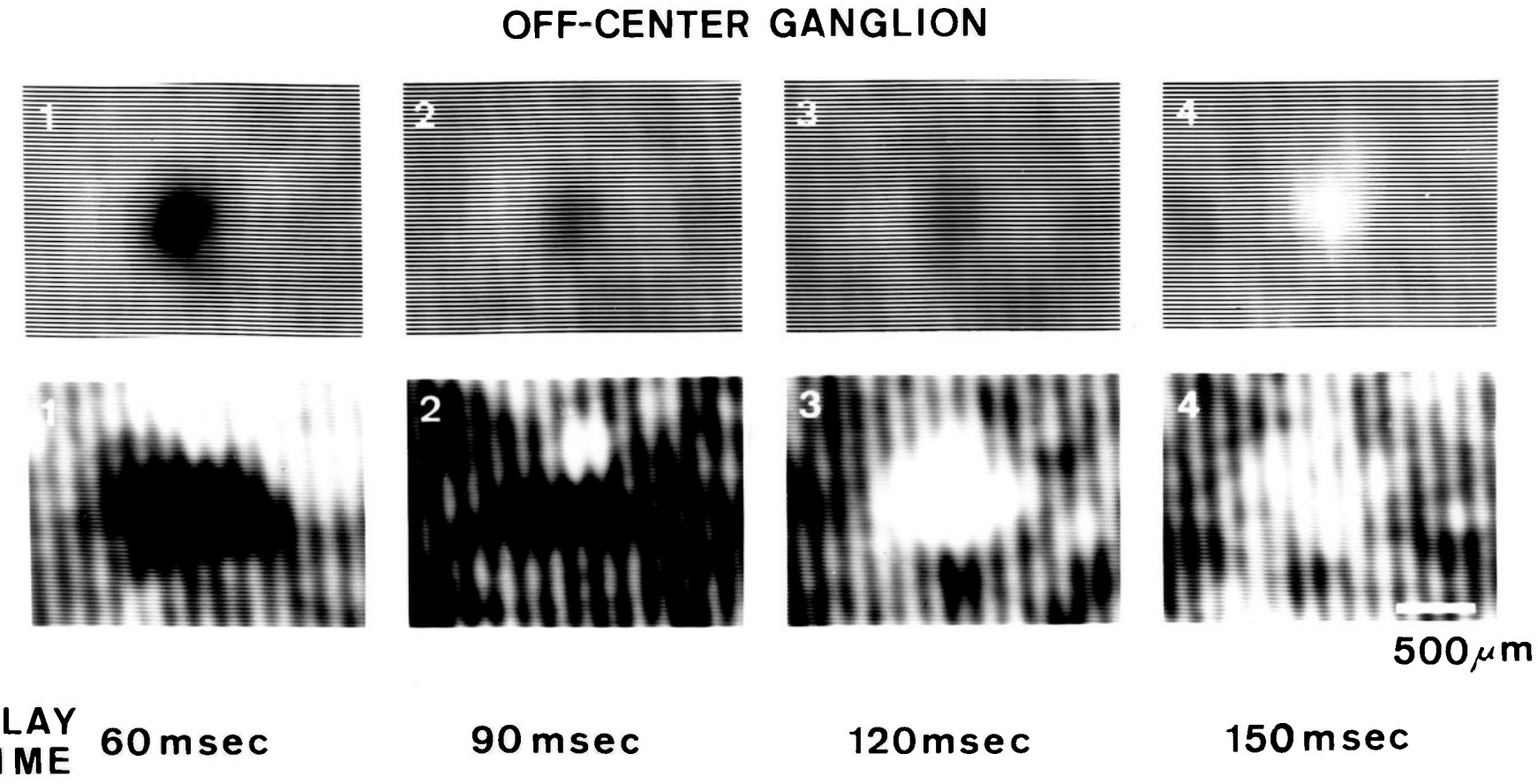

OFF-CENTER GANGLION
1
2
3
4
1
2
3
4
500μm
DELAY TIME
60msec
90msec
120msec
150msec

Fig. 3.13

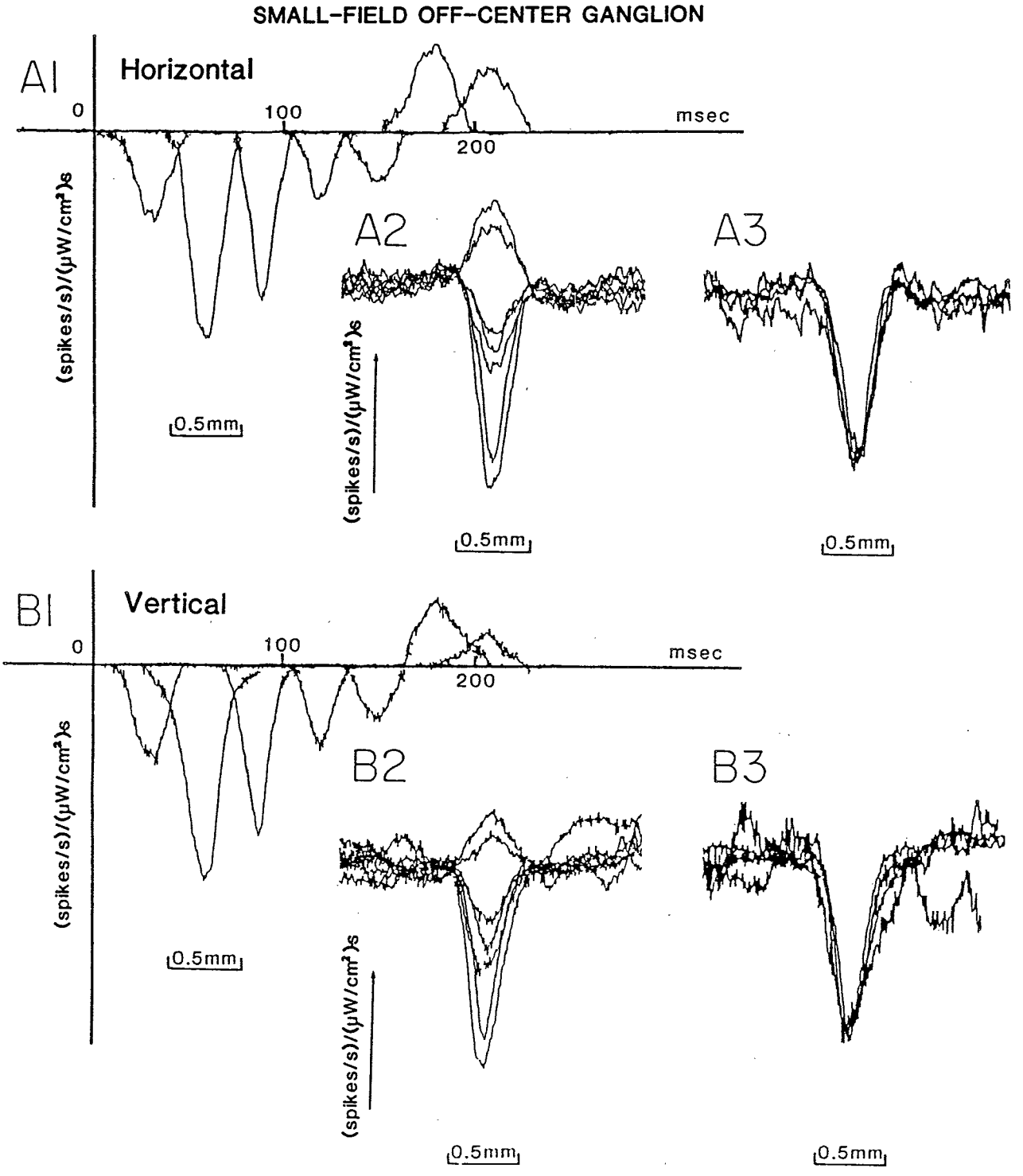

SMALL-FIELD OFF-CENTER GANGLION
A1
Horizontal
0
100
200
msec
(spikes/s)/(μW/cm²)s
0.5mm
A2
(spikes/s)/(μW/cm²)s
0.5mm
A3
0.5mm
B1
Vertical
0
100
200
msec
(spikes/s)/(μW/cm²)s
0.5mm
B2
(spikes/s)/(μW/cm²)s
0.5mm
B3
0.5mm

Fig. 3.14

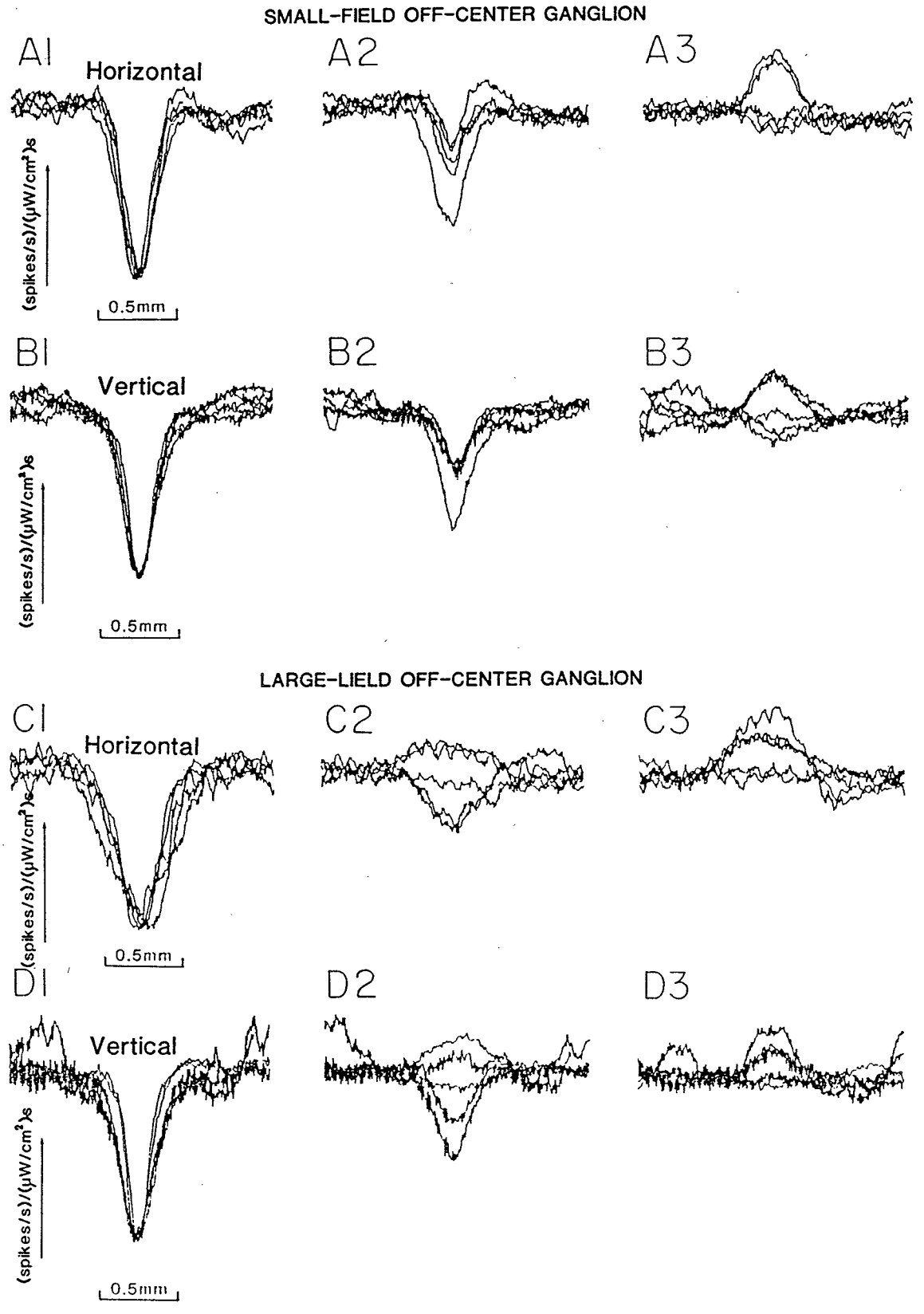

SMALL-FIELD OFF-CENTER GANGLION
A1
Horizontal
A2
A3
(spikes/s)/(μW/cm²)s
0.5mm
B1
Vertical
B2
B3
(spikes/s)/(μW/cm²)s
0.5mm
LARGE-LIELD OFF-CENTER GANGLION
C1
Horizontal
C2
C3
(spikes/s)/(μW/cm²)s
0.5mm
D1
Vertical
D2
D3
(spikes/s)/(μW/cm²)s
0.5mm
DELAY: 60msec
120msec
180msec

Fig. 3.15

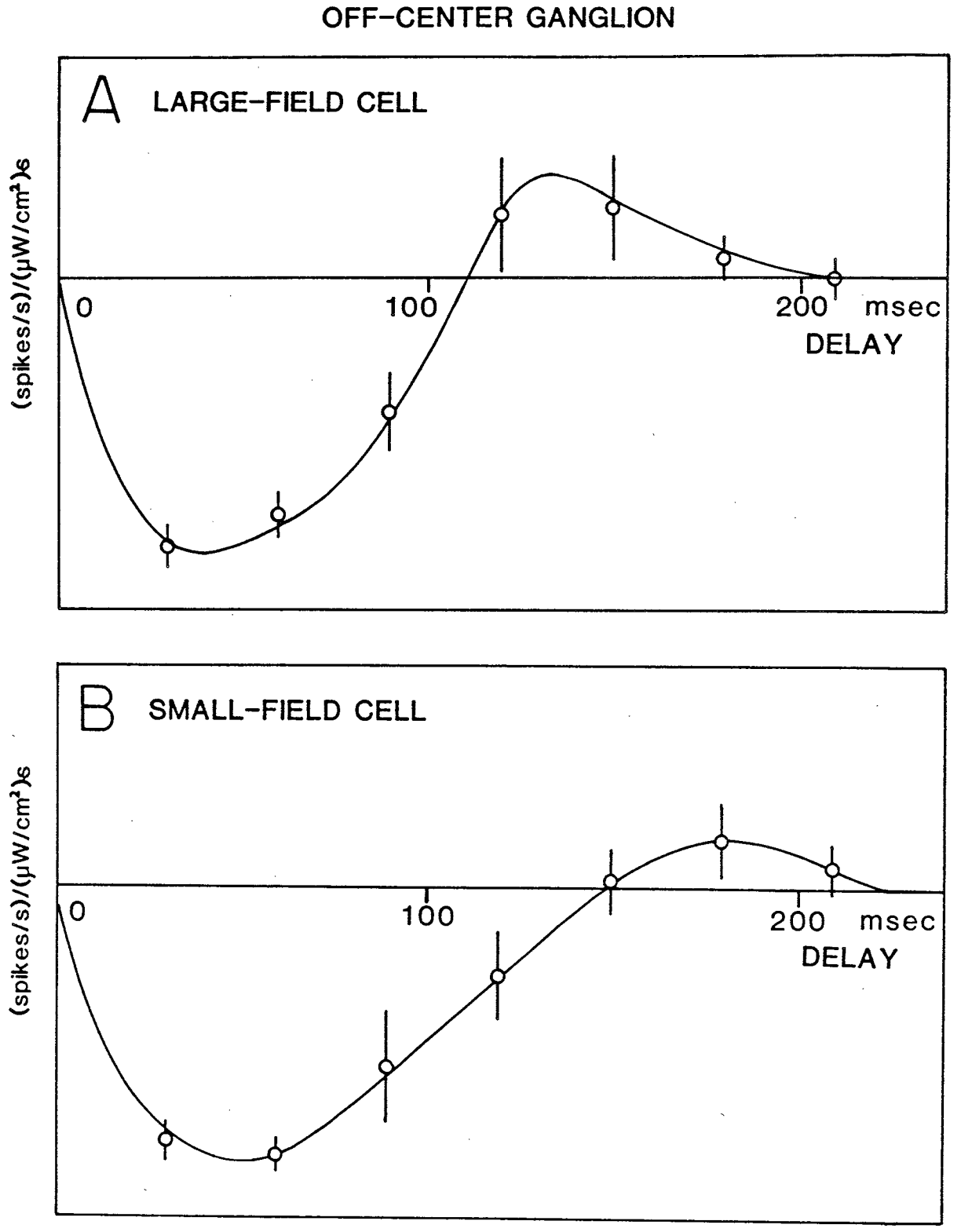

OFF-CENTER GANGLION
A
LARGE-FIELD CELL
(spikes/s)/(μW/cm²)s
0
100
200
msec
DELAY
B
SMALL-FIELD CELL
(spikes/s)/(μW/cm²)s
0
100
200
msec
DELAY

Fig. 3.16

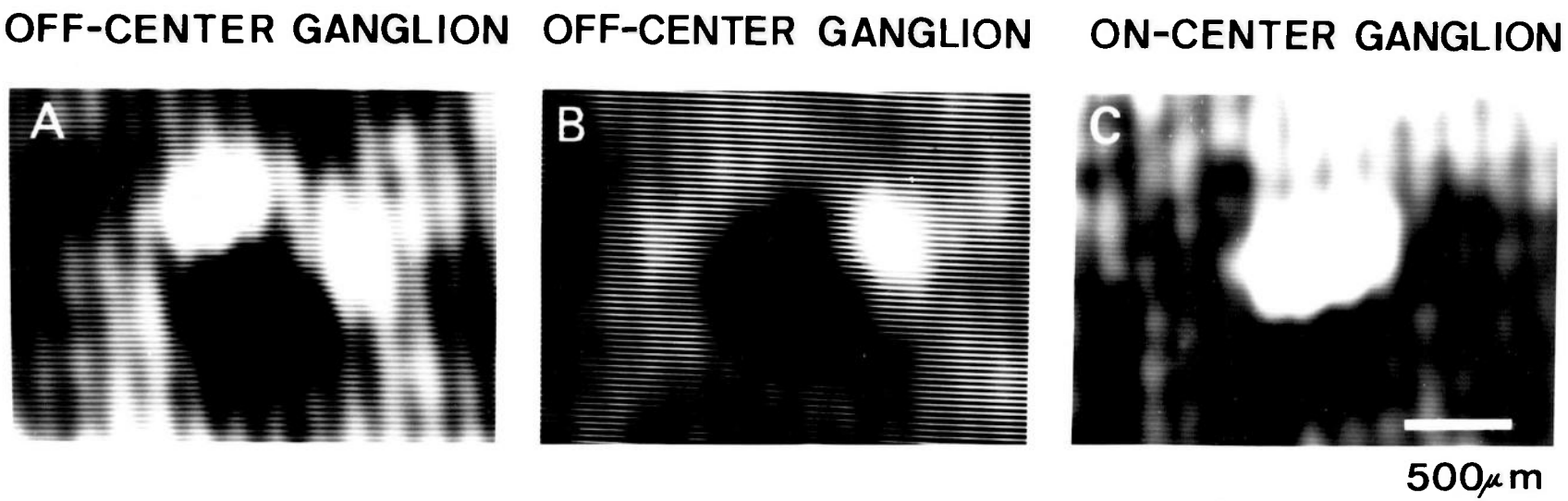

OFF-CENTER GANGLION
OFF-CENTER GANGLION
ON-CENTER GANGLION
A
B
C
500μm
DELAY TIME 60msec

Fig. 3.17

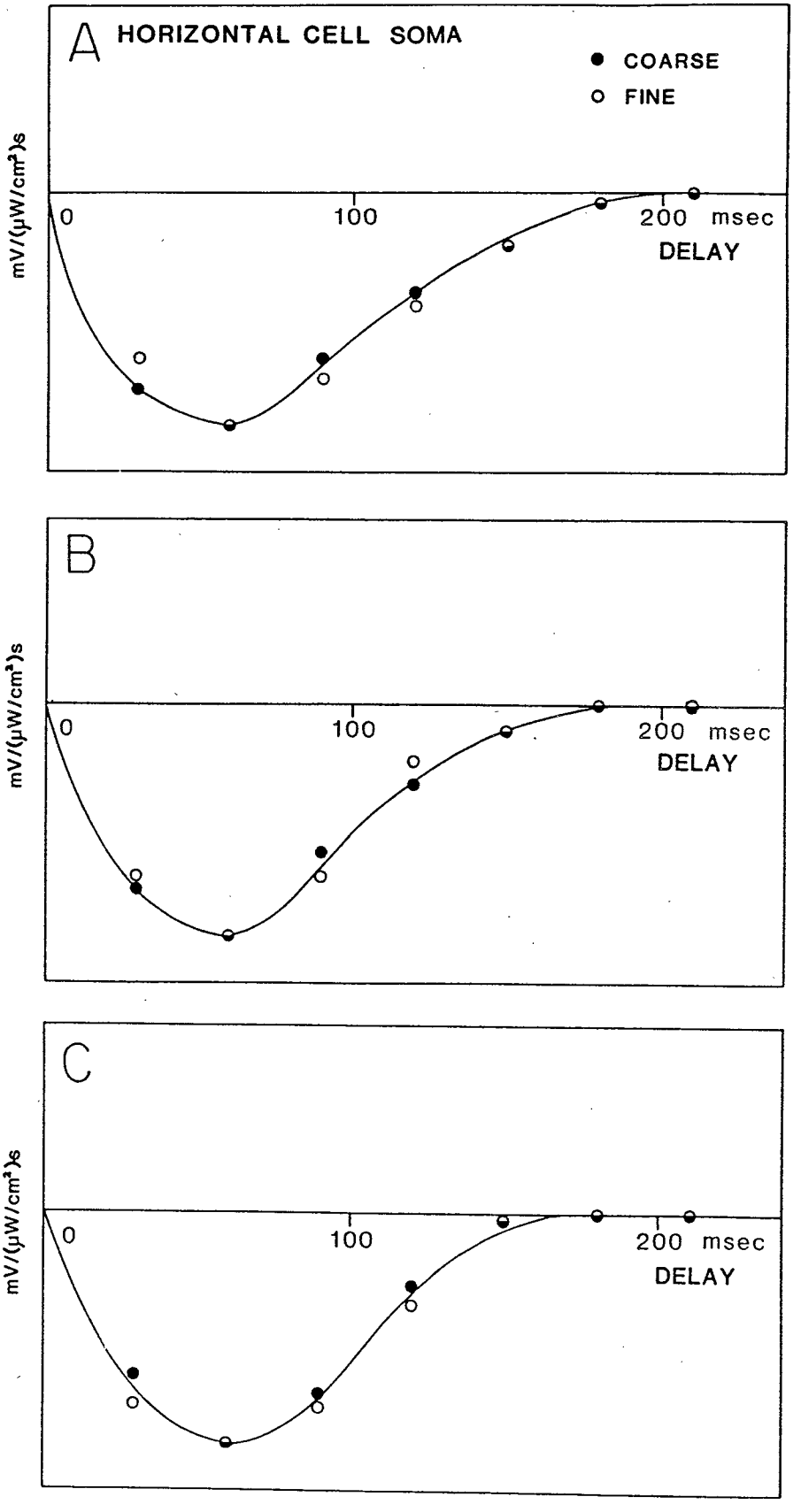

A
HORIZONTAL CELL SOMA
COARSE
FINE
mV/(μW/cm²)s
0
100
200 msec
DELAY
B
mV/(μW/cm²)s
0
100
200 msec
DELAY
C
mV/(μW/cm²)s
0
100
200 msec
DELAY

Fig. 3.18

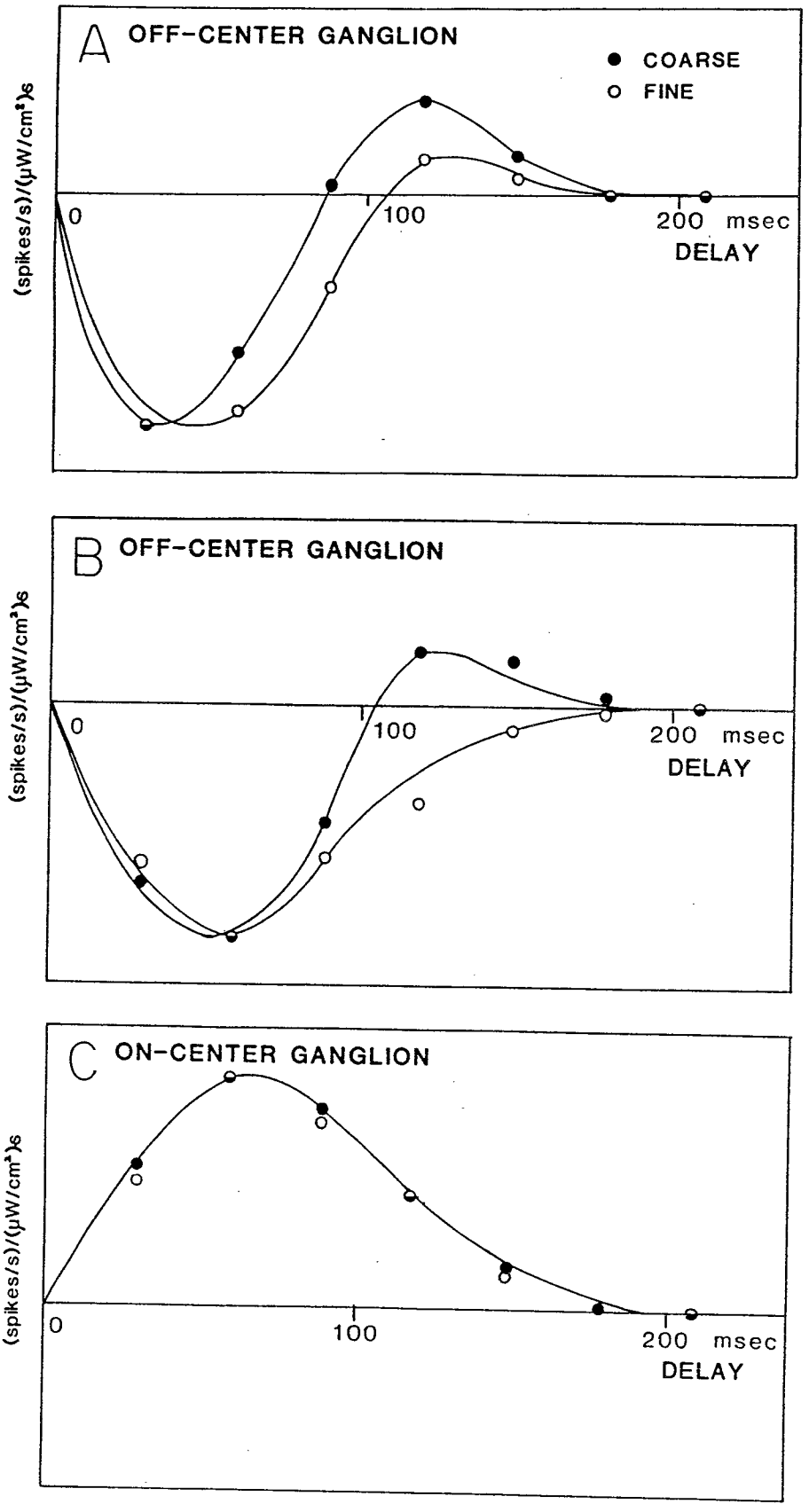

A
OFF-CENTER GANGLION
COARSE
FINE
(spikes/s)/(μW/cm²)s
0
100
200 msec
DELAY
B
OFF-CENTER GANGLION
(spikes/s)/(μW/cm²)s
0
100
200 msec
DELAY
C
ON-CENTER GANGLION
(spikes/s)/(μW/cm²)s
0
100
200 msec
DELAY

Fig. 3.19

STRF characteristics of catfish retinal interneurons

	Recorded cell number	Analysed cell number	Half-width of receptive field(um)#
Horizontal cell soma	30	21	H: 451 ± 86 V: 428 ± 64
Bipolar cell			
On-center	24	13	H: 228 ± 39 V: 226 ± 41
Off-center	35	22	H: 182 ± 24 V: 184 ± 24
Amacrine cell			
NA (on)	47	29	H: 423 ± 113 V: 299 ± 59
NB (off)	26	16	H: 382 ± 73 V: 283 ± 41
C (on-off)	21	4	H: 208 ± 32 V: 191 ± 40

Half-width of the receptive field was defined as the half-width of the receptive field center profile at a delay of 60 msec.

H: horizontal profile, V: vertical profile

Table 3.1

STRF characteristics of catfish retinal ganglion cells

	Recorded cell number	Analysed cell number	Half-width of receptive field(um)#	
On-center				
Small-field	14 (3)##	9	H:	379 ± 71
(hot spot)###	2		V:	374 ± 64
Large-field	13 (2)	8	H:	609 ± 96
(hot spot)	2		V:	372 ± 57
Undetermined	3			
Off-center				
Small-field	51 (19)	21	H:	315 ± 59
(hot spot)	6		V:	301 ± 57
Large-field	43 (27)	15	H:	575 ± 89
(hot spot)	5		V:	331 ± 71
Undetermined	10			

Half-width of the receptive field was defined as the half-width of the receptive field center profile at a delay of 60 msec.

Number in ( ) shows the number of cells which showed the polarity reversal of the receptive field.

(hot spot) shows the number of cells which had localized surround.

H: horizontal profile, V: vertical profile

Table 3.2

CHAPTER 4

SPATIO-TEMPORAL REGULATION OF RECEPTIVE FIELD CENTER BY SURROUND MECHANISMS IN BIPOLAR AND GANGLION CELLS OF CATFISH RETINA

Introduction:

In chapter 3, spatio-temporal receptive fields as revealed by TV snow noise were described and discussed. The results strongly support the idea that receptive field center predominantly acts as the local detector of the spatio-temporal changes of incident light. This chapter focuses on how the response properties of receptive field center are regulated by the surround mechanisms in catfish retinal bipolar and ganglion cells. Bipolar and ganglion cells in catfish retina have receptive field organization composed of center and antagonistic surround (Naka and Ohtsuka, 1975).

Intensive physiological study showed that surround stimulation modified center response in bipolar (Werblin, 1974; Thibos and Werblin, 1978a) and in ganglion cells (Maffei, 1968; Kruger and Fischer, 1973; Enroth-Cugell and Lennie, 1975; Enroth-Cugell et al., 1975) depending on the intensity of surround illumination. Such modification includes lateral inhibition (Kuffler, 1953; Fiorentini and Maffei, 1968; Kaneko, 1973) and shift of I-V relation (Werblin, 1974). These mechanisms result in contrast enhancement and the expansion of response dynamic range respectively. Furthermore, evidence has accumulated to show that center response of ganglion cells is sensitive to spatio-temporal changes of light (Werblin and Copenhagen, 1974; Thibos and Werblin, 1978b; Enroth-Cugell and Jakiela, 1980);illumination

of moving pattern to receptive field surround induces the suppression of center response. With all functional significance of the receptive field surround in bipolar and ganglion cells, parameters surround mechanism detects to modify the central dynamics, and what mechanisms reside in the modification of spatio-temporal properties of the center, are not thoroughly characterized.

In the meanwhile, psychophysical study (Robson, 1966; Kelly, 1972) has shown that human visual system possesses spatio-temporal interaction properties so as to make the best of constituent channel capacity. Namely, visual system behaves as spatial lowpass filter when temporally rapidly changing stimulus and vice versa. Such spatio-temporal interaction may be indicative of higher-order adaptation mechanism in visual system. Physiological investigations (Derrington and Lennie, 1982; Enroth-Cugell et al., 1983; Dawis et al., 1984) have shown that spatio-temporal interaction takes place in cat retinal ganglion cells in a similar way to the results from human visual system. This evidence suggests that retinal neurons may be responsible for spatio-temporal coupling properties in visual system. However, cellular mechanism underlying such spatio-temporal interactions is poorly understood.

The aim of this chapter is twofold; one is to elucidate the difference in surround mechanisms between bipolar and ganglion cells in order to understand the functional structure of hierarchical signal processing within the retina. Another is intended to clarify where spatio-temporal interaction arises in

the retina by relating to receptive field center and surround mechanisms. The investigation was predominantly carried out in off-center bipolar and ganglion cells. Off-units are more readily encountered in electrophysiological experiments. In fact, the sampling population of off-center cells was estimated to be about four times of that of on-center ones (Naka, 1977).

Materials and Methods:

Recording procedure:

Experiments were performed with eye-cup preparations of the channel catfish (Ictarulus punctatus). The eye-cup was placed in a chamber where a moisted oxygen(100%) was continuously supplied. The responses from bipolar cells and horizontal cells' somata were recorded intracellularly with glass capillary electrode filled with 2M potassium citrate. Extracellular spikes from ganglion cells were recorded with platinized tangsten electrode.

Micro-computer system for spatio-temporal receptive field analysis:

System configuration:

The system employed in this experiment was composed of a micro-computer(PC-8001; NEC) with a 64K-byte RAM, and an I/O unit equipped with a 31-bit shift register, an analog-to-digital converter(PCN-1209; Neolog) and an interrupt generating circuit(Fig. 4.1). A monitor television set(PM-52T; Ikegami) was used to display the stimulus pattern. The system was equipped with two minifloppy disk drives to store data analysis programs on one and experimental data on the other. Data analysis programs were written in the Fortran-80 and Macro-80(Microsoft) which

operated under CP/M(Digital Research).

Generation of spatio-temporal white-noise pattern:

The stimulus was a 16x16-pixel random checkered pattern refreshed at every 16.7msec corresponding to the interval of the non-interlace picture monitor display(Fig. 4.1). A pseudorandom binary noise(M-sequence) for the spatio-temporal random pattern was generated by using a 31-bit shift register with a 31-stage feedback circuit driven by a 5-MHz clock. The lower 16 bits were transferred to a V-RAM area of the PC-8001 to generate each horizontal sweep of each frame. After this, the shift register was shifted 31 times to the left. 16 times repetition of this process yielded a frame of 16x16-pixel random checkered pattern which was displayed on a TV monitor screen. This was imaged on the retina through the focusing lens(Fig. 4.1). The mean illuminance of the random pattern was 1.0 $\mu W/cm^2$ on the retinal surface. The vertical synchronizing signal from PC-8001 refreshed the random pattern every 16.7 msec(60 times/sec) through one of the interrupts(Fig. 4.1). The 31-bit shift register produced 8.39 million checkered patterns and the same pattern would appear once every 2330 min, which of course was long enough for every experiment conducted.

Data acquisition:

Suppose a spike discharge was detected within a time bin of 16.7 msec. Then, the 31 bits of M-sequence, corresponding to the current random checkered pattern were stored in memory. Thus, the exact timing of the spike discharge was known since each spike discharge was uniquely identifiable from the shift register's 31

bit output. Thus, a checkered pattern could be reconstructed by knowing only the initial 31 bits. If more than two spikes were detected within a bin, the initial value was stored as many times as spike occurrences to reconstruct identical checkered pattern. When a spike discharge was detected during a video-refresh interrupt, a priority interrupt control was used to store the spike and to refresh the checkered pattern. The size of memory limited the maximal number of spike events which could be stored at 4096. In the case of non-spiking cells such as bipolar and horizontal cells, the analog potential was sampled and digitized by a 12-bit analog-to-digital converter(PCN-1209; Neolog) and was then stored on a minifloppy disk via I/O unit. The sampling interval was set at a value of 16.7msec(once every refreshed frame), so that the sampling was triggered by the vertical synchronizing signal.

Cross-correlation:

Cross-correlation analysis involving spike-generating ganglion cells was made by the following procedure. For each occurrence of a spike discharge(registered by the first 31 bits of M-sequence), ten preceding checkered patterns were reconstructed and were accumulated in ten bins. The spike discharge occurred 16.7 msec after the first checkered pattern, 33.3 msec after the second and so on. This process was repeated until 4096 spike discharges occurred, and ten averaged frames were produced. Such ten frames could cover spatio-temporal receptive field properties of catfish retinal neurons.

In the non-spiking case of bipolar and horizontal cells, the

conventional cross-correlation was performed by associating the analog response of the membrane potential with the input frames which were reconstructed from the values of M-sequence(1's of bright elements and 0's of dark pixels). As was the case of ganglion cells, ten successive frames from 0 to 210 msec of delay times were calculated. The duration for obtaining one complete STRF was 90 sec in bipolar cells and horizontal cell somata. A somewhat modified random pattern was also prepared for the spatio-temporal stimulus, which was a 4X4-pixel one surrounded by steady light in both time and space domain or temporally binary-modulated spatially uniform light. Prior to the recording from each unit, the receptive field at a delay of 51msec was measured. Then, the central position of the receptive field was centered on a checkered pattern by use of a focusing mirror.

Analysis of spatio-temporal receptive field mechanism:

Spatio-temporal properties of the receptive field center was quantitatively analysed on the basis of the following procedure. To reveal the time-varing aspect of the receptive field center, the magnitude of the receptive field center was plotted against each successive delays(Fig. 4.1). This graph indicates linear impulse response function and is referred to as (first-order) temporal kernel (Sakuranaga et al., 1986). The incremental sensitivity of the receptive field center can be approximated by the peak-to-peak amplitude of this kernel (Naka et al., 1979). Spatial map of the receptive field center was shown at each delay. To simplify the observation, only horizontal profiles were selectively shown below.

Results:

Spatio-temporal properties of receptive field center depend on the surround mean illuminance:

The response properties of bipolar and ganglion cells were largely affected by the irradiance of the surround region. Fig. 4.2B shows responses of an off-center bipolar cell to dark surround and to steady surround illumination of several illuminance levels. A sustained hyperpolarization resulted from illumination of 4x4 random checkered pattern with a mean illuminance of 1.0 $\mu W/cm^2$ on center region without surround stimulation. The response to spatio-temporal changes of the random checkered pattern was usually too small to be recognized. As shown in the middle and lower traces of Fig. 4.2B, illumination of a steady uniform light to the surround area drastically altered the response characteristics to the random checkered pattern. The surround illumination decreased the sustained hyperpolarization followed by appearance of a fluctuating response to spatio-temporal changes of the center stimulus light. The amplitude of membrane potential fluctuation increased with increase of the surround illumination, accompanied by diminution of the sustained hyperpolarization. Furthermore, the initial large hyperpolarization rapidly returned nearly to the resting potential level in the dark accompanied by appearance of a vigorous fluctuating response to the random checkered pattern of the central region.

The response properties of off-center bipolar cells were examined by reconstructing the temporal kernel as shown in Fig.

4.2A. Without surround illumination, the cell responded very slowly to spatio-temporal changes of light with very low incremental sensitivity. By increasing the intensity of surround stimulation, the incremental sensitivity of the center area increased monotonically and the response was quickened. In addition, the response waveform changed from monophasic to biphasic. These observations indicate that off-center bipolar cells can detect better changes of center light if the intensity of surround illumination is raised. Such dependence on the surround illumination was similarly examined in off-center ganglion cells.

Fig. 4.3A shows changes of the incremental sensitivity and temporal property of small-field ganglion cell in relation with the surround illumination. The center stimulation by the 4x4 checkered pattern without surround illumination caused very little response to spatio-temporal changes of light. When the intensity of surround illumination was raised, the incremental sensitivity increased and also response waveform changed from monophasic to biphasic, showing that the cell responded better to spatio-temporal changes of light. Fig. 4.3B illustrates the relationship between the incremental sensitivity and the intensity of surround illumination. In the absence of surround stimulus, the incremental sensitivity of ganglion cells was about 25% of its maximal value which was attainable by equal center and surround illuminances. The incremental sensitivity was raised monotonically with increase in the intensity of surround illumination. When the mean illuminance was the same for center

and surround stimulations, the incremental sensitivity nearly reached the maximal value. Once the surround illuminance exceeded the center mean illuminance, the incremental sensitivity did not further increase but remained nearly constant.

Fig. 4.4 shows receptive field profiles of an off-center bipolar and an off-center ganglion cell shown in Fig. 4.2A and Fig. 4.3A, respectively. A1 and B1 are the horizontal profiles of the off-center bipolar cell for four levels of surround illumination at delays 51msec(A1) and 102msec(B1). Their normalized profiles are shown in A2 and B2, indicating that the spatial property was little affected by the mean illuminance level of surround stimulation. Similar features were observed in off-center ganglion cells as is evident from the horizontal profiles at delays 51msec(C1) and 85msec(D1). These normalized profiles of C1 and D1 show that spatial property of an off-center ganglion cell was nearly invarient with respect to the surround illuminance. In conclusion, bipolar and ganglion cells show similar dynamical changes that depend on the intensity of surround illumination. However, no significant difference was found between small-field and large-field cells, concerning spatio-temporal properties and incremental sensitivity in the presence of steady surround illumination.

Spatio-temporal properties of receptive field center of bipolar and ganglion cells depend on spatio-temporal changes of surround light:

Spatio-temporal receptive-field analysis of bipolar and ganglion cells was undertaken by using two sorts of stimuli which

are shown in Fig. 4.5. One type was a 16x16-pixel random checkered pattern which illuminated the whole area of the receptive field. The other type was a 4x4-pixel random checkered pattern for the center stimulus and a steady uniform light for the surround area. In both types, the mean illuminance of the surround was equal to that of the center stimulus. Each picture element of each random checkered pattern was 120μm x 120μm on the retinal surface. The 4x4 pattern covered the entire receptive field center of bipolar and of small-field ganglion cells. The method for measuring spatio-temporal properties of the receptive field center was the same as that used in the previous section. Fig. 4.5 shows temporal kernels(A1,B1) and spatial profiles(A2,B2) of the receptive field center of off-center bipolar cells obtained by the illuminations of two kinds of stimuli. The results of (A1, A2) and (B1,B2) were acquired from two different off-center bipolar cells. It is seen that the temporal property was the same for 16x16 and 4x4 random patterns. The incremental sensitivity measured as the peak-to-peak amplitude of the first-order kernel was also nearly equal in two stimuli. The 16x16 pattern reduced only slightly(<8%) the incremental sensitivity, in comparison with the case of 4x4 stimulus(11 cells). Also, spatial profiles of the receptive field center were almost identical with the two stimulus patterns. Hence, it seems that properties of the receptive field center of bipolar cells are not much influenced by the stimulus condition in the surround region.

As regards ganglion cells, however, the incremental

sensitivity was evidently affected by the surround. This is shown in Fig. 4.6 for three off-center ganglion cells in which the left column(A1,B1,C1) represents the temporal kernels obtained by center-field(4x4; ○) and whole-field random patterns (16x16; ●); the incremental sensitivity declined by a factor of 45~60% when the random stimulation was extended to the surround area. However, if normalized, the results turned out to be nearly the same for the stimulus condition(A2, B2, C2). This indicates that the response time course is determined primarily by the center mechanism and not much by the surround stimulation. The same can also be said with respect to the receptive field profile(A3, B3, C3).

Next, the dependence of spatio-temporal characteristics of the receptive field center on the coarseness of surround stimulus was examined by using the stimuli shown in top row of Fig. 4.7. The center stimulus was a 4X4-pixel random checkered pattern whereas the surround stimulus was varied from 16X16(a) to 1X1(e). The mean illuminance of these stimuli was kept constant in center and surround regions. Such surround condition exerted two types of effects depending on the particular unit of off-center ganglion cells; one is shown in Fig. 4.7A1 and A2, and the other is in Fig. 4.7B1 and B2. A1 and B1 show temporal kernels from the stimuli (a)-(e) and their normalized kernels are shown in A2 and B2. In twenty-six units out of thirty-two cells analysed, the incremental sensitivity decreased monotonically with the size of pixels associated with the surround pattern. But, the pixel size did not affect the response time course(A1,

A2). In the remaining six cells, however, response time course quickened slightly and the incremental sensitivity decreased somewhat with the size of noise element(B1 and B2). Receptive field center profiles of off-center ganglion cells, did not change with the coarseness of surround stimulus despite the considerable changes of incremental sensitivity with the size of noise element(not illustrated).

Spatio-temporal properties of bipolar and ganglion cells depend on fluctuation of the whole-field spatio-temporal random stimuli:

Dependence of spatio-temporal properties on the coarseness of center stimulation was examined in bipolar, ganglion, and horizontal cells. Configurations of the stimulus patterns used in this experiment are shown in the second row of Fig. 4.7; the center stimulus was a 1X1 random checkered pattern fluctuating in binary form, and the surround stimulus was chosen from 1X1(j), 2X2(i), 4X4(h), 8X8(g) patterns and steady uniform illumination(f). The mean illuminance was constant for all such stimulus patterns including both center and surround region.

Fig. 4.8 shows a representative response properties of off-center bipolar cells. As shown in B1, the response to 1X1 center illumination surrounded by the steady uniform light showed a more rapid time course than in the case of the 1X1 center illumination surrounded by the uniform light fluctuated in a binary way. Such change in the temporal property was also observed with the 4X4 center stimulation(A1 and A2 of Fig. 4.8). As shown in C, however, spatial property was not much influenced by the spatial content of surround stimulus. Furthermore, temporal kernels from

1X1 center stimulus and 4X4 center stimulus were quite similar, suggesting that the temporal property of bipolar cells was little affected by coarseness of center stimulus. Fig. 4.8D demonstrates the dependency of incremental sensitivity on the coarseness of center and surround stimuli. This graph was obtained from eight off-center bipolar cells with six stimuli shown in (a,e,f,h,j) as well as with the random checkered pattern surrounded by the steady uniform light. The relative sensitivity of the receptive field center in ordinate was normalized to the incremental sensitivity measured when surround was stimulated by steady uniform light. The incremental sensitivity with the 16x16 surround was nearly identical to the result of steady surround stimulation. In both 4x4 and 1x1 center patterns, the incremental sensitivity with the 1x1 surround was reduced to about half of that with steady surround.

There was a remarkable difference between off-center ganglion and off-center bipolar cells, as regards dependence of the temporal properties upon the coarseness of center stimulus noise. Thus, Fig. 4.9 shows results from off-center ganglion cells, indicating that the incremental sensitivity decreased monotonically with the coarseness of surround stimuli although the response time course remained unchanged(B1, B2). Furthermore, the kernel time course was much faster with 1x1 than with 4x4 center stimulation(A1, A2). Such acceleration of response speed was observed consistently in the cells whose temporal kernels were not much influenced by the coarseness of surround illumination. Spatial profiles of the receptive field of the cell

of A1 are shown in C, demonstrating that the spatial property is invarient with respect to the surround pattern as is the case in off-center bipolar cells. D shows changes of the incremental sensitivity as a function of the size of checker element in center and surround stimuli(eighteen off-center ganglion cells). In both 1x1 and 4x4 center stimulations, the incremental sensitivity decreased monotonically with the coarseness of surround stimuli. The incremental sensitivity was reduced more in 4x4 than in 1x1 center stimulation irrespective of the coarseness of surround stimulus. Furthermore, the incremental sensitivity with the 16x16 whole-field pattern(a;Fig. 4.7) decreased by about 25% compared with the case of the 4x4 random checkered pattern surrounded by steady uniform light. With the 4x4 center stimulation, the incremental sensitivity was nearly the same in the 16x16 and 8x8 surrounds; thus the incremental sensitivity presumably decreases by 25% if the surround stimulus becomes finer than 16x16.

Spatio-temporal property of horizontal cell soma is unaffected by the coarseness of stimulus noise:

Fig. 4.10 shows that the spatio-temporal property of horizontal cell somata was unaffected by the coarseness of the noise. Temporal kernels of a horizontal cell soma with the stimulus patterns of Fig. 4.7 are shown in A1. The incremental sensitivity decreased with the size of surround noise element. The response time ccurse did not, however, change with the coarseness of surround stimulus as is evident from normalized temporal kernels in A2. The similar situation was observed when

the 1X1 random checkered pattern was used for the center(B1, B2; Fig. 4.10). Temporal kernels of the cell of A1 and the corresponding normalized kernels are shown in B1 and B2, respectively. The reduction of incremental sensitivity associated with the change in the coarseness of surround stimulus was more prominent than when the 4x4 center pattern was used(cf. A1). The response time course did not, however, change with different surround patterns. Pattern-dependent changes of the incremental sensitivity (twenty-two units of the horizontal cell soma) are plotted in Fig. 4.10D, indicating that incremental sensitivity decreases with the coarseness of stimulus pattern in a manner similar to the situation of off-center bipolar cells(cf. Fig. 4.8).

Discussion:

Functional difference in the receptive field surround between bipolar cells and ganglion cells:

A striking difference in response properties between bipolar cells and ganglion cells lies in the incremental sensitivity to the fluctuation of light falling on the surround area. The incremental sensitivity of bipolar cells was not affected by the 16x16 fluctuating surround illumination(Fig. 4.5), whereas that of ganglion cells was appreciably reduced by such stimulus(Fig. 4.6). It was reported that the flash sensitivity of bipolar cells of mudpuppy retina was affected exclusively by the mean illuminance of surround stimulation without being influenced by spatio-temporal changes of surround stimulus pattern (Werblin, 1974; Thibos and Werblin, 1978a). Therefore, the surround of

vertebrate bipolar cells' receptive field is thought to be predominently concerned with detection of the mean illuminance level of incident light.

As regards ganglion cells, we have observed suppression of incremental sensitivity associated with spatio-temporal changes of the surround illumination(Fig. 4.6). The similar effect has been reported in cat (Enroth-Cugell and Jakiela, 1980) and in mudpuppy (Werblin and Copenhagen, 1974; Thibos and Werblin, 1978b). The suppression of incremental sensitivity or responsiveness in ganglion cells may be interpreted in two ways; one is the decrement of incremental sensitivity by the surround mechanism which signals the movement of visual images, another being the suppression by the contrast signals that arise in association with spatio-temporal changes of the surround stimulation. As described afterwards, spatio-temporally changing visual scenes such as moving patterns of light possibly induce contrast signals by on-off amacrine cells. Suppose that the latter mechanism is present in catfish retina, the suppression of incremental sensitivity by the surround illumination of random checkered pattern may be caused by the mechanism of contrast gain control as reported in cat retinal ganglion cells(Shapley and Victor, 1978, 1979). So is the case, it seems that the incremental sensitivity is so regulated as to decrease according to the magnitude of contrast signal. A high contrast means wide dynamic range of incident light. If the incremental sensitivity is constant irrespective of the contrast of stimulus, high contrast pattern of light may cause the saturated response due to

the very limited coding capacity of ganglion cells (Kuffler, 1953; Barlow, 1981); resulting in the distortion or cut-off in detecting spatio-temporal changes of light. This situation is illustrated in Fig. 4.11. Therefore, modification of the incremental sensitivity as a function of the contrast signal may serve to adjust the incremental sensitivity of the center. The scheme would help to detect local spatio-temporal changes of light with minimal distortion over a wide range of contrast as well as of the mean illuminance.

The role of receptive field center and surround in bipolar and ganglion cells:

Receptive field surround of bipolar and ganglion cells revealed by random checkered pattern was very faint or nearly recognizable except for rare examples (Fig. 4.12) seen in the cells with localized non-concentric surround. Nevertheless, illumination of light on the surround area remarkably altered the response property of the center, indicating a functional significance of the surround on center response(Fig. 4.2, Fig. 4.3). Hence, it is inferred from the present results that the receptive field center and the surround are imposed on separate but cooperative functional role in order to signal the prerequisite information to the follower neurons. Receptive field center of bipolar and ganglion cells contributes to detect the local spatio-temporal changes of light whereas the surround operates as a detector for the statistical parameter such as mean illuminance(Fig. 4.13), which characterizes the statistical feature of light impinged on the receptive field and is used for

the modification of center response. To have a large surround area is prerequisite for the averaging of signals from separate areas. In this way, the relevant statistical parameters can be evaluated through replacement of temporal averaging of center signal by spatial averaging on the surround area.

Center-surround interaction in the retinal neurons may well be so organized as to adjust maximally spatio-temporal dynamics of the center, under the assumption that signals from the surround provide the information about statistics of the light falling on the center(Fig. 4.13). Hence, any mismatch in center-surround interaction would hamper the normal dynamics of the center, and such mismatch arises when the statistics of the light falling on the center is different from that of the surround illumination. As shown in Fig. 4.2 and Fig. 4.3, mismatch caused by bright center stimulation without surround illumination results in prominent deterioration of the incremental sensitivity and response speed.

A possible mechanism for contrast detection:

Despite several lines of evidence to support the presence of contrast gain control of ganglion cells (Shapley and Victor, 1978, 1979; Victor and Shapley, 1979), the exact mechanisms of contrast detection have not yet been elucidated. Hence, a possible scheme is presented which mediates the retinal contrast signal by on-off amacrine cells. Key to this proposal are three features that pertain to on-off amacrine cells; (1)high-pass(AC) filtering as exemplified by the transient response to a step of light(Fig. 4.14A), (2)full-wave rectification as can be seen as

the transient depolarization to both initiation and cessation of light(Fig. 4.14A), (3)gap-junctional connections between on-off amacrine cells (Naka and Christensen 1981; Zimmerman, 1983).

Full-wave rectification property of on-off amacrine cell reverses the sign of negative output signals from high-pass filter to utilize rectified results for the calculation of the contrast(Fig. 4.14B). If high-pass filtered output is not rectified, positive signals involved in the filtered output are canceled with its negative signals in the process of spatial summation, producing no substantial depolarization. The rectified output in individual on-off amacrine cells is added through the gap junctions between on-off amacrine cells to average the membrane potentials whose DC component is closely related to the contrast of stimulus light(Fig. 4.14B). The contrast signal extracted by on-off amacrine cells is fed into ganglion cells presumably via amacrine to ganglion cell synapses to modify the incremental sensitivity according to the contrast of the incoming light(Fig. 4.13).

Spatio-temporal interactions in bipolar and ganglion cells:

Spatio-temporal properties seem to be quite different in bipolar and ganglion cells. In bipolar cells, increase in size of the surround noise element delayed the response time course, but the size of the center noise element did not much affect the response time course(Fig. 4.8). As regards ganglion cells, on the other hand, the response time course was primarily affected by the size of the center noise element and the surround stimulus condition appears to be minor importance in this respect(Fig.

4.9). Furthermore, it is recalled here that the spatio-temporal properties of horizontal cell somata did not change with the coarseness of either center or surround pattern(Fig. 4.10). These pieces of evidence suggest that spatio-temporal interaction properties similar to those in cat retinal ganglion cells (Derrington and Lennie, 1982; Enroth-Cugell et al., 1983; Dawis et al., 1984) and in the human visual system(Robson, 1966; Kelly, 1972) arise at the ganglion cell level, perhaps with active participation of amacrine cells.

Quasi-constant spatial properties of bipolar and ganglion cells revealed by random checkered pattern:

It is important to note that receptive fields obtained in this study demonstrate not only the static but also the time-varing aspect of the receptive field. In bipolar and ganglion cells, spatial profiles of the receptive field were nearly identical(Fig. 4.8, Fig. 4.9) for different kinds of surround stimuli. The temporal feature, however, changed significantly depending on the surround stimuli(Fig. 4.8, Fig. 4.9). While a spatial resolution of 120 μm was imposed on the stimulus used in the present study, Maffei et al., (1971) reported a similar result that cat retinal ganglion cells explored by sinusoidal grating showed nearly identical spatial profiles in the center region. Hence, a regulatory mechanism by which to keep a constant size for the receptive field center may very well be a general entity in the vertebrate retina.

Figure Legends:

Fig. 4.1: Schematic diagram for measuring the spatio-temporal receptive fields of retinal neurons. A random checkered pattern composed of 16X16-pixels(A) (or 4X4-pixels surrounded by a steady uniform light(B)) was generated by using both an M-sequence generating circuit and a personal computer PC-8001. The pattern was displayed on a picture monitor screen through the VRAM area. The cross-correlation between the stimulus and the evoked response was carried out in PC-8001. A spatio-temporal receptive field thus obtained was composed of a series of three-dimensional pictures showing the receptive field profile at each delay. Temporal property can be shown as the first-order temporal kernel which was obtained by plotting the magnitude of receptive field against the delay time. Spatial property was examined by measuring horizontal and/or vertical receptive field profiles at each delay.

Fig. 4.2:

A: Temporal kernels of an off-center bipolar cell obtained with surround stimuli of different mean illuminance level. The center stimulus was composed of 4X4-pixel random checkered pattern and its mean illuminance was 1.0$\mu W/cm^2$. The surround illuminance level was varied from dark, 0.4, 0.75, to 1.0 times of the center illuminance. STRFs were measured using the response record during 90 sec after 20sec of prestimulus.

B: Responses of the off-center bipolar cell shown in A. Without the surround illumination, the cell responded with a sustained hyperpolarization of about 5mV in amplitude. When the surround

light of the same mean illuminance was presented, the cell gave rise to a depolarizing response after about 5sec delay, reflecting the response to spatio-temporal changes of light. Lower trace shows response to the stimulus whose surround intensity was 1.5 times of the center illuminance.

Fig. 4.3:

A: Temporal kernels of an off-center ganglion cell to steady uniform surround illuminations with different mean illuminances. Center stimulation was the 4X4-pixel random checkered pattern with the mean illuminance of 1.0 $\mu W/cm^2$. The mean illuminance of surround was 0, 0.4, 0.75, 1.0 times of the mean illuminance of the center. The procedure to measure STRFs was the same as of Fig. 4.2A.

B: The relationship between the mean illuminance level of surround stimulus and the incremental sensitivity of the receptive field center of off-center ganglion cells. This result was an average from fifteen off-center ganglion cells. The relative intensity of surround stimulus in abscissa was normalized to the mean illuminance of center stimulus. The relative sensitivity of the receptive field center in ordinate was normalized to the incremental sensitivity measured in the presence of the surround stimulation which had the same mean illuminance as center.

Fig. 4.4: Receptive field profiles of an off-center bipolar and an off-center ganglion cells with the surround stimulation of several mean illuminance levels. Horizontal profiles from the cell of Fig. 4.2 are shown at delays of 51msec(A1) and

102msec(B1). A2 and B2 are the normalized versions of A1 and B1, respectively. The illuminance level of surround stimulus was varied from the complete dark, 0.4, 0.75, to 1.0 times of the mean illuminance of center stimulation. Receptive field profiles without surround stimulation are not shown because the dark surround failed to yield a clear receptive field profile. Horizontal profiles from the cell of Fig. 4.3A are depicted at delays of 51msec(C1) and 85msec(D1). C2 and D2 are the normalized versions of C1 and D1, respectively. At a delay of 85msec, the polarity of receptive field was reversed with the mean center illuminance of 1.0 and 0.75. (Without surround stimulation, the receptive field map did not yield a clear result at this delay time). For the sake of comparison in D2, normalized profile with the mean surround illuminance of 0.4x center illuminance, was reversed in polarity.

Fig. 4.5: The top panel shows two stimulus patterns used in the experiment; type I was a 16x16-pixel random checkered pattern covering the whole area of the receptive field, and type II was composed of a 4x4-pixel random pattern in the center region and a steady uniform light in the surround region. The pixel had the same size(120μm x 120μm) for both types. A1 and B1 show temporal kernels from different off-center bipolar cells(type I stimulus ●, and type II stimulus o). No significant difference can be seen between ● and o in either A1 or B1. A2 and B2 are normalized horizontal profiles of the receptive field at a delay of 51 msec from the cells of A1 and B1 respectively. The receptive field maps corresponding to ● and o were again almost identical.

Fig. 4.6: Spatio-temporal properties of three off-center ganglion cells(A, B, C) for the stimuli shown in Fig. 4.5; temporal kernels(left column), their normalized versions(middle column) and normalized horizontal receptive-field profiles(right column) at a delay of 51msec.

Fig. 7: (a),(b),(c),(d), and (e) are photic stimuli composed of 4x4-pixel random checkered pattern in the center region and 16x16, 8x8, 4x4, 2x2, and 1x1 in the surround, respectively. On the basis of the results using (a) to (e), off-center ganglion cells fell into two categories shown A and B. A1 shows temporal kernels from a cell whose response time course was not influenced by the coarseness of surround random stimuli. A2 shows normalized versions of A1. The incremental sensitivity decreased monotonically with the size of surround noise element. B1 shows a set of temporal kernels from the cell whose response time course was affected by the coarseness of surround noise. Normalized temporal kernels corresponding to B1 are shown in B2. The time-to-peak was 15msec shorter with the stimulus (a) than with (e).

Fig. 4.8: Spatio-temporal properties of off-center bipolar cells for the various random checkered patterns ((a) - (e) of Fig. 4.7). A1 shows temporal kernels measured with the stimuli, (a), (e), and (h). A2 shows their normalized forms. B1 shows temporal kernels with the stimuli, (f),(h),(j), and their normalized version are given in B2. All these kernels in A1 and B1 were from the same off-center unit. C illustrates the normalized horizontal receptive field profiles(at a delay of 51msec) from the stimuli,(a) and (e). D shows the dependence of incremental

sensitivity on the coarseness of center and surround stimuli. The relative sensitivity of the receptive field center in ordinate was normalized to the incremental sensitivity measured in the presence of the steady uniform surround stimulation. Abscissa shows checker patterns of surround stimuli.. This graph was compiled from eight off-center bipolar cells.

Fig. 4.9: Spatio-temporal properties of an off-center ganglion cell with various random checkered pattern stimuli of Fig. 4.7. A1 shows temporal kernels obtained from the stimuli, (a), (b), (c), (d), (e), and their corresponding normalized kernels are shown in A2. The result with the stimulus, (h) is also shown for comparison. The kernel waveform was influenced by the fineness of surround noise. B1 shows temporal kernels with the stimuli, (f), (g), (h), (i), and (j), and B2 shows the normalized kernels corresponding to (f) and (j). In the 1x1 center stimulus, the kernel time course was not affected by the coarseness of surround noise. A1 and B1 are from same off-center cell. C shows normalized receptive field profiles at a delay of 51msec for the stimuli, (a), (b), and (e). D is a graph obtained from eighteen off-center ganglion cells, showing dependence of the incremental sensitivity on the coarseness of the noise size in center and surround patterns. The relative sensitivity of the receptive field center in ordinate was normalized to the incremental sensitivity when surround was stimulated by steady uniform light. Abscissa shows checker patterns of surround stimuli. In contrast with off-center bipolar cells(cf. Fig. 4.8), incremental sensitivity with the 16x16 whole-field pattern was reduced by 25%

compared with the case of steady uniform surround illumination. Moreover, the incremental sensitivity with the 16x16 surround stimuli was nearly the same as that with 8x8.

Fig. 4.10: Spatio-temporal properties of horizontal cell somata with various random checkered patterns of Fig. 4.7. A1 shows temporal kernels for the stimuli, (a), (b), (c), (d), and (e). Of these, kernels corresponding to (a) and (e) were normalized and shown in A2. B1 shows temporal kernels for the stimuli, (f), (g), (h), (i), and normalized kernels are shown in B2 for (f) and (j). These data indicate that the kernel waveform does not change with the coarseness of center and surround stimuli. Temporal kernels in A1 and B1 are from the same cell. C shows normalized receptive field profiles with the stimuli, (a), (b), and (e). D shows dependence of the incremental sensitivity on the coarseness of center and surround patterns(twenty-two somata). The relative sensitivity of the receptive field center in ordinate was normalized to the incremental sensitivity measured in stimulating the surround by steady uniform light. Abscissa shows checker patterns of surround stimuli. Unlike the case of off-center ganglion cells, the incremental sensitivity estimated with the 8x8 surround stimulation was lower than that with 16x16 whole-field stimulation.

Fig. 4.11: Schematic illustration for the need of sensitivity regulation dependent on the contrast of incident light in ganglion cells. Consider the case where one-dimensional sinusoidal grating moving at a constant speed illuminates the whole receptive field of an on-center ganglion cell. In low

contrast stimulation(A1), the cell changes its spike frequency sinusoidally(B1). If mean illuminance level of stimulus is constant and AC dynamics of the cell behaves linearly, illumination of high contrast stimulus(A2) results in the saturation or cut-off of spike discharges(B2).

Fig. 4.12: A spatio-temporal receptive field of an off-center ganglion cell with localized surrounds. The field was taken at different delay times 17, 34, 51, 68, 85, 102, 119, 136 msec for records 1-8. Upper deflection shows an off-region, and localized surrounds are indicated by arrows.

Fig. 4.13: Schematic diagram of the neural circuitry and response regulation in catfish retina. The mean intensity of incident light is detected by horizontal cells' somata which modify the response property of bipolar cells. The contrast signal of incident light is presumably generated by on-off amacrine cells which regulate the response property of ganglion cells. Thus, at least two steps of hierarchical dynamical control system may be present in catfish retina. An enormous wide range of incident light is covered by these regulatory system. Resistance in this diagram shows gap junctions.

Fig. 4.14:

A: Response of an on-off amacrine cell to field step of light with the mean illuminance of 1.0 $\mu W/cm^2$. The cell shows a transient depolarization(high-pass filtering) at initiation and termination(full-wave rectification characteristics) of step of light.

B: Functional properties of an on-off amacrine cells can be

described as the block diagram shown in (a). DC component of input signal is eliminated by a high-pass filtering(b). Negative signal component of the high-pass filtered output is reversed by full-wave rectification property(c). Spatial summation from numerous on-off amacrine cells which produce positive(depolarizing) fluctuation, results in the sustained depolarization of individual on-off amacrine cells(d). This DC component reflects the contrast of incident light(cf. (b1)-(d1), (b2)-(d2)).

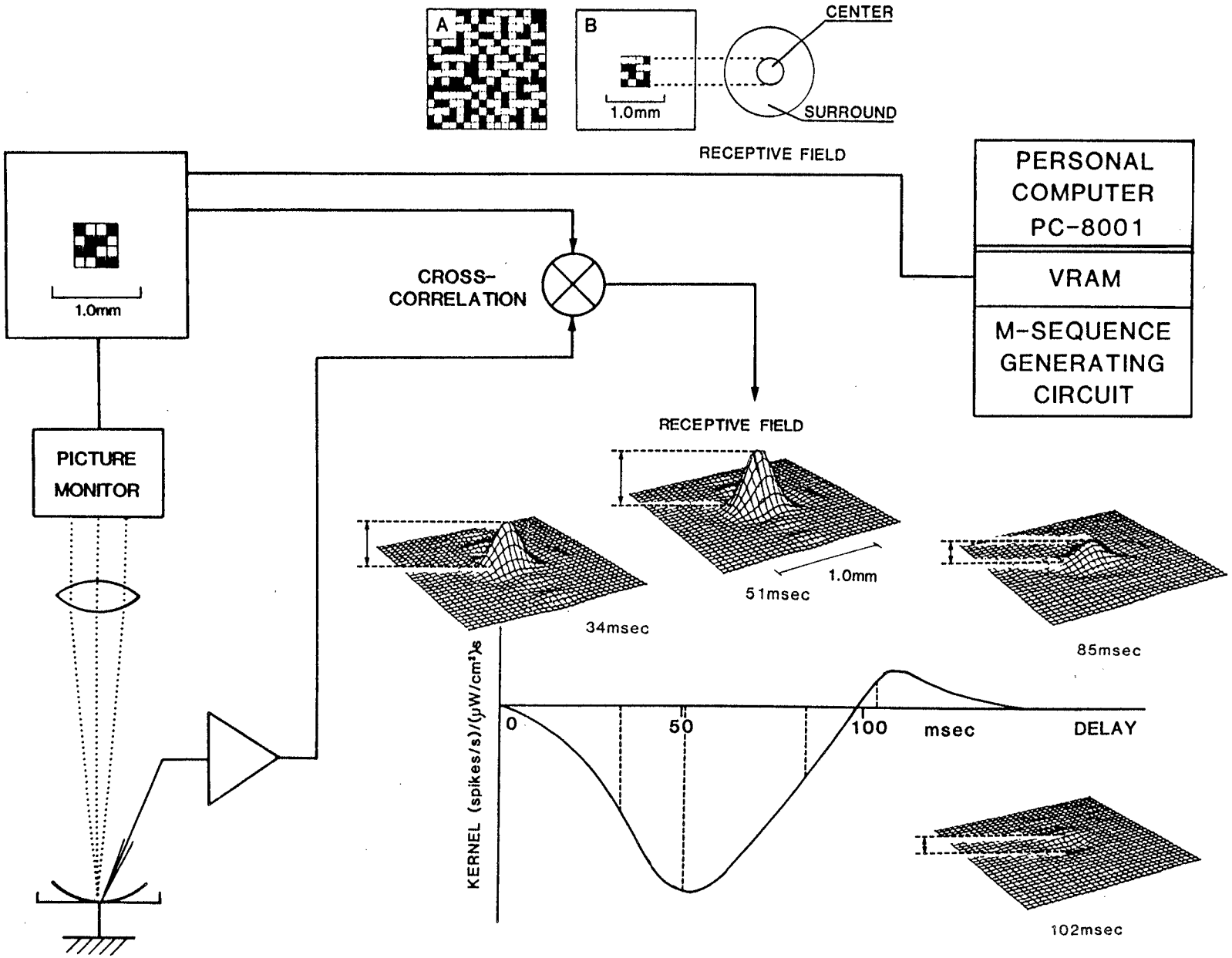

A
B
1.0mm
CENTER
SURROUND
RECEPTIVE FIELD
PERSONAL COMPUTER PC-8001
VRAM
M-SEQUENCE GENERATING CIRCUIT
1.0mm
CROSS-CORRELATION
PICTURE MONITOR
RECEPTIVE FIELD
1.0mm
51msec
34msec
85msec
KERNEL (spikes/s)/(μW/cm²)s
0
50
100
msec
DELAY
102msec

Fig. 4.1

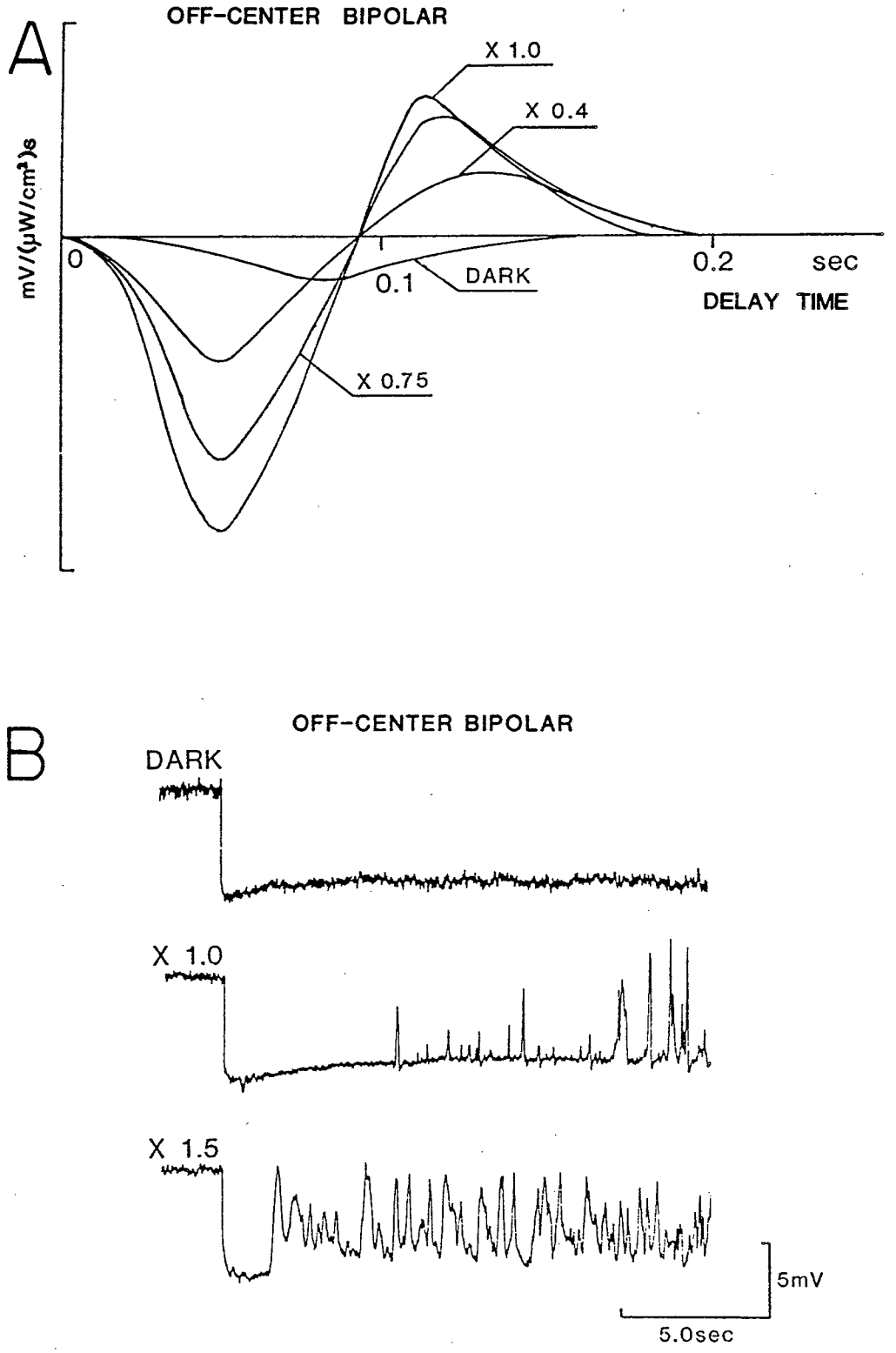

A
OFF-CENTER BIPOLAR
X 1.0
X 0.4
mV/(μW/cm²)s
0
0.1
DARK
0.2
sec
DELAY TIME
X 0.75
B
OFF-CENTER BIPOLAR
DARK
X 1.0
X 1.5
5mV
5.0sec

Fig. 4.2

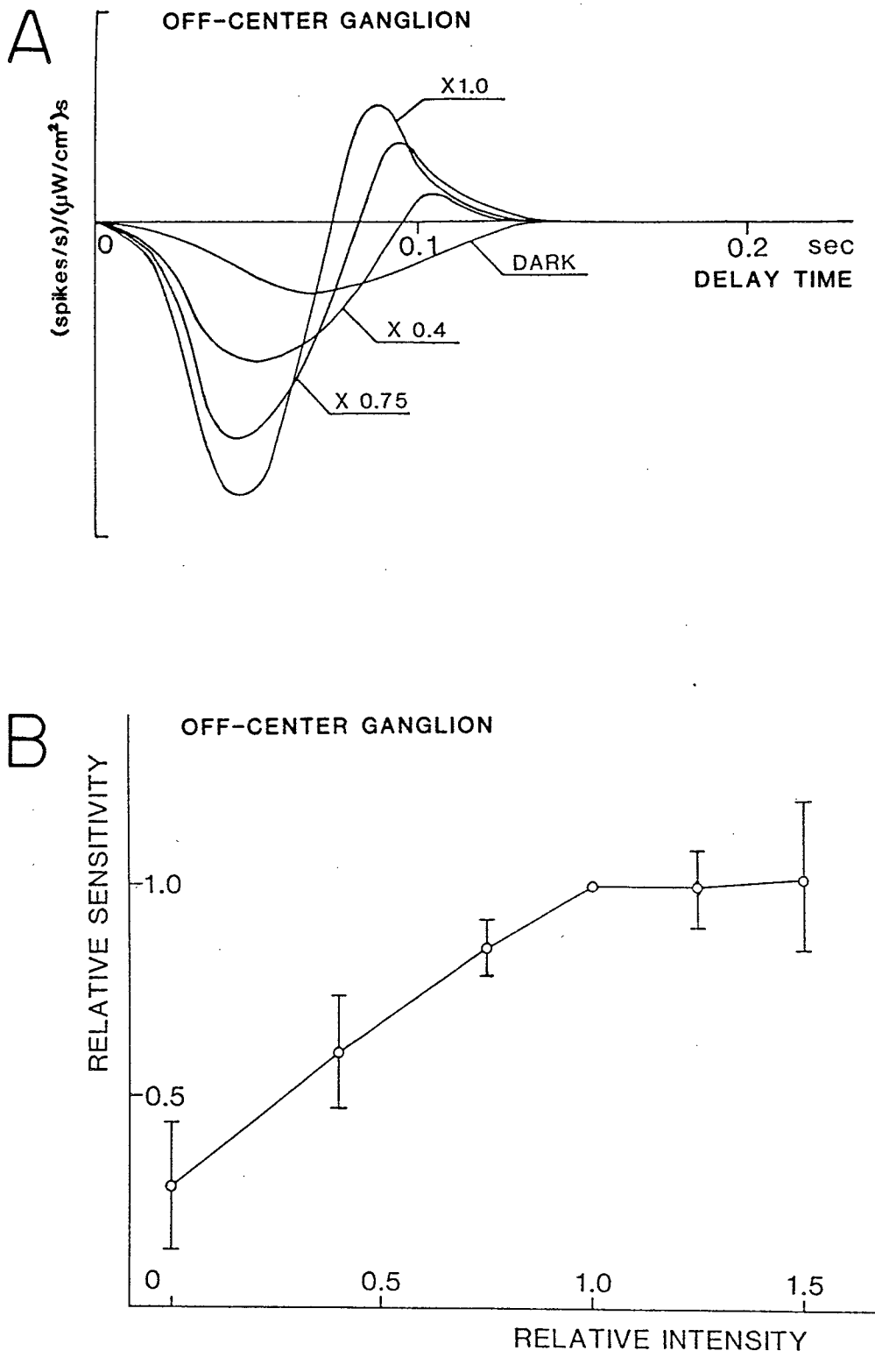

A
OFF-CENTER GANGLION
X1.0
(spikes/s)/(μW/cm²)s
0
0.1
0.2 sec
DELAY TIME
DARK
X 0.4
X 0.75
B
OFF-CENTER GANGLION
RELATIVE SENSITIVITY
1.0
0.5
0
0.5
1.0
1.5
RELATIVE INTENSITY

Fig. 4.3

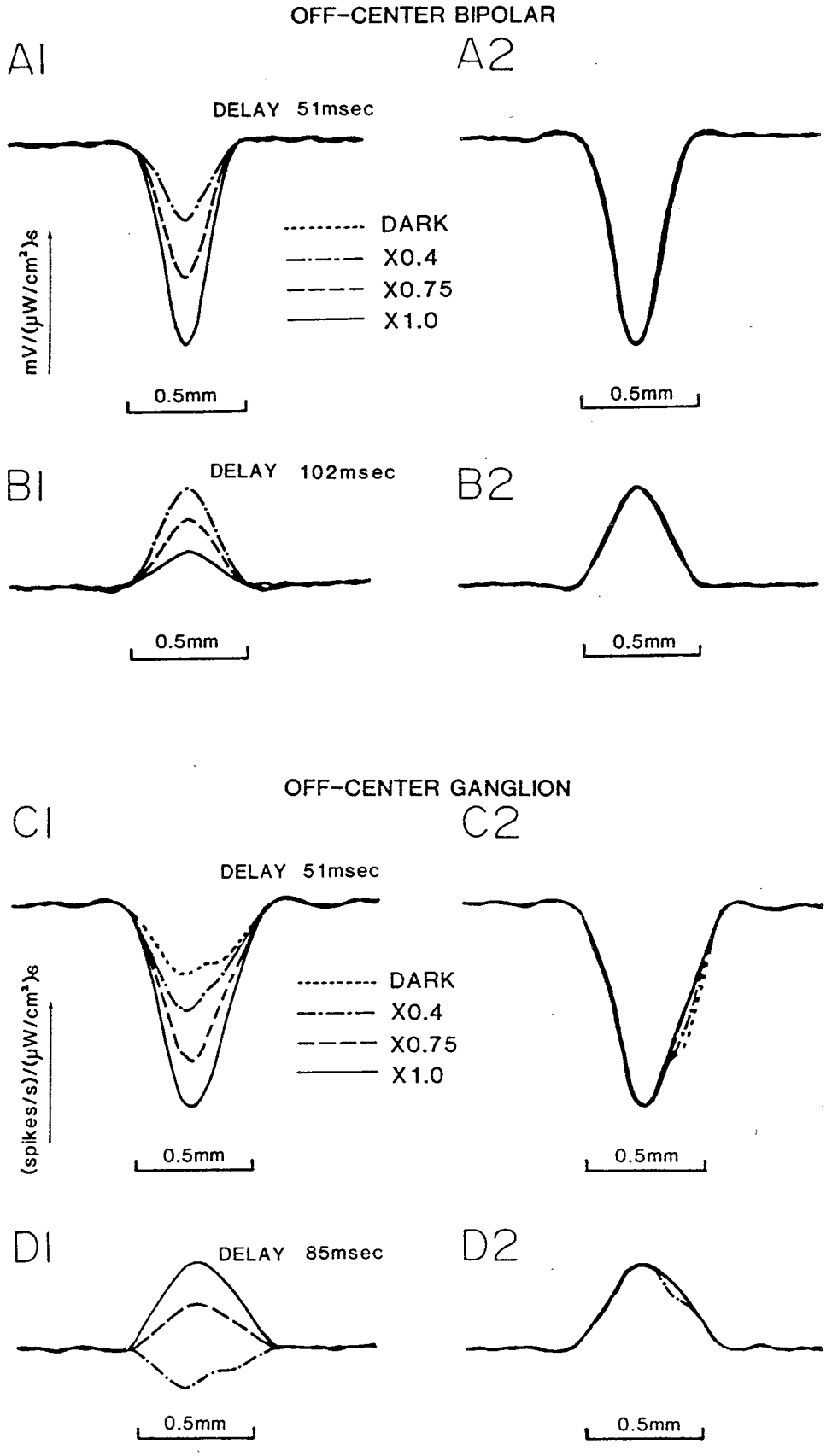

OFF-CENTER BIPOLAR
A1
A2
DELAY 51msec
DARK
X0.4
X0.75
X1.0
mV/(μW/cm²)s
0.5mm
0.5mm
B1
DELAY 102msec
B2
0.5mm
0.5mm
OFF-CENTER GANGLION
C1
C2
DELAY 51msec
DARK
X0.4
X0.75
X1.0
(spikes/s)/(μW/cm²)s
0.5mm
0.5mm
D1
DELAY 85msec
D2
0.5mm
0.5mm

Fig. 4.4

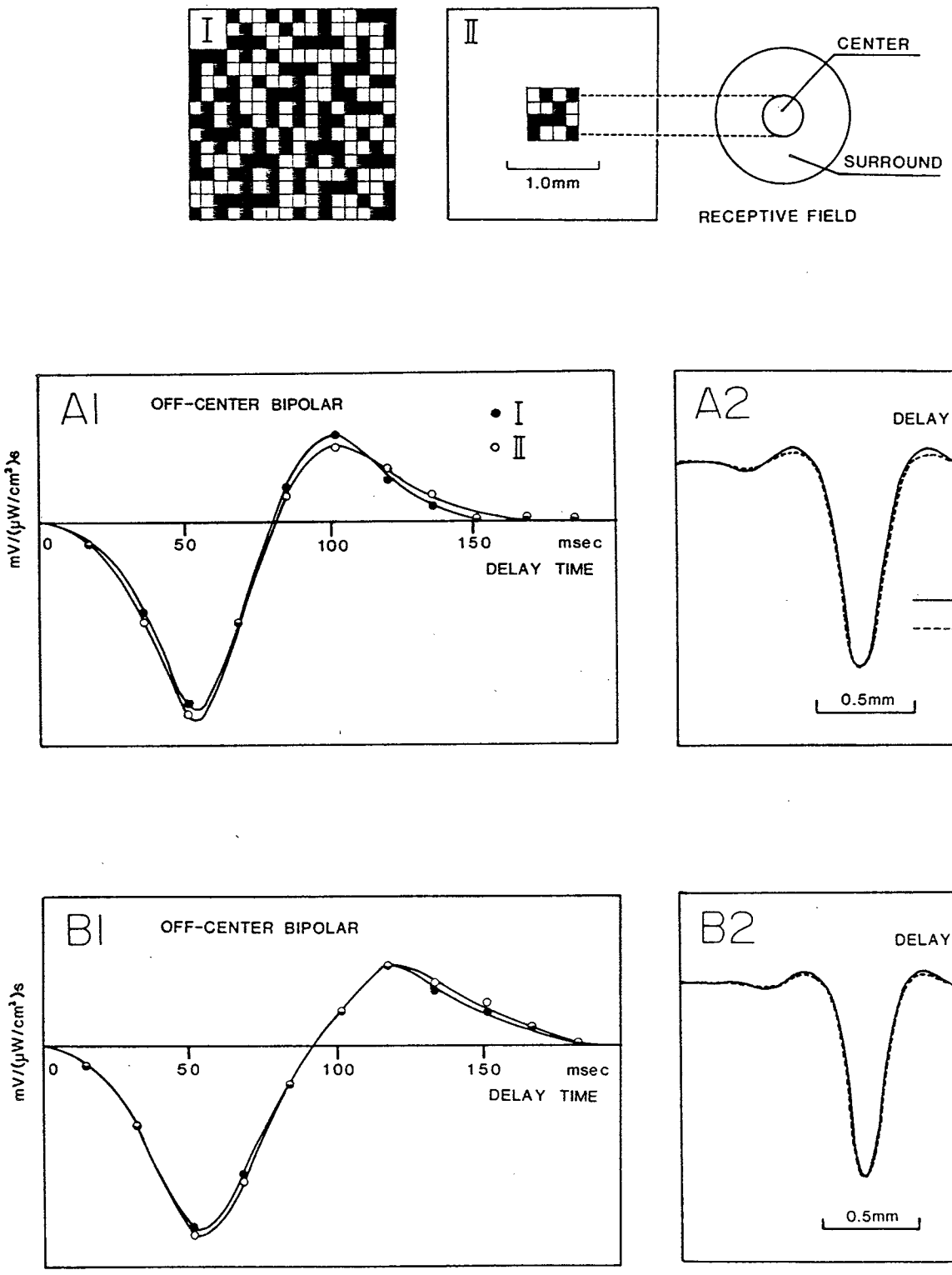

I
II
CENTER
SURROUND
1.0mm
RECEPTIVE FIELD
A1
OFF-CENTER BIPOLAR
I
II
mV/(μW/cm²)s
0
50
100
150
msec
DELAY TIME
A2
DELAY 51msec
I
II
0.5mm
B1
OFF-CENTER BIPOLAR
mV/(μW/cm²)s
0
50
100
150
msec
DELAY TIME
B2
DELAY 51msec
0.5mm

Fig. 4.5

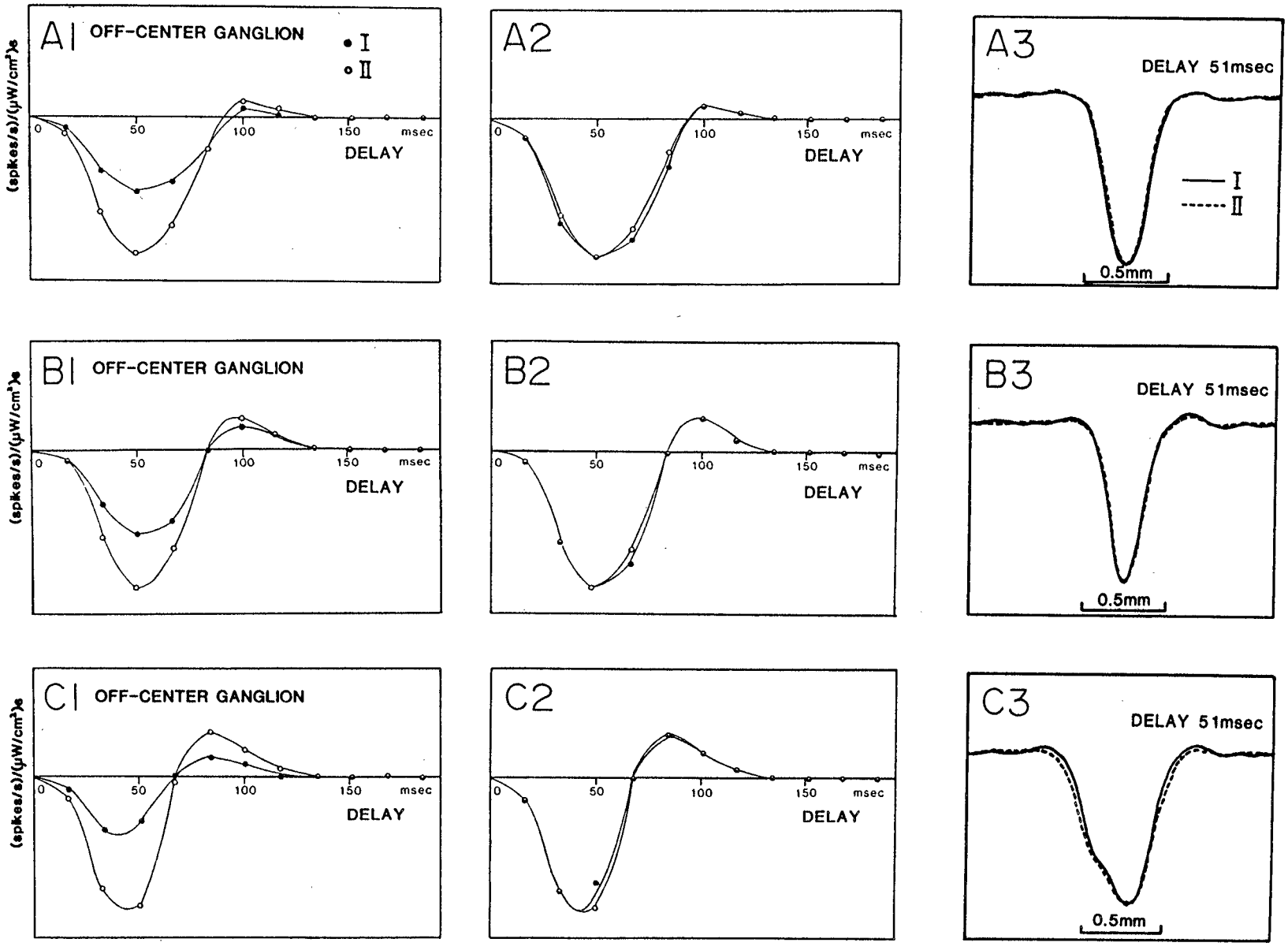
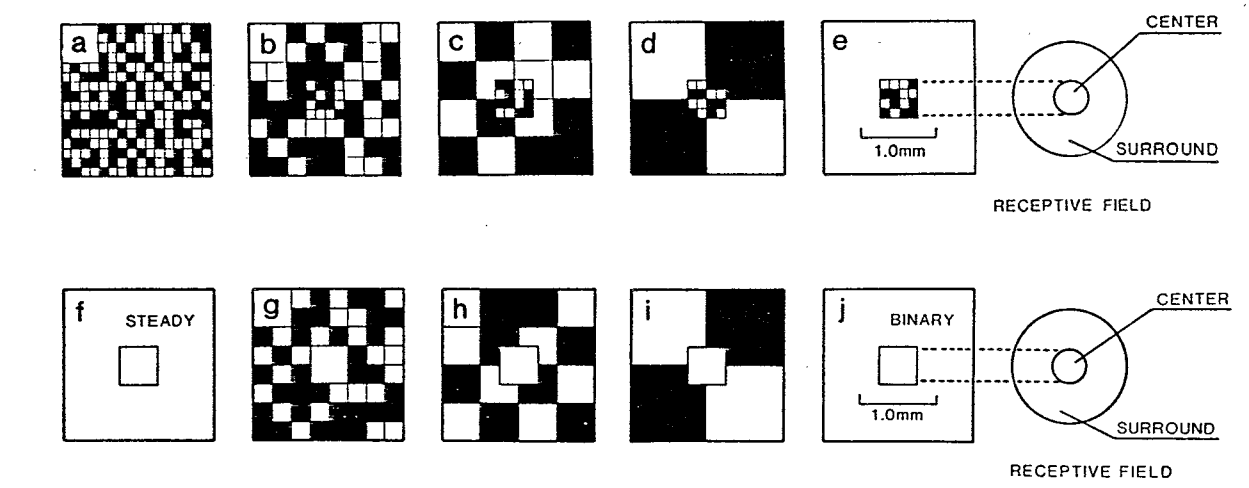

A1 OFF-CENTER GANGLION
• I
○ II
(spikes/s)/(μW/cm²)s
0
50
100
150
msec
DELAY
A2
DELAY
A3
DELAY 51msec
I
II
0.5mm
B1 OFF-CENTER GANGLION
B2
B3
C1 OFF-CENTER GANGLION
C2
C3

Fig. 4.6


a
b
c
d
e
CENTER
1.0mm
SURROUND
RECEPTIVE FIELD
f
STEADY
g
h
i
j
BINARY
CENTER
1.0mm
SURROUND
RECEPTIVE FIELD

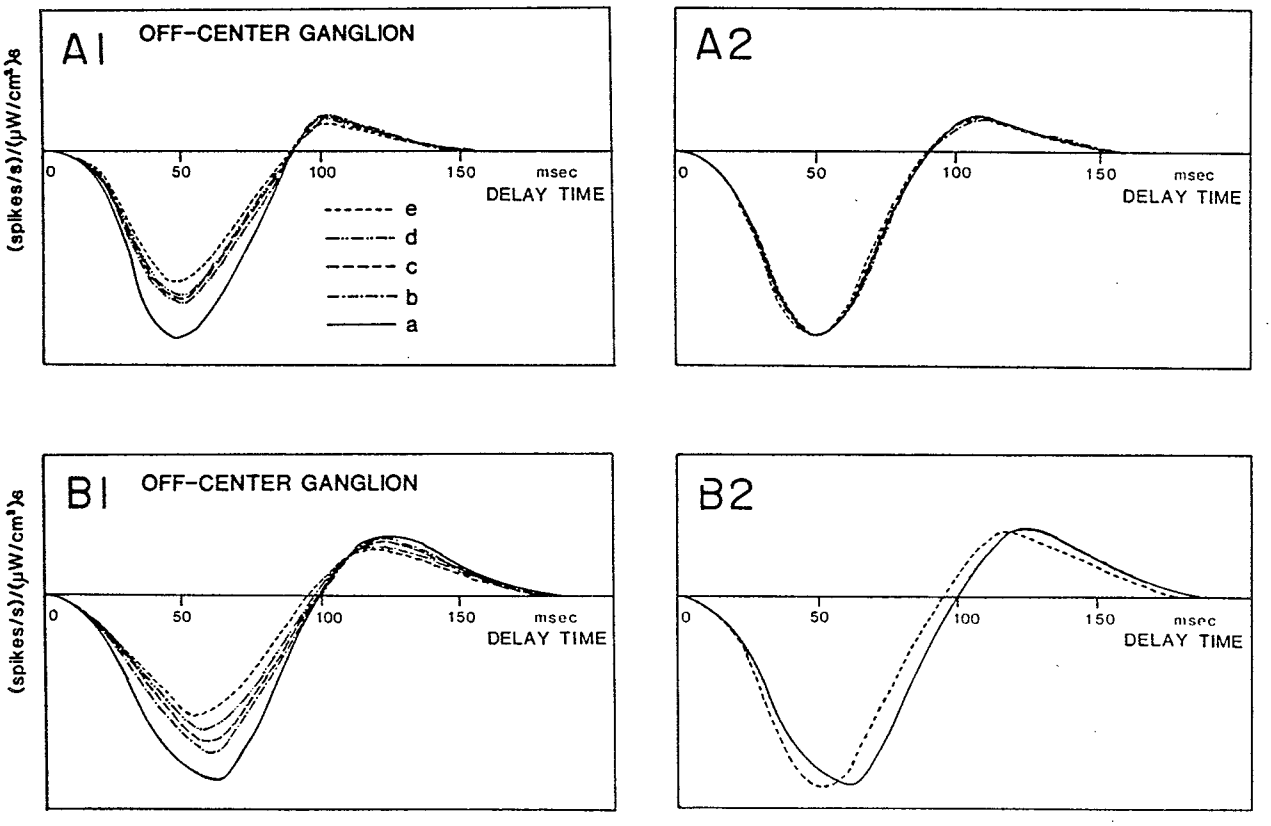

A1
OFF-CENTER GANGLION
(spikes/s)/(μW/cm²)ⁿ
0
50
100
150
msec
DELAY TIME
e
d
c
b
a
A2
0
50
100
150
msec
DELAY TIME
B1
OFF-CENTER GANGLION
(spikes/s)/(μW/cm²)ⁿ
0
50
100
150
msec
DELAY TIME
B2
0
50
100
150
msec
DELAY TIME

Fig. 4.7

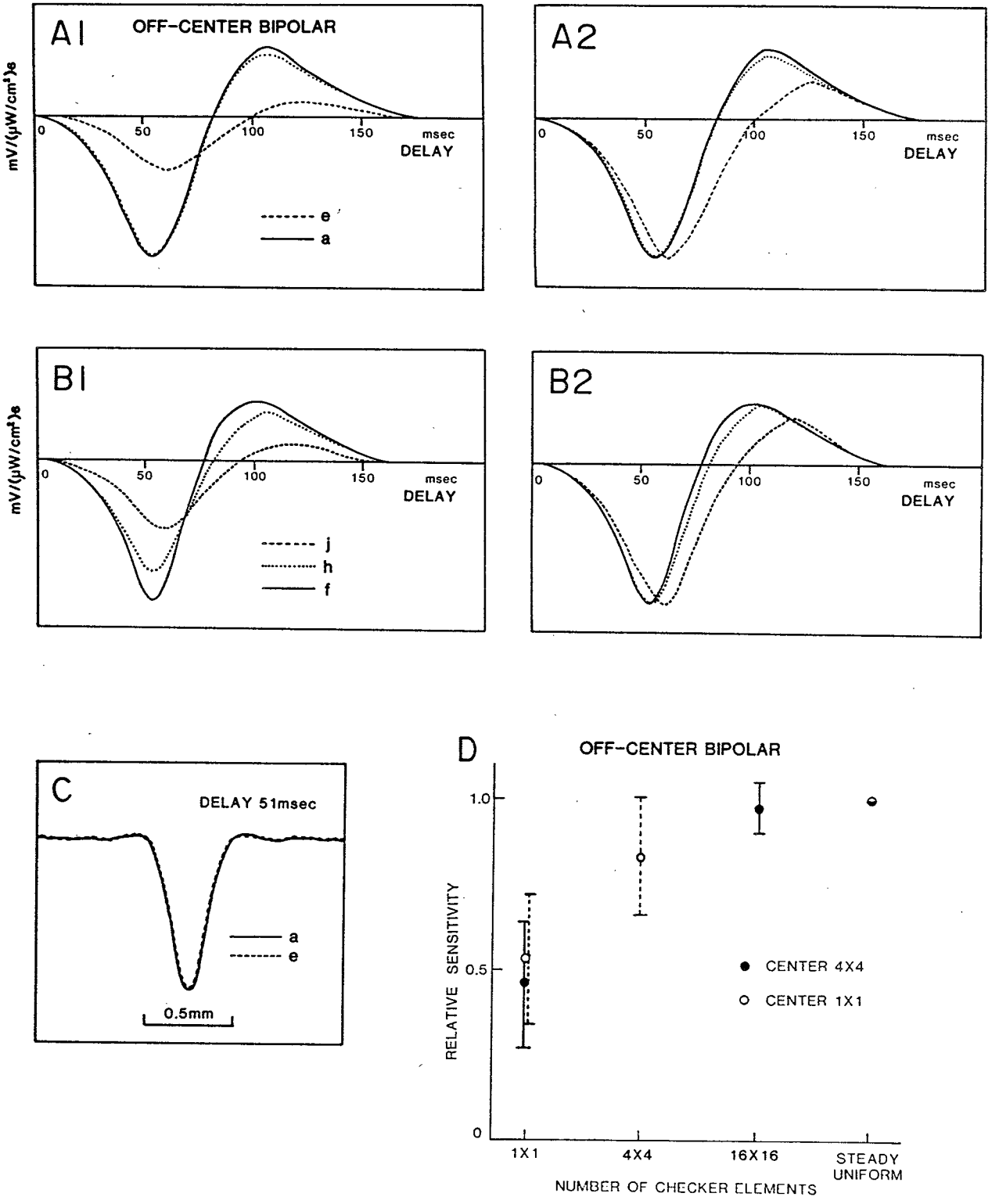

A1
OFF-CENTER BIPOLAR
mV/(μW/cm²)s
0
50
100
150
msec
DELAY
e
a
A2
B1
j
h
f
B2
C
DELAY 51msec
0.5mm
D
OFF-CENTER BIPOLAR
RELATIVE SENSITIVITY
1.0
0.5
0
CENTER 4X4
CENTER 1X1
1X1
4X4
16X16
STEADY UNIFORM
NUMBER OF CHECKER ELEMENTS

Fig. 4.8

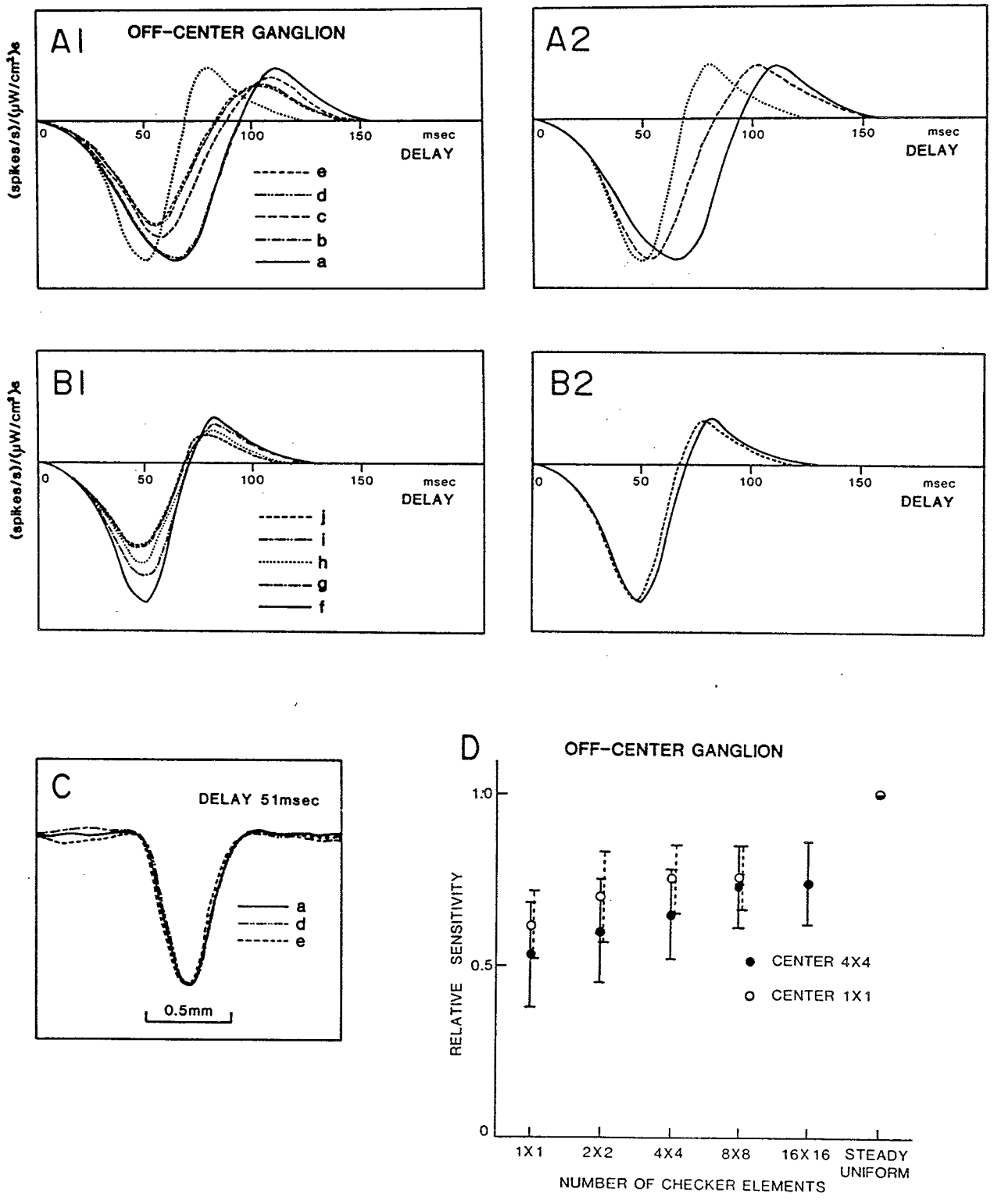

A1
OFF-CENTER GANGLION
(spikes/s)/(μW/cm²)s
0
50
100
150
msec
DELAY
e
d
c
b
a
A2
B1
j
i
h
g
f
B2
C
DELAY 51msec
0.5mm
D
OFF-CENTER GANGLION
RELATIVE SENSITIVITY
1.0
0.5
0
CENTER 4X4
CENTER 1X1
1X1
2X2
4X4
8X8
16X16
STEADY UNIFORM
NUMBER OF CHECKER ELEMENTS

Fig. 4.9

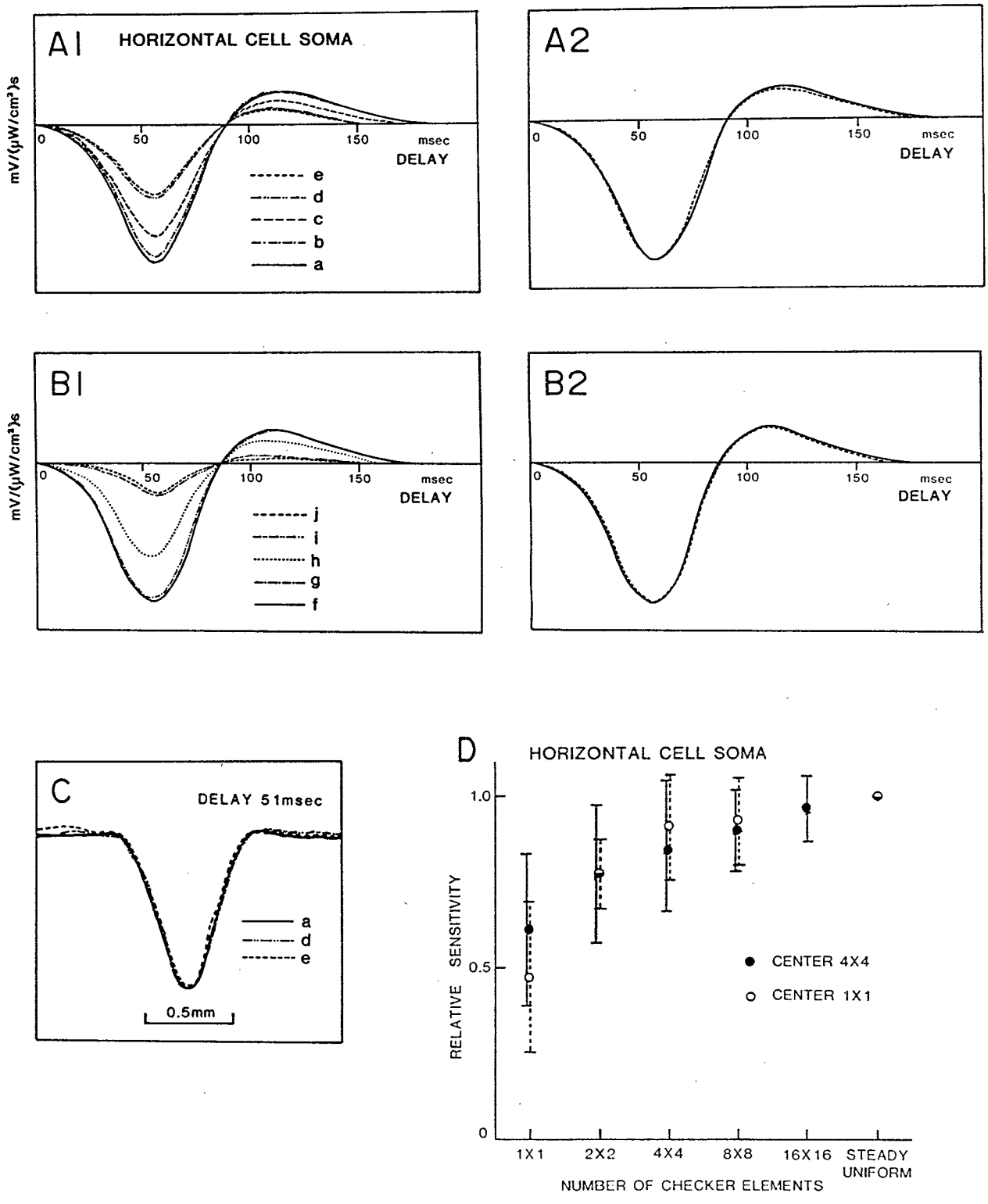

A1
HORIZONTAL CELL SOMA
mV/(μW/cm²)s
0
50
100
150
msec
DELAY
e
d
c
b
a
A2
0
50
100
150
msec
DELAY
B1
mV/(μW/cm²)s
0
50
100
150
msec
DELAY
j
i
h
g
f
B2
0
50
100
150
msec
DELAY
C
DELAY 51msec
a
d
e
0.5mm
D
HORIZONTAL CELL SOMA
RELATIVE SENSITIVITY
1.0
0.5
0
CENTER 4X4
CENTER 1X1
1X1
2X2
4X4
8X8
16X16
STEADY UNIFORM
NUMBER OF CHECKER ELEMENTS

Fig. 4.10

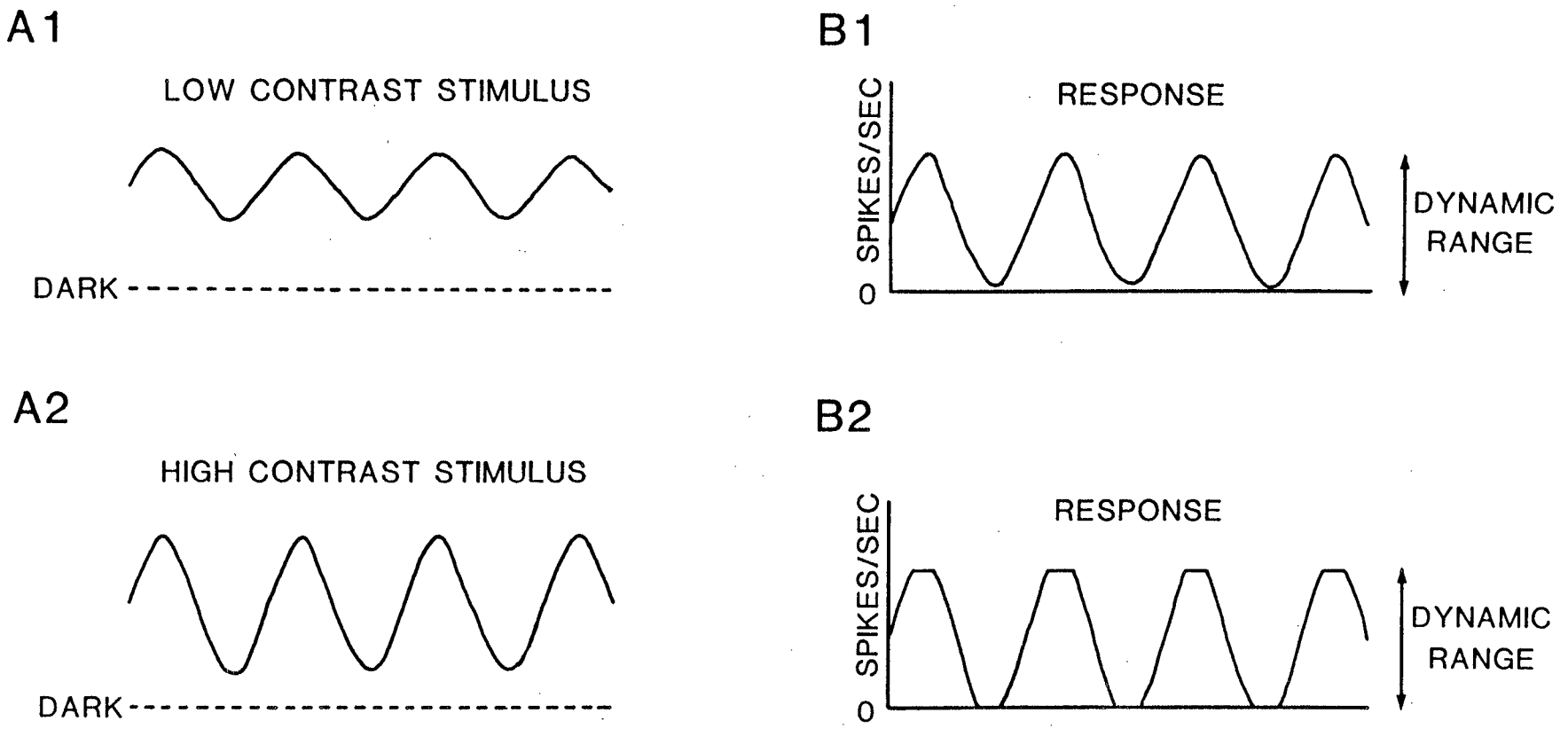

A1
LOW CONTRAST STIMULUS
DARK
A2
HIGH CONTRAST STIMULUS
DARK
B1
RESPONSE
SPIKES/SEC
0
DYNAMIC RANGE
B2
RESPONSE
SPIKES/SEC
0
DYNAMIC RANGE

Fig. 4.11

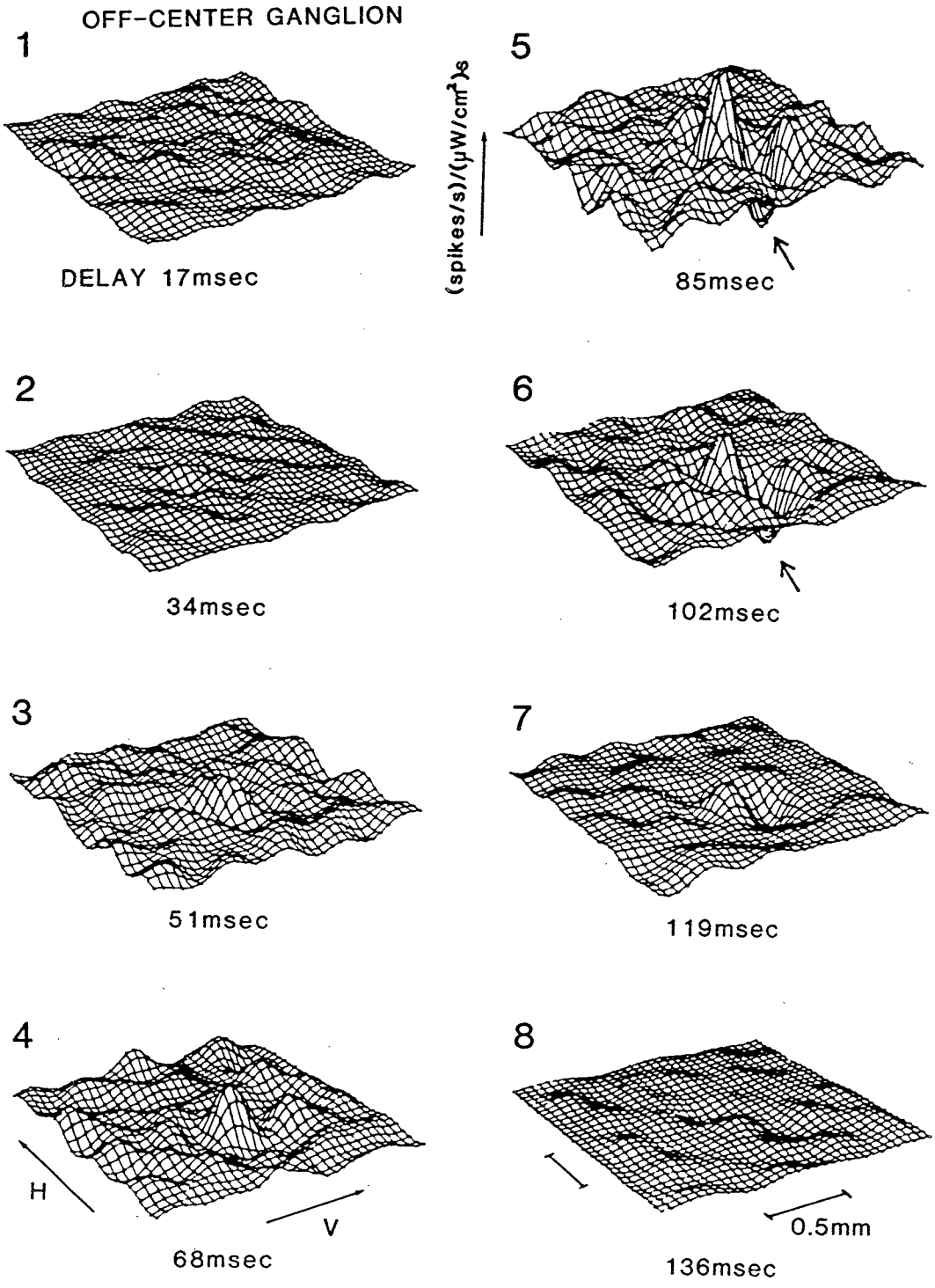

OFF-CENTER GANGLION
1
DELAY 17msec
2
34msec
3
51msec
4
H
V
68msec
5
85msec
6
102msec
7
119msec
8
0.5mm
136msec
(spikes/s)/(μW/cm²)s

Fig. 4.12

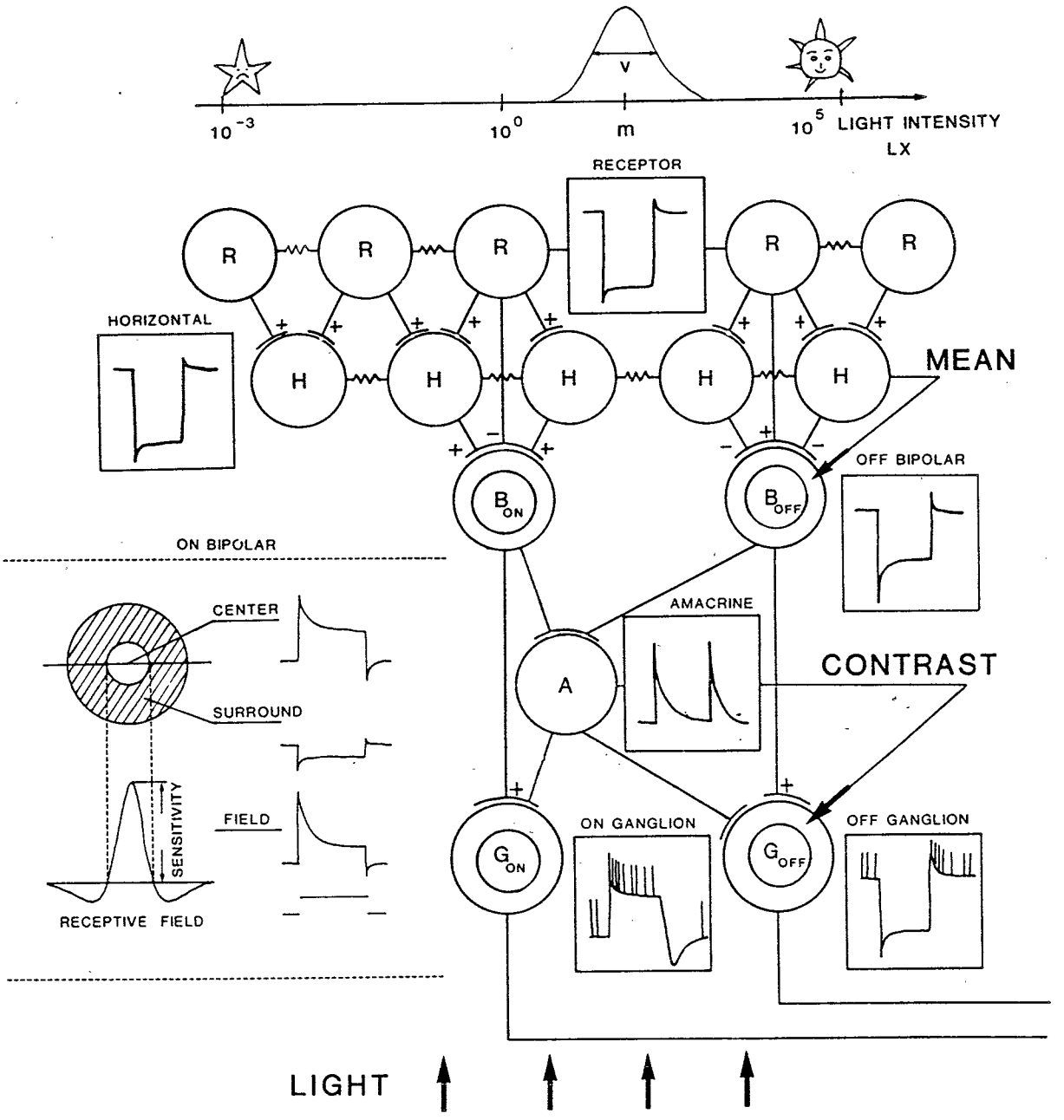

V
10^{-3}
10^{0}
m
10^{5}
LIGHT INTENSITY
LX
RECEPTOR
R
HORIZONTAL
H
MEAN
OFF BIPOLAR
B_{ON}
B_{OFF}
ON BIPOLAR
CENTER
SURROUND
FIELD
SENSITIVITY
RECEPTIVE FIELD
AMACRINE
A
CONTRAST
ON GANGLION
OFF GANGLION
G_{ON}
G_{OFF}
LIGHT

Fig. 4.13

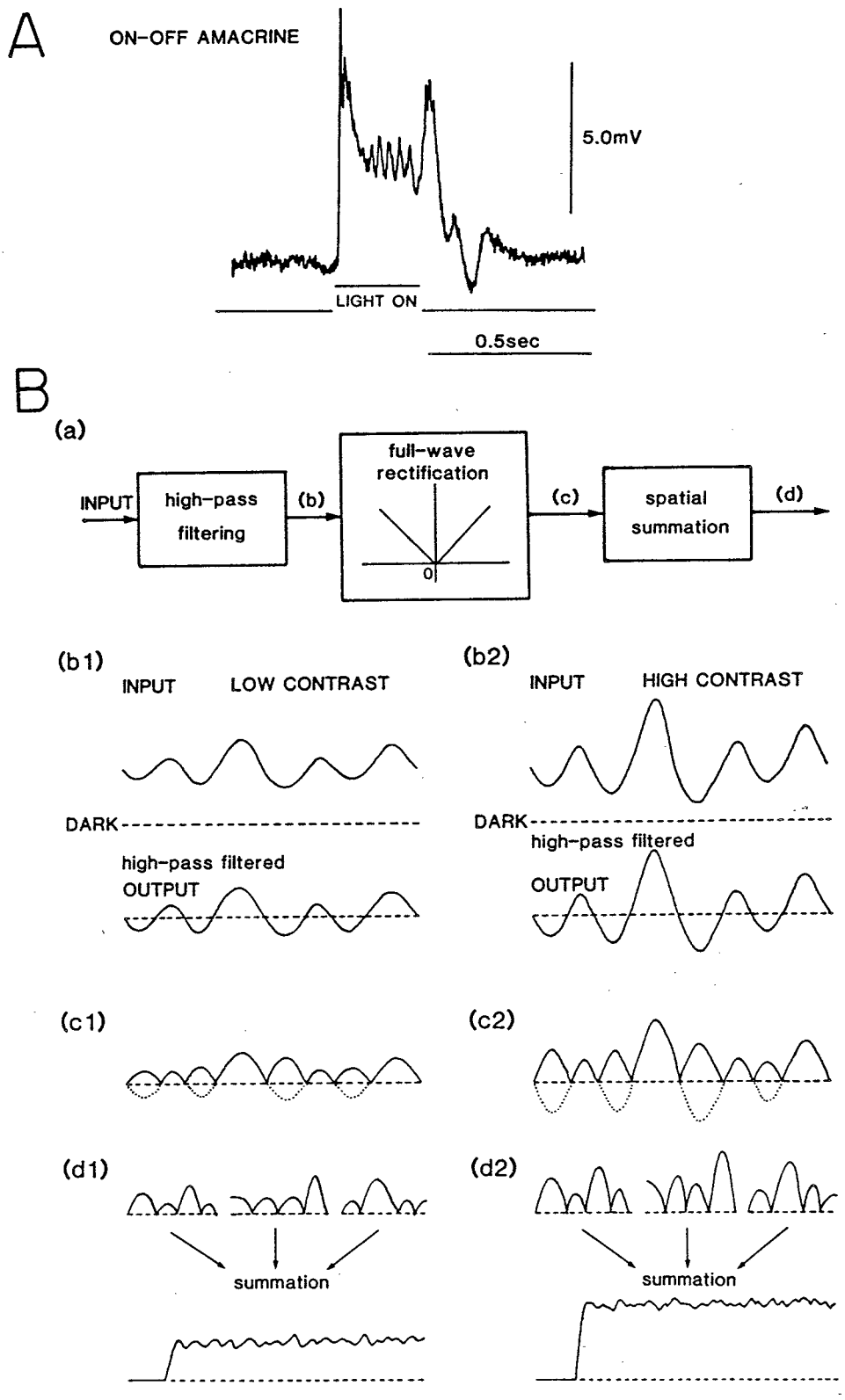

A
ON-OFF AMACRINE
5.0mV
LIGHT ON
0.5sec
B
(a)
INPUT
high-pass filtering
(b)
full-wave rectification
0
(c)
spatial summation
(d)
(b1)
INPUT
LOW CONTRAST
DARK
high-pass filtered OUTPUT
(b2)
INPUT
HIGH CONTRAST
DARK
high-pass filtered OUTPUT
(c1)
(c2)
(d1)
summation
(d2)
summation

Fig. 4.14

CHAPTER 5

REGULATORY EFFECTS OF DOPAMINE ON SPATIO-TEMPORAL DYNAMICS OF CATFISH RETINAL NEURONS

Introduction:

There are several lines of evidence to suggest that dopamine is a neurotransmitter in the retina. Dopamine(DA) is synthesized in the retina (Iuvone et al., 1978) and is confined to either amacrine or interplexiform cells (Dowling and Ehinger, 1978) and can be released by light stimulation (Kramer, 1971). Furthermore, it is reported that in the carp retina DA stimulates adenylate cyclase (Brown and Makman, 1972; Watling and Dowling, 1981), and that a DA-sensitive adenylate cyclase (Watling et al., 1979) is localized to horizontal cells (Van Buskirk and Dowling, 1981).

The functional role of DA in the retina has been intensively studied in horizontal cells. Exogenously applied DA results in the shrinkage of receptive field profile accompanied by the augmentation of the center response (Negishi and Drujan, 1979; Cohen and Dowling, 1983). DA has also been shown to decrease the diffusion of fluorescent dye(Lucifer-yellow) between horizontal cells (Teranishi et al., 1983b; Teranishi et al., 1984; Piccolino et al., 1984; Negishi et al., 1985). Electrical coupling resistance between horizontal cells greatly increases by the application of DA in both intact retina (Piccolino et al., 1984, 1985) and recoupled dissociated cells (Lasater and Dowling, 1985), suggesting that narrowing of the receptive field profile is due to the alteration of electrical coupling between horizontal cells (Negishi et al., 1985). In the dark adapted

retina, horizontal cell somata show alterations in responsiveness and receptive field size very similar to those induced by DA (Mengel and Dowling, 1985). This result suggests that DA plays an important role in the dark adaptation mechanism.

In carp bipolar cells, DA enhances the central response to light, and depresses the surround response (Hedden and Dowling, 1978). In rabbit retinal ganglion cells, DA increases the spontaneous activity of off-center cells and decreases spontaneous and light-induced responses of on-center cells (Ames and Pollen, 1969). Furthermore, DA antagonists reduce the leading edge response of on-off directionally selective cells (Jensen and Daw, 1983, 1984). In the cat retina, spontaneous and light-induced responses of all ganglion cells are suppressed by DA (Thier and Alder, 1984).

Thus, in spite of considerable amount of knowledge about DA effects on retinal neurons, DA's functional role in retinal information processing remains to be fully understood. The aim of this section is to explore the functional role of DA in signal processing of horizontal, bipolar, and ganglion cells by relating with their surround mechanisms. The first part of this chapter describes effects of DA on horizontal cell somata and their axons in the catfish retina. In the next part, effects of DA on bipolar and ganglion cells are analysed by the use of spatio-temporal random noise.

Materials and Methods:

Experiments were conducted with the eye-cup preparation of channel catfish, Ictalurus punctatus. In some fish, dopamine-

containing cells were destroyed by intraocular injection of 6-hydroxydopamine(10 μg/eye, two times on successive days) 2-3 weeks prior to electrophysiological experiments (Negishi et al., 1982, Negishi et al., 1983). In the analysis of bipolar and ganglion cells, suppression of release of DA from dopamine-containing cells was performed by hypodermic injection of reserpine(1.0mg/fish) one or two days prior to the experiments. To analyse spatial properties of horizontal cells, a spot of light on a X-Y display(608; Sony Tektronix) was projected onto the retinal surface. Measured on the retina, the spot was 100 μm in diameter and 10 $\mu W/cm^2$ in irradiance. The spot was flashed and displaced, for each flash, in 90-μm steps or was swept back and forth(without interruption) along a straight line at a speed of 0.95 mm/sec. Intracellular recordings were made from the soma or the axon terminal of photopic L-type horizontal cells. The two parts of the horizontal cell could easily be identified based on their receptive-field size; the soma field measured by a slit of light had a half-width of 0.45 to 0.55 mm , and the axon field had a half-width of more than 1 mm (Davis and Naka, 1980). Some cells(15 somas and 12 axons) were morphologically identified by procion yellow dye, and all of them satisfied the criterion of the receptive field size. In the experiment on bipolar and ganglion cells, spatio-temporal random noise(random checkered pattern) was employed to reveal both spatial and temporal properties of the cell. Dopamine was applied as a brief jet(2-4 mM in the Ringer's solution) from a nebulizer. The concentration of DA applied as a jet was assumed to be 20-40 μM (Sugawara and

Negishi, 1973).

After electrophysiological experiments, the eye-cup preparations were fixed in a paraformaldehyde(4%)/glutaraldehyde (0.5%)/sucrose(35%)(FGS) solution for several hours. The retina was then isolated from the sclera, choroid, and, if possible, from the pigment epithelium, flat-mounted with the vitreal side facing up on a glass plate, and dried over Zeolite(Wako) in a desiccator for several hours. The flat-mounted retinas were examined under a fluorescence microscope(Nikon EF). Some retinas were softened again in the FGS solution and were cross-sectioned to 15-μm thickness. The retinal sections were dried, sealed with Entellan(Merk), and examined microscopically. In this manner, cells that had accumulated DA were seen in both flat-mounts and cross sections.

Results:

Typical responses from a single L-type horizontal cell soma are shown in Fig. 5.1; the upper traces(A,B) are the responses to stepwise displacement of a flashing spot; the lower traces(C,D), those to a sweeping spot. The potential amplitude was maximal when the spot was placed on the recording site. In both traces, the responses at the left side(A,C) were obtained before, and those at the right side(B,D) after, application of DA. Upon DA application, irregular artificial shifts occurred in the potential trace in some cases. Subsequently, the resting potential behaved in various manners depending on individual cells; 13 cells depolarized, 10 cells hyperpolarized in a range of several millivolts, and the other 28 cells were unchanged.

Consistent changes in the light-evoked response were observed regardless of the directions of the resting potential shift induced by DA. The amplitude of the response evoked at the recording site increased, whereas that of the responses evoked by an eccentric spot decreased. This was seen in the sharper slope of the decremental amplitude curves of response with spot displacement(e.g., compare curves B and D with A and C, respectively). The maximum amplitude (at the recording site) was 11.4±3.0(SD)mV before(n=32) and 18.1±4.4(SD)mV after DA application(n=29). The responses from axon terminals were less affected by DA, as will be shown later. The maximal amplitude of the control axon-terminal responses was 5.7±0.6mV(n=24) and with DA the amplitude increased to 6.5±1.8mV(n=20). In general, the DA effects appeared immediately or in a few minutes after DA application and lasted for 10 to 20 min afterward. The application could be repeated 3-4 times after 30-min intervals for each preparation.

Fig. 5.2A shows the normalized response of horizontal-cell soma to a sweeping spot; each trace represents responses of four different somata to a single sweep of the spot. The half-decay width of response curves is approximately 0.64 ± 0.06(SD) mm(n=28). Upon DA application, the response curve became sharper, the average half-decay width being 0.29 ± 0.03 mm(n=24)(Fig. 5.2B). The same experiment was conducted in the retinas from which DA cells had been deprived by a prior treatment with 6-hydroxydopamine(6-OHDA). In general, the amplitude of S-potentials recorded from treated retinas was smaller(by about

20%) than that from normal retinas. The response curve to a sweeping spot was relatively wide, the half-decay width being 0.84 ± 0.10 mm(n=18)(Fig. 5.2C). Upon DA application to treated retinas, the response curve had nearly the same half-decay width of 0.30 ± 0.06(n=16) as that of DA-applied normal retinas(Fig. 5.2D).

Application of DA had little effect on the responses recorded from the horizontal cell axon in the normal or DA-deprived retinas. Examples are shown in Fig. 5.3, in which horizontal cells' receptive fields were plotted with a sweeping spot of light. The half-decay width was 1.10 ± 0.12(SD) mm(n=23) and 1.33 ± 0.12 mm(n=17) in normal(A) and DA-cell-deprived retinas(C), respectively, and they were unchanged after DA application(1.11 ± 0.12mm(n=18) in B and 1.33 ± 0.16 mm(n=14) in D). The peak of the curve appears to be slightly sharper after DA application.

Fluorescence photomicrographs(Fig. 5.4) show cells that had accumulated DA applied during electrophysiological experiments. In normal retinas(A and C), DA was taken up by both DA cells(larger in size) and indoleamine-accumulating(IA) cells(smaller). Since DA cells were destroyed in retinas previously treated with 6-OHDA, only IA cells that had accumulated the applied DA can be seen in flat-mounts(B) and cryosections(D).

Effects of dopamine on ganglion cells in the normal retina:

Horizontal cells are thought to play an important role in the formation of the receptive field surround of ganglion cells

(Maksimova, 1970, Naka and Nye, 1971). It is reasonable, therefore, to suppose that dopamine-induced changes of spatial properties in horizontal cells may also affect the response properties of ganglion cells. First, effects of dopamine on ganglion cells in normal retinas were examined by measuring spatio-temporal receptive fields(STRFs). Fig. 5.5 shows the typical example of the effects of DA on off-center ganglion cells. The cell of Fig. 5.5 had the receptive field with circular shape. The receptive field profile did not change by DA application(A2). By contrast, the incremental sensitivity increased by 30% after DA administration(A1). Furthermore, return to the zero level of temporal kernel(cf. Materials and Methods of chapter 4) was slightly quickened by DA. This effect appeared at 2-3 min after the application of DA and returned to the original level 20min later. The recovery time was similar to that of horizontal cell somata. These results were consistently obtained in thirty-two off units examined. On the other hand, DA did not alter the incremental sensitivity of nor the receptive field of on-center ganglion cells(Fig. 5.6).

Effects of DA on ganglion cells in reserpine-treated retinas:

Effects of DA on ganglion cells were examined in reserpine-treated retinas. Reserpine is thought to inhibit the vesiclar storage of DA in dopaminergic cells(Cooper et al., 1982). Therefore, as a result of depletion of endogenous DA, DA is not released from DA-releasing dopaminergic cells in reserpine-treated retinas. Experiments were carried out one or two days after hypodermic injection of reserpine. As shown in Fig.5.7, an

on-center ganglion cell tonically responded to the field stimulation without marked reduction of spike discharge(upper trace of A1). When DA was applied, the response time course drastically changed, i.e., initial sudden rise of spike frequency followed by rapid decrement of spike production to about half of the initial spike frequency(lower trace of A1). The initial peak of spike frequency was similar before and after DA application.

However, the temporal property of the receptive field center of an on-center ganglion cell to the 16x16 random checkered pattern changed significantly depending upon the presence or absence of DA. A2 of Fig. 5.7 shows the temporal kernel of the receptive field center of an on-center ganglion cell obtained with 16X16 random checkered pattern. The temporal property of the center is characterized by the monophasic and sluggish kernel time course in addition to the low incremental sensitivity. DA application resulted in the acceleration of kernel time course accompanied by a marked increase of incremental sensitivity. Furthermore, the kernel waveform changed from monophasic to biphasic. On the other hand, as shown in A3 of Fig. 5.7, the spatial profile of the receptive field was nearly identical before and after application of DA.

Similar results were obtained in off-center ganglion cells. In the reserpine-treated retina, field illumination caused off-center ganglion cells to show slow decrement of spike discharges and the vigorous off-response followed by sluggish decrement of spike frequency(B1 of Fig. 5.7). Administration of DA induced rapid changes of the response time course. The initial spike

frequency of 110 spikes/sec in the off-response phase and the mean spike frequency of 50 spikes/sec after the cessation of stimulus were nearly identical before and after DA application. The temporal kernels of B2 indicate that sluggish and monophasic responses changed to brisk and biphasic reponses together with drastic increase in the incremental sensitivity. The spatial property underwent only minor changes(B3); the receptive field profile after DA application gave rise to a small inflection in the second peak. However, the half width of receptive field profile changed little after DA application.

Fig. 5.8 shows effects of DA on the temporal property of receptive field center of an off-center ganglion cell in the presence or absence of the surround illumination. The stimulus pattern was the 16x16 random checkerd pattern(in both cases of center and surround illumination) or the 4x4 random checkered pattern falling on the center region(in the case of center stimulation) ; the size of one checker element was 120 um on the retinal surface. The stimulus intensity of 0 Log unit was 1.0 $\mu W/cm^2$ and the intensity was attenuated from 0 Log to -4 Log with neutral density filters. The temporal kernels of Fig. 5.8 were obtained by cross-correlating between unattenuated light and responses. In the reserpine-treated retina, temporal kernels of off-center cells showed a monophasic time course, indicating a lowpass filtering characteristics in time. The amplitude of temporal kernels increased monotonically according to the diminution of stimulus intensity in both field illumination(A1) and center illumination(A2). The time-to-peak of temporal kernels

delayed monotonically from 55 msec(0 Log) to 110 msec(-3 Log) with the decrease of stimulus intensity in both field(A1) and center illuminations(A2). The application of DA induced drastic changes in the temporal property associated with field illumination. After administration of DA, the temporal kernels from 0 Log, -1 Log, -2 Log stimulation became biphasic and their kernel amplitudes increased greatly compared with those prior to the DA application. The temporal kernels from field illumination of -3 Log intensity were similar before and after the DA administration, except for reduction in the latency of kernel. Unlike before DA application, the amplitude of temporal kernels decreased monotonically with the diminution of stimulus intensity. Latency to the peak of temporal kernels delayed with decrease of the illumination intensity as was seen before DA application. On the other hand, the temporal property with center illumination(B2) did not seem to change after DA application. These observations suggest that the receptive field surround does not work well without DA in spite of the surround illumination. These results were obtained irrespective of the size of the receptive field center in both on-center and off-center cells.

Effects of DA on bipolar cells:

The results from ganglion cells strongly suggest the participation of DA on center-surround interaction. On- and off-center ganglion cells receive their signals from on- and off-center bipolar cells, respectively (Famiglietti and Kolb, 1976; Naka, 1977). Hence, receptive field properties of ganglion cells reflect much those of bipolar cells.

As shown in Fig. 5.9, effects of DA on bipolar cells were quite similar to those on ganglion cells. Preparations examined were reserpine-treated retinas in which DA is not released from DA-releasing dopaminergic cells as a result of depletion of endogenous DA(Cooper et al., 1982). The off-center bipolar cell of A in the reserpine-treated retina showed a sustained hyperpolarization of about 5mV to the field illumination. When DA was applied, this off-center bipolar cell responded with an initial large hyperpolarization of about 5 mV followed by a prominent decrease of sustained hyperpolarization to about 1.5mV. The amplitude of initial hyperpolarization was nearly identical before and after DA application. These response features were similar to those produced by spot and field illuminations on the receptive field of bipolar cells in normal retinas (Naka and Ohtsuka, 1975). In the reserpine-treated retina, the response to field illumination was similar to spot illumination.

The response from receptive field surround was examined by a sweeping slit moving to one direction at a speed of 0.95mm/sec(0.1mm x 4mm in size and 5$\mu W/cm^2$ in irradiance). Fig. 5.9, C shows the responses of an off-center bipolar cell in the reserpine-treated retina to the moving slit of light before and after DA application. Before DA application, the receptive field profile was composed of a center region with the half-width of about 200 μm without clear surround component. DA application induced a unanimous appearance of surround component whose amplitude was about one-fourth of the center amplitude, whereas the receptive field profile of center region was nearly identical

with that obtained before DA application.

Drastic effects were also observed in the response to random checkered pattern illuminating the whole receptive field. Thus, B shows the response of the off-center bipolar cell to the 16x16 random checkered pattern which had the spatial configuration of Fig. 5.8. In the reserpine-treated retina, the cell showed a sustained hyperpolarization of about 5mV. DA application drastically reduced this level, and produced random membrane fluctuation, which is indicative of the responsiveness to spatio-temporal changes of the stimulus light. The temporal property of the receptive field center of an off-center bipolar cell in a reserpine-treated retina was examined before and after DA administration(Fig. 5.9D). The temporal kernel showed a monophasic time course which was very slow. After DA application, the incremental sensitivity increased greatly in addition to the speed up of kernel time course. Furthermore, the kernel waveform changed from monophasic to biphasic. Similar results were obtained in on-center bipolar cells(not illustrated).

Relationship between S-potentials and the incremental sensitivity of ganglion cells:

The results described so far suggested that the surround illumination without DA does not fully contribute to the regulation of the receptive field center. At least two factors for causing these phenomena in reserpine-treated retinas(cf. Figs. 5.7, 5.8, 5.9) can be inferred; one is extreme reduction of the S-potentials in the absence of DA, so that there should be little surround signal to regulate the center mechanism.

Alternatively, the surround signal in itself may be adequately generated, but its transmission to the receptive field center is blocked. To examine these possibilities, the following experiments were performed.

As shown in Fig. 5.10A, the S-potential from a horizontal cell soma in the reserpine-treated retina responded with a slow hyperpolarization of 15mV to field illumination. The response reached its plateau level(15mv from the dark level) in about 0.6sec after the initiation of light. DA application induced changes in the response waveform to the same step illumination of field light. The hyperpolarization became maximal at about 0.1sec. Hyperpolarization after DA increased by 7.5mV compared with that before DA.

As shown in Fig. 5.10B, similar results were obtained with the 16x16 random checkered pattern. The membrane fluctuation of horizontal cell somata in the reserpine-treated retina was hardly discernible, suggesting that the spatial summation area may be substantially larger than in the normal retina. When DA was administrated, the amplitude of hyperpolarization increased by 8mV accompanied by the appearance of vigorous random fluctuation that appeared to reflect the responsiveness to spatio-temporal changes of light.

Fig. 5.10C shows the changes of hyperpolarization amplitude induced by DA ; the amplitude of S-potentials to the 16x16 random checkered pattern in the reserpine-treated retinas was 62 ± 6%(SD)(n=25) of that after DA application. On the other hand, the incremental sensitivity of off-center ganglion cells in

reserpine-treated retinas was 26 ± 8 (SD)%(n=11) of that after DA application(Fig. 5.10D). The incremental sensitivity of ganglion cells and sustained hyperpolarization level of S-potentials to the random checkered pattern were nealy identical in DA-applied normal retinas and DA-applied reserpine-treated retinas.

Then, the contribution of sustained hyperpolarization level to the incremental sensitivity in off-center ganglion cells was examined in DA-applied normal retinas. Without the surround illumination, the incremental sensitivity of off-center ganglion cells was 28±12(SD)%(n=15)(Fig. 5.10E) of that obtained in the presence of steady surround illumination of the same mean illuminance as that of center stimulation. When the surround illumination was adjusted to produce S-potentials to about 60% of those induced by the surround illumination with the same mean illuminance as the center illumination, the incremental sensitivity was reduced to 57±10(SD)% (n=15)(Fig. 5.10E). These results suggest the possibility that DA directly modifies the center-surround interaction in bipolar and ganglion cells as well as the S-potential of horizontal cells.

Discussion:

Effects of DA on horizontal cells:

A schematic diagram of retinal morphology(Fig. 5.11) shows a neural connectivity that provides an explanation of the present results. The somas of L-type horizontal cells(H-S) receive signals from red-sensitive cones(C) and connect to one another with gap junctions(↔), and may send signals to the axon terminals(H-AT) via a slender axon(AX) which presumably has a

high conduction resistance. The axon terminals are also coupled electrically to one another with gap junctions. In the fish retina, somas of dopamine-containing interplexiform cells(IP) are located at the innermost level of the inner nuclear layer and send an ascending process(A-P) toward the outer plexiform layer(OPL) where they make synapses on horizontal cells and bipolar cell dendrites. Externally applied dopamine(DA) may produce an effect that simulates a functional influence of interplexiform cells on photopic L-type horizontal cells in the fish retina. The present results confirmed the earlier findings (Davis and Naka, 1980) that the half-decay width of receptive field profile to a sweeping spot is narrower in the soma than in the axon terminal of photopic L-type horizontal cells in the catfish retina, and revealed that externally applied dopamine(DA) narrowed the width of the receptive field from the soma but not that from the axon terminal. A similar observation was reported in the carp retina (Teranish, 1983).

In the fish retina, DA appears to prevent electrical coupling at gap junctions between the somata of horizontal cells but not between their axon terminals. In contrast, L-type horizontal cells of the turtle retina appear to be electrically coupled, mainly at the axon terminal levels, where the spatial properties are modulated by gamma-aminobutyric acid(GABA) (Piccolino et al., 1982) and by DA (Neyton et al., 1982). At present, it is hard to explain why DA narrowed the spatial profile of responses recorded from the soma without affecting the axon terminal. The DA effect in question is certainly mediated

via a DA-receptor mechanism, because pretreatment by haloperidol(5-10 mM solution), a dopaminergic blocker, prevents the appearance of DA effect(not illustrated; but see Teranishi et al., 1983). It is of interest to point out that the half-decay width from the sweeping-spot experiment was wider for the soma(Fig. 5.2) as well as for the axon terminal(Fig. 5.3) in DA-cell-deprived retinas than in normal retinas. DA, applied to DA-cell-deprived retinas, restored the normal sensitivity of the soma potential to DA, indicating that DA-receptors of horizontal cells remained intact in such retinas. DA does not modify the spatial profile of the axon potential, because the membrane property of the axon terminal may differ from that of the soma, at least concerning the sensitivity to DA. It is revealed, however, that the responses recorded from the axon terminal were slightly enlarged in amplitude with the response peak being somewhat sharpened by DA. These subtle changes appear to reflect the action of DA on the soma, not a direct effect on the axon terminal itself. Hence, the spatial properties of photopic L-type S-potentials are modulated by DA, probably at gap junctions among horizontal-cell somas in the catfish retina. As is the case in other retinas (Teranishi et al., 1983; Teranishi et al., 1984; Piccolino et al., 1984; Lasater and Dowling, 1985), DA increases the gap-junctional resistance and thus prevents the lateral spread of S-potentials and shrinks the receptive field of horizontal cell soma.

Modification by DA of response properties of bipolar and ganglion cells:

Modulatory effects of DA on bipolar and ganglion cells are well understood in reserpine-treated retinas in which the DA cells cannot release DA. In reserpine-treated retinas, response properties of bipolar and ganglion cells for the field illumination were very similar to those elicited by the center illumination(Fig. 5.7, Fig. 5.8, and Fig. 5.9), suggesting that DA is required for the normal center-surround interaction in bipolar and ganglion cells. Furthermore, similar effects of DA on both bipolar and ganglion cells suggest that DA-induced response changes in ganglion cells are a reflection of DA's effects on bipolar cells. On the other hand, the center machanism was little affected by DA(Fig. 5.7, Fig.5.8, Fig. 5.9).

The lack of normal center-surround interaction in DA-deficient retinas may be ascribed to two causes. One is the decreased response amplitude of horizontal cells to light. Decreased signal from horizontal cells may hinder improvement of the center response property of bipolar and ganglion cells. Another possibility is that the mechanism of center-surround interaction cannot normally operate without DA even though the normal interaction signal is supplied from the surround. The result of Fig. 5.10 suggests that the decreased S-potential amplitude does not fully account for why the center response property deteriorates without DA in bipolar and ganglion cells. If so is the case, DA may control the photoreceptor-bipolar transmission(modified by horizontal cells) via synapse from DA-releasing interplexiform cell to bipolar cells(Fig. 5.11). Recently, it is reported that in cultured fish horizontal cells,

DA enhances ionic conductances gated by L-glutamate, the foremost putative neurotransmitter released from photoreceptors (Lasater and Dowling, 1982) and also by its agonist (Knapp and Dowling, 1987). DA may also regulate photoreceptor-bipolar transmission by a similar mechanism. In any case, the center-surround interaction is thought to be an important mechanism underlying light adaptation (Dowling, 1967). The present results strongly suggest that DA plays an important role in the process of light adaptation.

It has been reported in rat that depletion of DA significantly increased the time-to-peak of flash-evoked potentials from the visual cortex, lateral geniculate nucleus, and optic tract (Dyer et al., 1981). Furthermore, visual evoked potentials(VEP) of Parkinson's disease patients significantly delayed compared with normal subjects (Bodis-Wollner and Yahr, 1978). The present results from catfish retinal bipolar and ganglion cells suggest that these cortical response delays originate in the retina.

Figure Legends:

Fig. 5.1: Step responses and response curves to a sweeping spot and a flashing spot of light, and their changes following exogenous application of dopamine. A flashing spot(100-μm diameter) was displaced in steps of 90 μm(A, B), or the steadily illuminating spot was swept back and forth along a 6-mm length over the retinal surface(C, D) at a speed of 0.95 mm/sec. Arrows below the potential tracings indicate the direction of sweep. Dopamine(2 to 4 mM in the Ringer's solution) was momentarily applied in a jet form via a nebulizer between the left(A, C) and right(B, D) tracings.

Fig. 5.2: Normalized response curves to a sweeping spot, obtained from the soma of photopic L-type horizontal cells; before(A, C) and after DA application(B, D). A and B are from normal retinas, while C and D from those in which DA cells had been destroyed by prior treatment with 6-OHDA(DA-cell deprived retinas). Scale(1 mm) represents the sweep length on the retinal surface.

Fig. 5.3: Normalized response curves to a sweeping spot of light, obtained from the axon terminal of photopic L-type horizontal cells; before(A, C) and after DA application(B, D). Each curve represents a single sweep of response obtained from different cells. Normal retinas(A, B) and DA-cell deprived retinas(C, D).

Fig. 5.4: Fluorescence photomicrographs of retinal preparations used in the electrophysiological experiment. (A, B) Horizontal view of flat-mounts. (C, D) Radial view of cryosections(15-μm thickness). A and C are from a normal retina, and B and D from a DA-cell-deprived retina. Large cells are DA-releasing

interplexiform cells(DA), and smaller cells belong to a class of indoleamine-accumulating amacrine cells(IA); both classes took up dopamine exogenously applied during the experiment. Scale bars indicate 20 μm and 5 μm for flat-mounts (A, B) and cryosections (C, D), respectively.

Fig. 5.5: Effects of exogenous DA on an off-center ganglion cell in the normal retina. A1 shows temporal kernels(cf. Materials and Methods in Chapter 4) obtained by 16X16-pixel spatio-temporal random noise stimulation before and after DA application. The recovery is also shown. A2 shows normalized horizontal profiles of the receptive field at a delay of 51 msec.

Fig. 5.6: Effects of DA on an on-center ganglion cell in normal retina. A1 shows temporal kernels obtained before and after DA application. Stimulus condition was identical to that of Fig. 5.5. Recovery record is also shown. A2 shows normalized horizontal profiles of receptive field at a delay of 51 msec.

Fig. 5.7: Effects of exogenous DA on ganglion cells of a reserpine-treated retina. The endogenous DA was depleted by hypodermic injection of reserpine prior to the experiment. A1 shows spike discharges of an on-center ganglion cell in response to field illumination(mean illuminance of 1.0 $\mu W/cm^2$) before and after DA administration. A2 shows the first-order temporal kernel(cf. Materials and Methods in Chapter 4) of the cell of A1 obtained by the 16x16-pixel spatio-temporal random pattern stimulation. DA increased the kernel amplitude(incremental sensitivity) and quickened the kernel time course. A3 shows the normalized horizontal profile of receptive field of the same unit

as of A1 at a delay of 68msec. The solid line and dotted line show profiles before and after DA application, respectively. B1 shows spike discharges of an off-center ganglion cells to the field illumination. B2 and B3 are temporal kernels and receptive field profiles of the cell of B1. The stimulus condition was identical to that of A2 and A3.

Fig. 5.8: Temporal properties of the receptive field center of an off-center ganglion cell in the presence or absence of surround stimulation in a reserpine-treated retina. A1 shows temporal kernels of the receptive field center obtained by the 16x16 random noise which illuminated the whole receptive field. The stimulus intensity changed from 0 Log unit(mean illuminance of 1.0$\mu W/cm^2$) to -3 Log unit by -1 Log unit steps. A2 shows temporal kernels of the cell of A1 when the stimulus region was restricted to the receptive field center by using the 4x4-pixel pattern(whose pixel size was equal to that of the 16x16-pixel pattern; 120 μm x 120 μm on the retinal surface). B1 shows temporal kernels of the cell of A1 obtained with a 16x16 random pattern after DA application. B4 shows temporal kernels when the stimulus area was restricted to the central 4x4 area of B1.

Fig. 5.9:

A: Responses of an off-center bipolar cell in a reserpine-treated retina to a field light before and after DA application. The mean illuminance of the field light was 1.0 $\mu W/cm^2$ on the retinal surface.

B: Responses of the off-center bipolar cell of A to the 16x16-pixel random noise pattern. The mean illuminance of random noise

was 1.0 $\mu W/cm^2$ with one pixel being 120 μm x120 μm on the retina.
C: Responses of the off-center bipolar cell of A to a moving slit of light. Measured on the retina, the slit was 0.1 mm x 4 mm with 5 $\mu W/cm^2$ in irradiance. The slit was swept back and forth(without interruption) along a straight line at a speed of 0.95 mm/sec. The response amplitudes are normalized.
D: Temporal kernels of the receptive field center of the off-center bipolar cell of B.

Fig. 5.10:

A: Responses of a horizontal cell soma in a reserpine-treated retina to the same field illumination as used in the experiment of Fig. 5.9A.
B: Responses of the horizontal cell soma of A to the 16x16 random noise employed in the measurement of Fig. 5.9B.
C: DA-induced changes in response amplitude of a horizontal soma in a reserpine-treated retinas. The stimulus was a 16x16 random noise(mean illuminance; 1.0 $\mu W/cm^2$). Response amplitudes in ordinate were ones normalized to S-potentials after DA application; compiled from twenty-five cells.
D: Changes in the incremental sensitivity of off-center ganglion cells of reserpine-treated retinas. The incremental sensitivity of receptive field center was measured by stimulating with the 4x4 random pattern on the center region surrounded by a steady uniform light. The 4x4 center region and steady surround area had an equal mean illuminance of 1.0 $\mu W/cm^2$. Sensitivity values in ordinate were normalized to the incremental sensitivity measured after DA application. Eleven cells.

E: Dependence of the incremental sensitivity upon surround illumination, which was observed in off-center ganglion cells when DA was exogenously applied to normal retinas(without reserpine pre-treatment). The stimulus was 4x4 random pattern surrounded by a steady uniform light. Sensitivity values in ordinate were normalized to the incremental sensitivity measured when the mean illuminance level of surround was equal to that of center region(1.0 value in abscissa). Zero in abscissa indicates dark surround.

Fig. 5.11: A summary diagram of the retinal morphology relevant to DA. C, cones; B, bipolar cell; G, ganglion cell; H-S, horizontal cell soma; AX, horizontal cell axon; H-AT, horizontal cell axon terminal; A, amacrine cell; IP(DA), dopamine-containing interplexiform cell; A-P, ascending process of IP; OPL, outer plexiform layer; IPL, inner plexiform layer; ↔ (two-way arrows), gap junction; ← (one-way arrow), synaptic connection; ⇄ (double arrows), mutual synaptic connection.

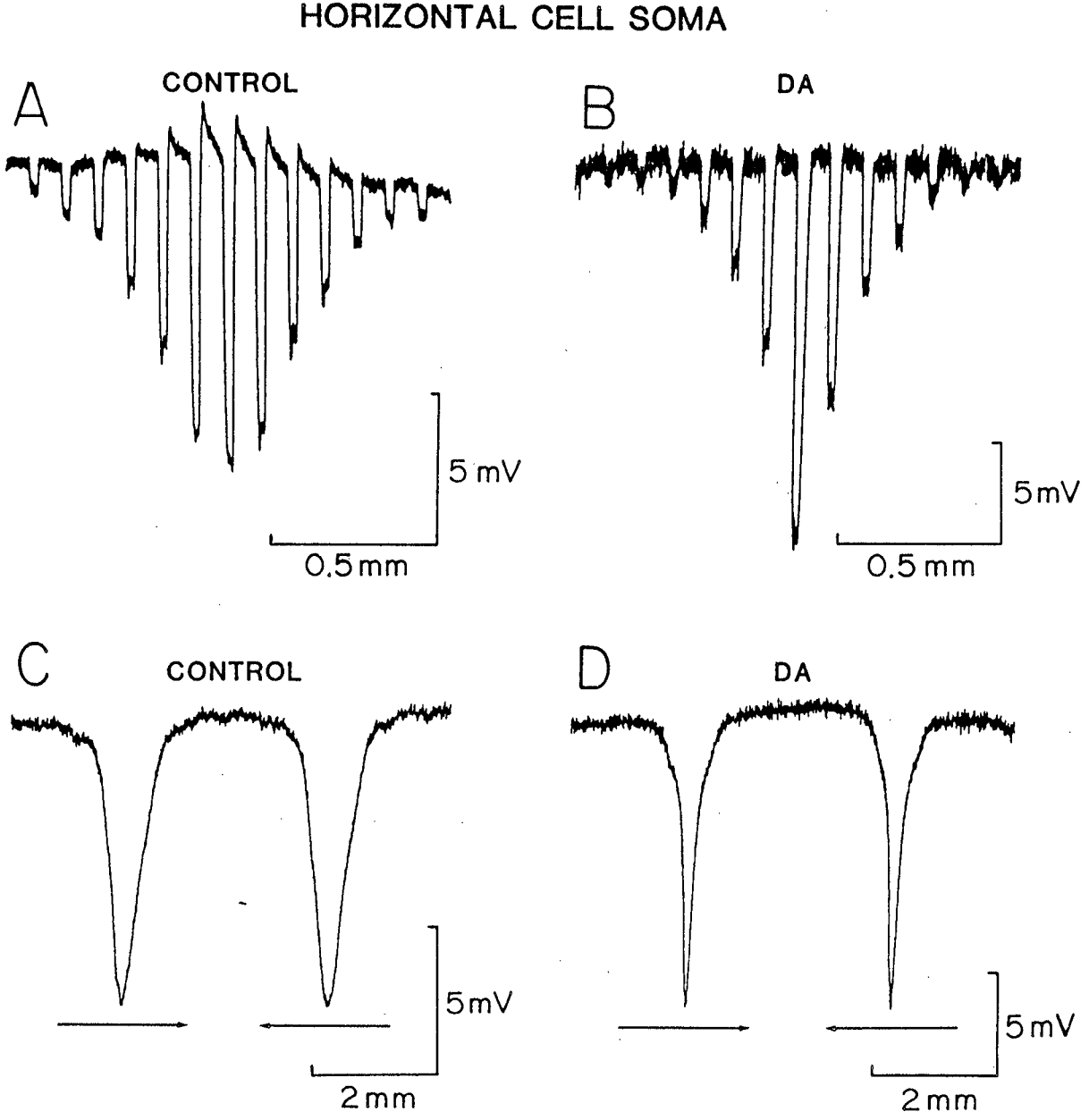

HORIZONTAL CELL SOMA
A
CONTROL
5 mV
0.5 mm
B
DA
5mV
0.5 mm
C
CONTROL
5mV
2mm
D
DA
5mV
2mm

Fig. 5.1

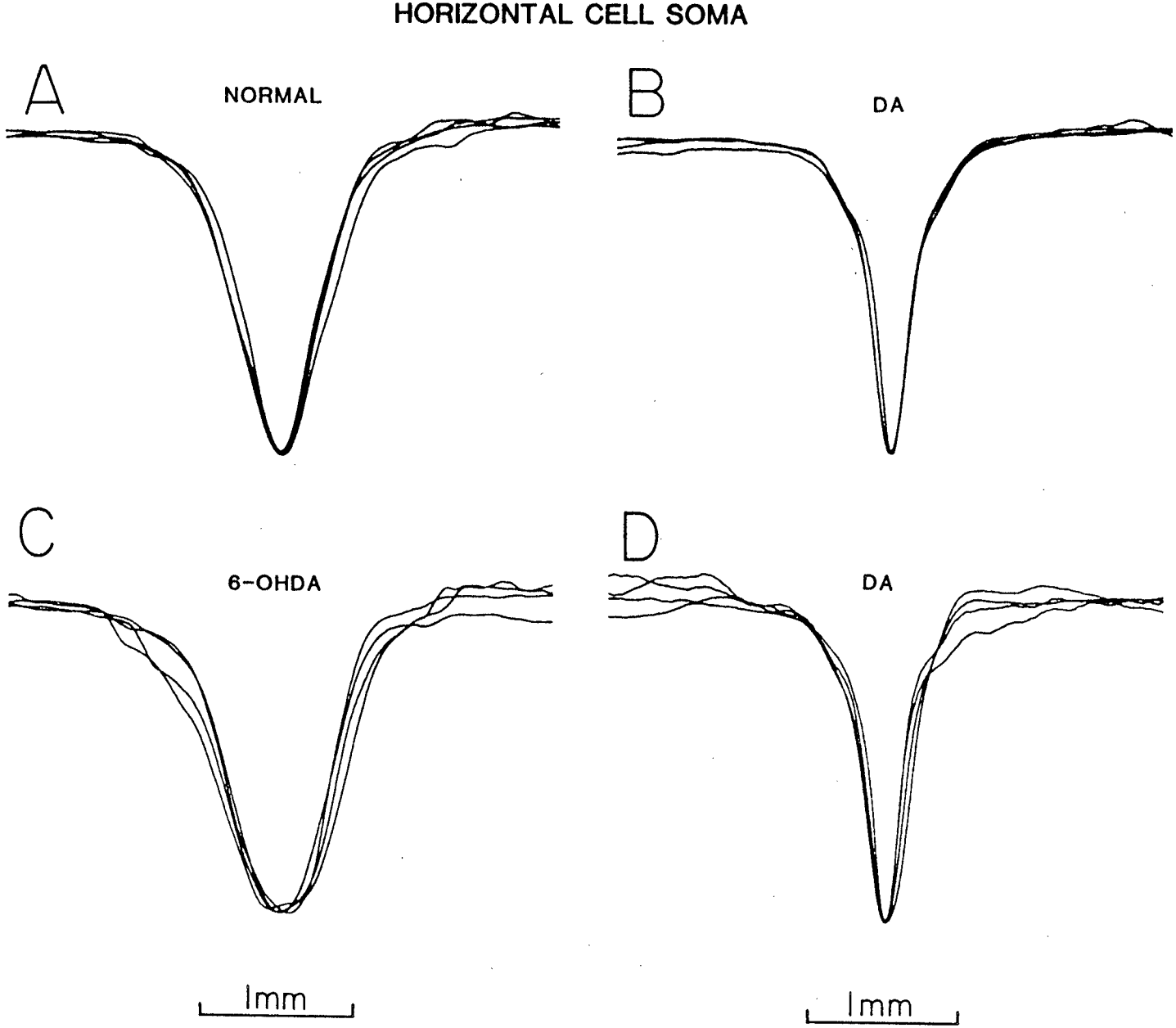


Fig. 5.2

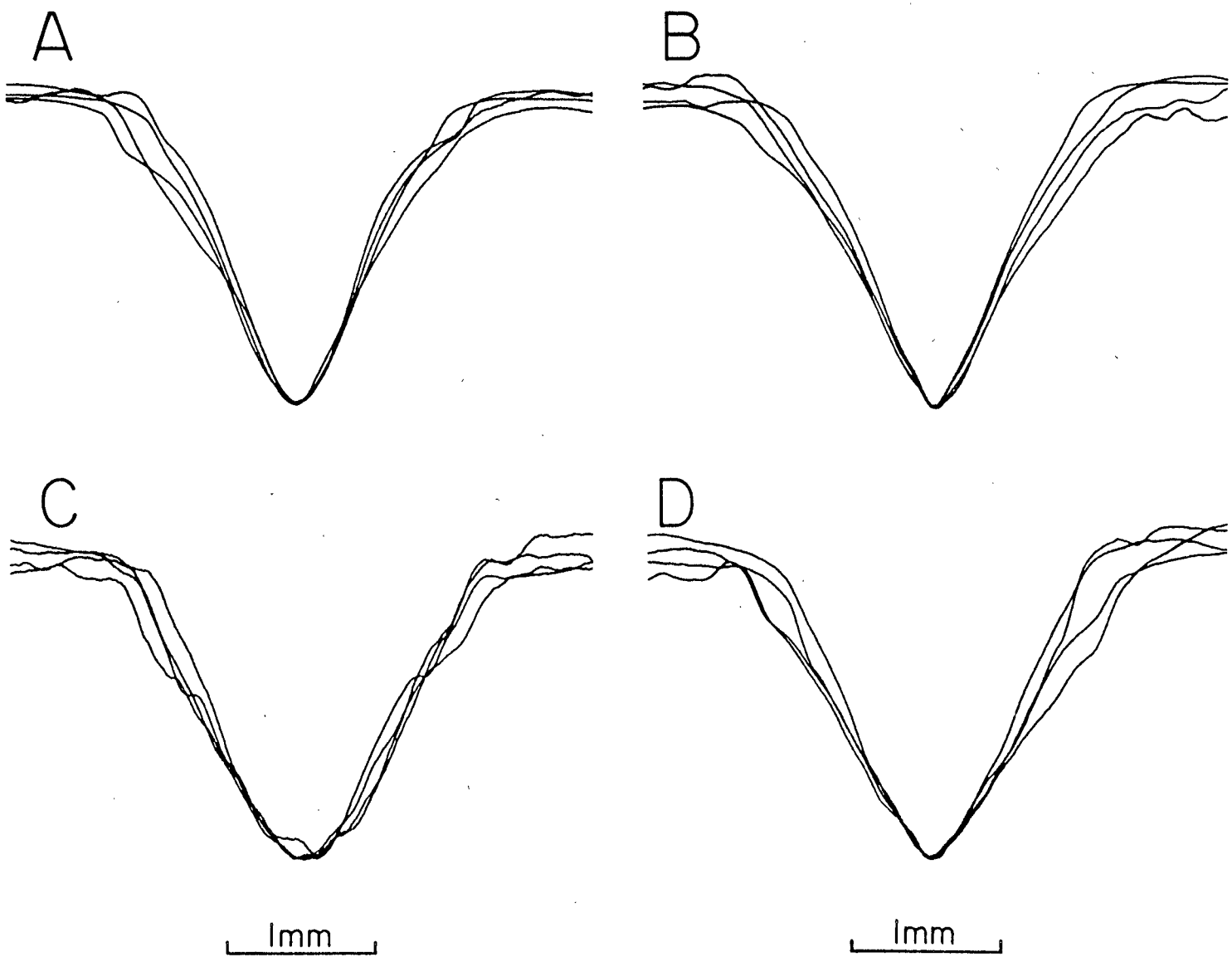


Fig. 5.3

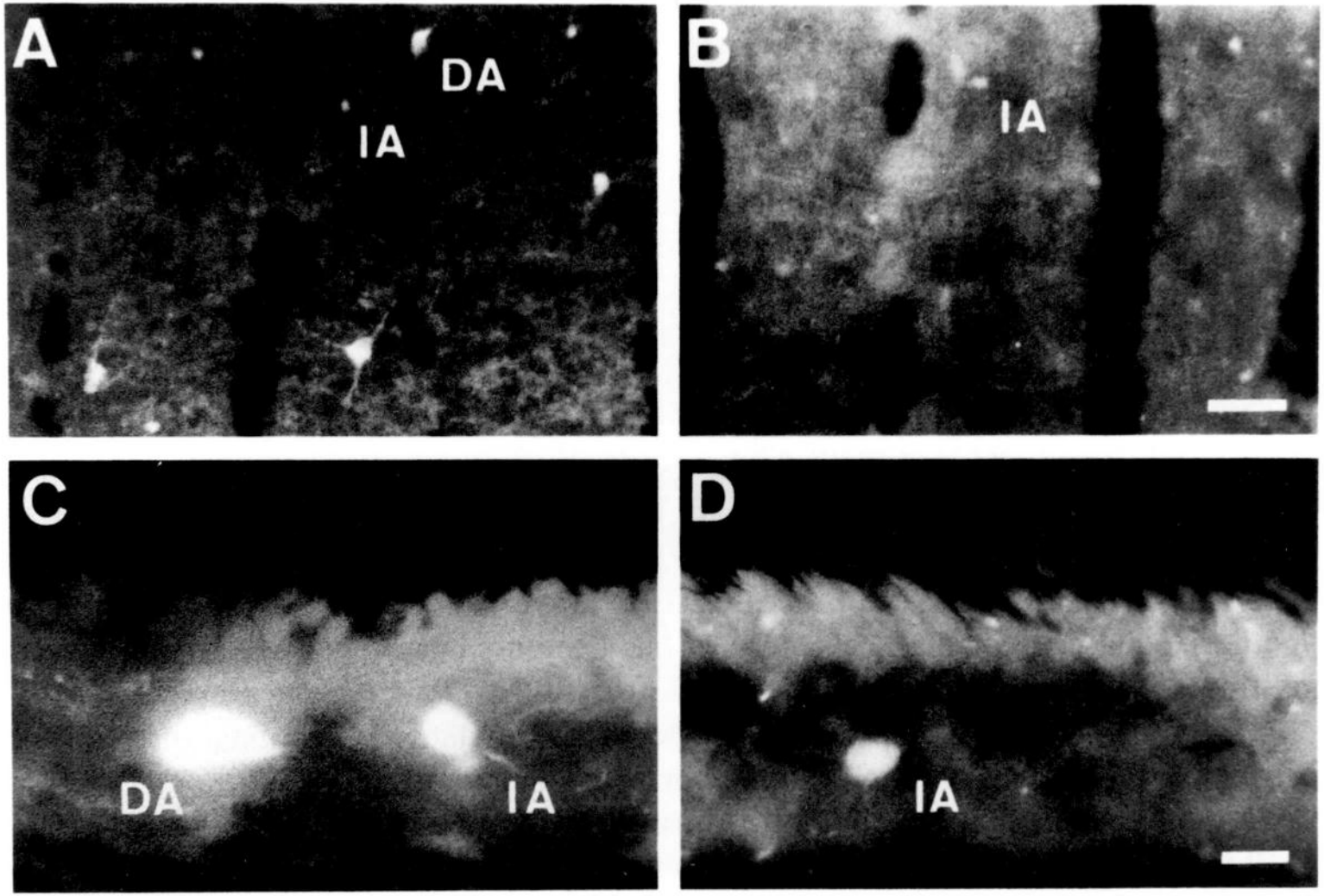


Fig. 5.4

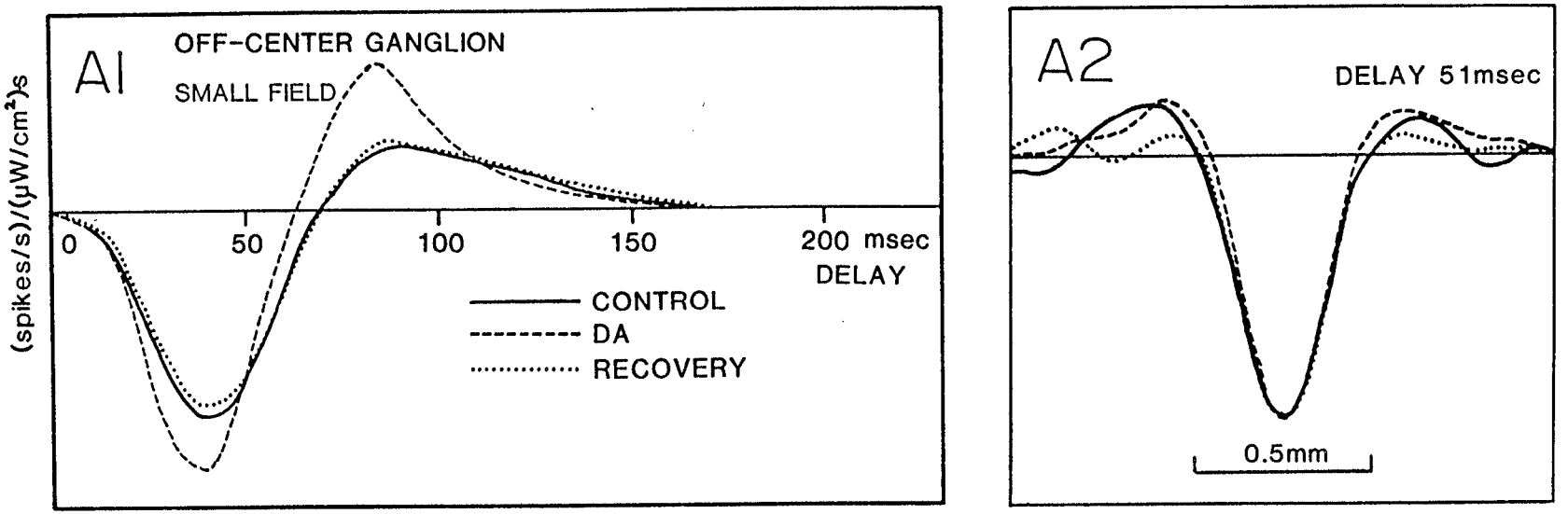

A1
OFF-CENTER GANGLION
SMALL FIELD
(spikes/s)/(μW/cm²)s
0
50
100
150
200 msec
DELAY
CONTROL
DA
RECOVERY
A2
DELAY 51msec
0.5mm

Fig. 5.5

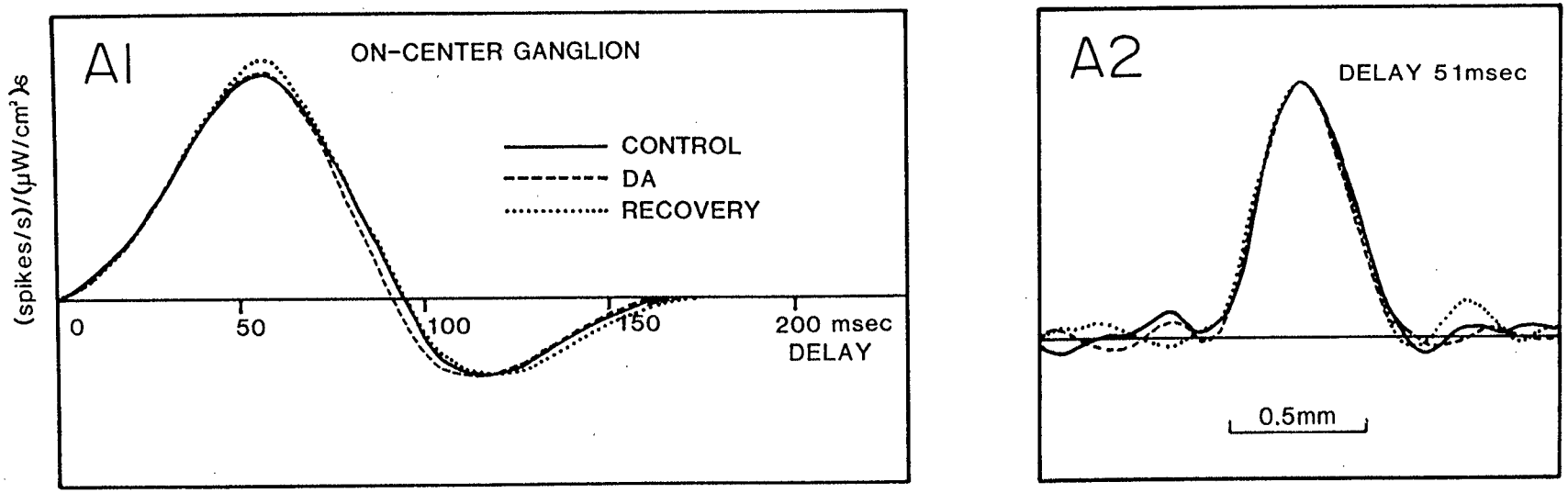

A1
ON-CENTER GANGLION
CONTROL
DA
RECOVERY
(spikes/s)/(μW/cm²)s
0
50
100
150
200 msec
DELAY
A2
DELAY 51msec
0.5mm

Fig. 5.6

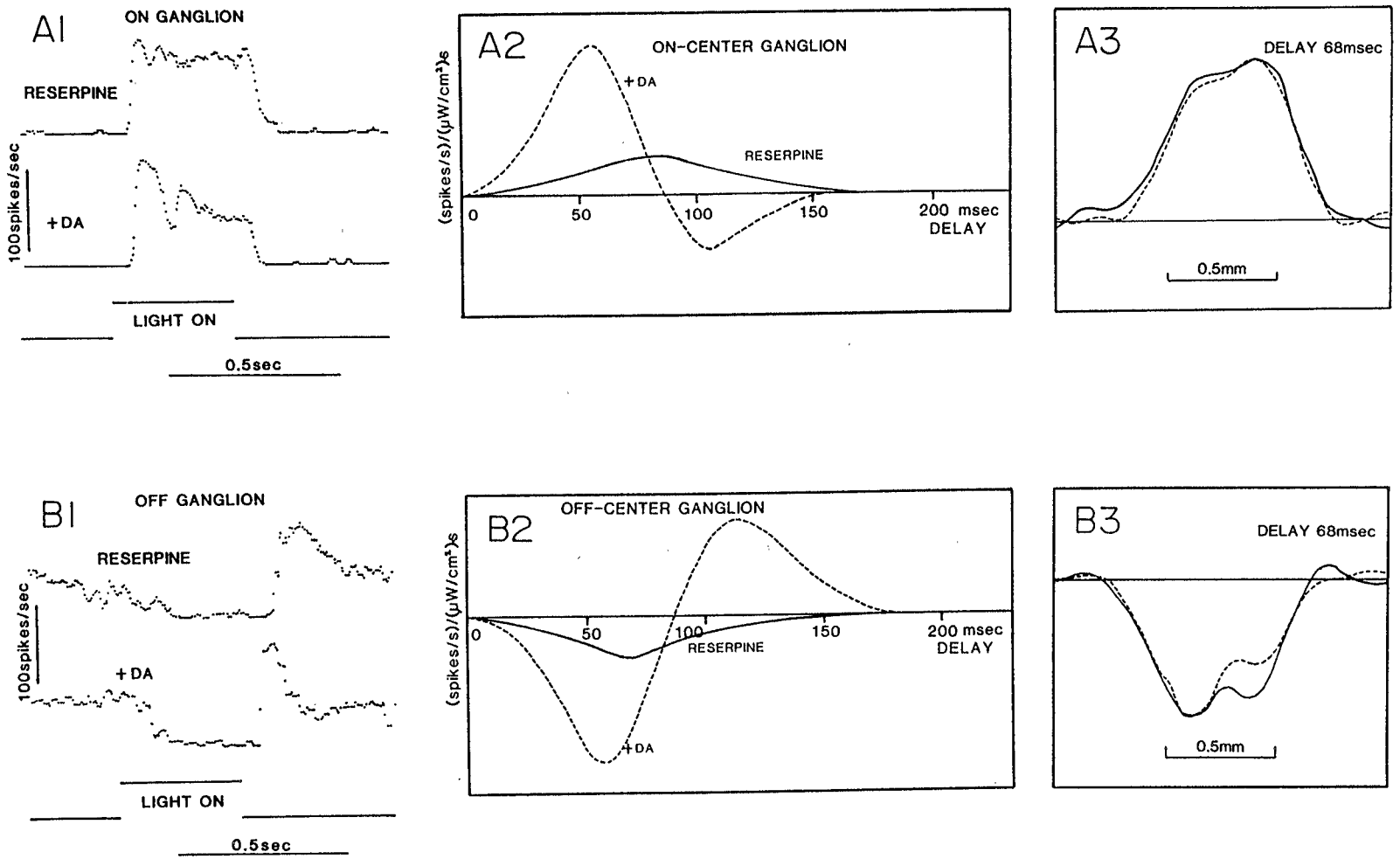

A1
ON GANGLION
RESERPINE
+DA
100spikes/sec
LIGHT ON
0.5sec
A2
ON-CENTER GANGLION
+DA
RESERPINE
(spikes/s)/(μW/cm²)s
0
50
100
150
200 msec
DELAY
A3
DELAY 68msec
0.5mm
B1
OFF GANGLION
RESERPINE
+DA
100spikes/sec
LIGHT ON
0.5sec
B2
OFF-CENTER GANGLION
(spikes/s)/(μW/cm²)s
0
50
100
150
200 msec
DELAY
RESERPINE
+DA
B3
DELAY 68msec
0.5mm

Fig. 5.7

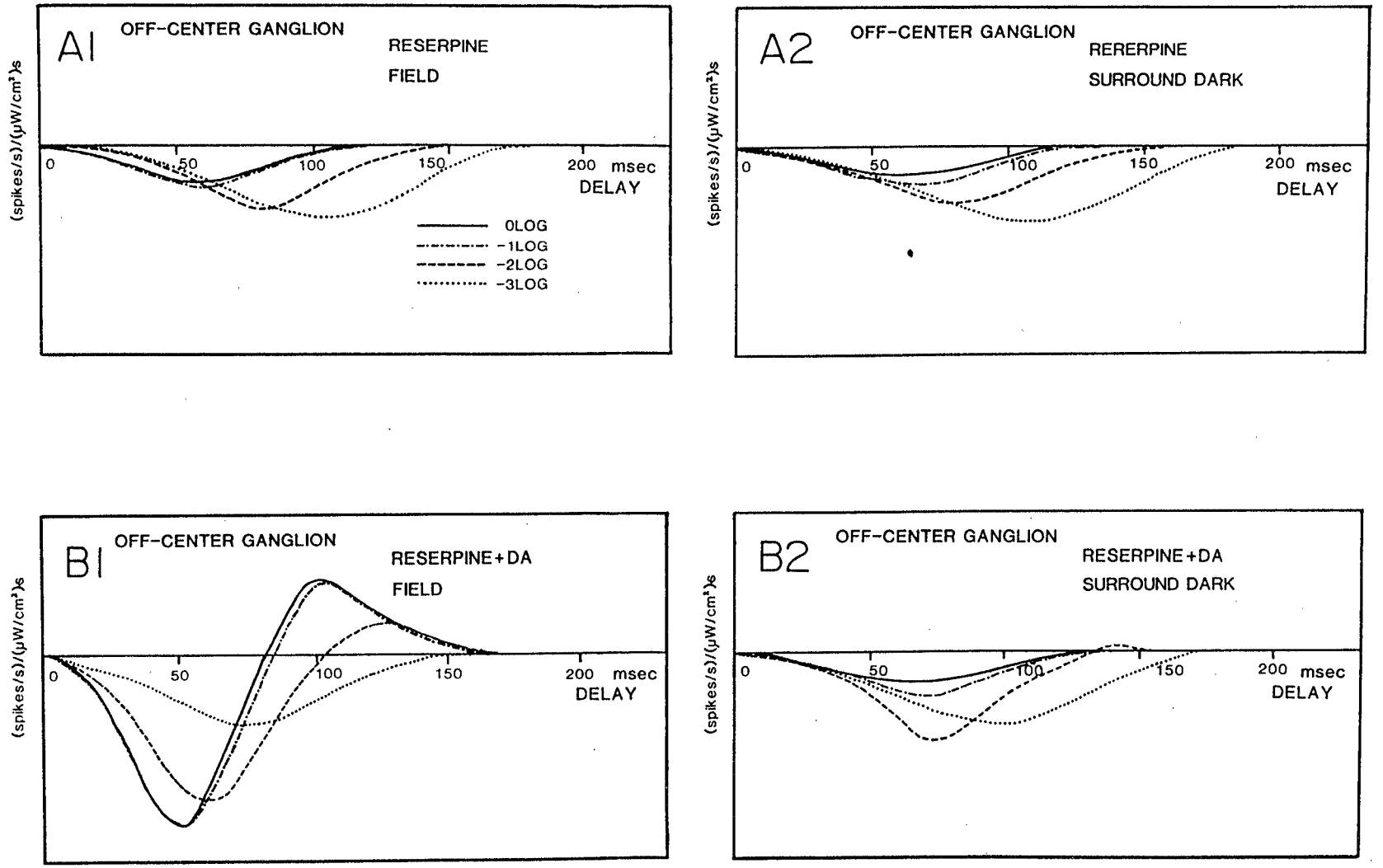

A1
OFF-CENTER GANGLION
RESERPINE
FIELD
(spikes/s)/(μW/cm²)s
0
50
100
150
200 msec
DELAY
0LOG
-1LOG
-2LOG
-3LOG
A2
OFF-CENTER GANGLION
RERERPINE
SURROUND DARK
B1
OFF-CENTER GANGLION
RESERPINE+DA
FIELD
B2
OFF-CENTER GANGLION
RESERPINE+DA
SURROUND DARK

Fig. 5.8

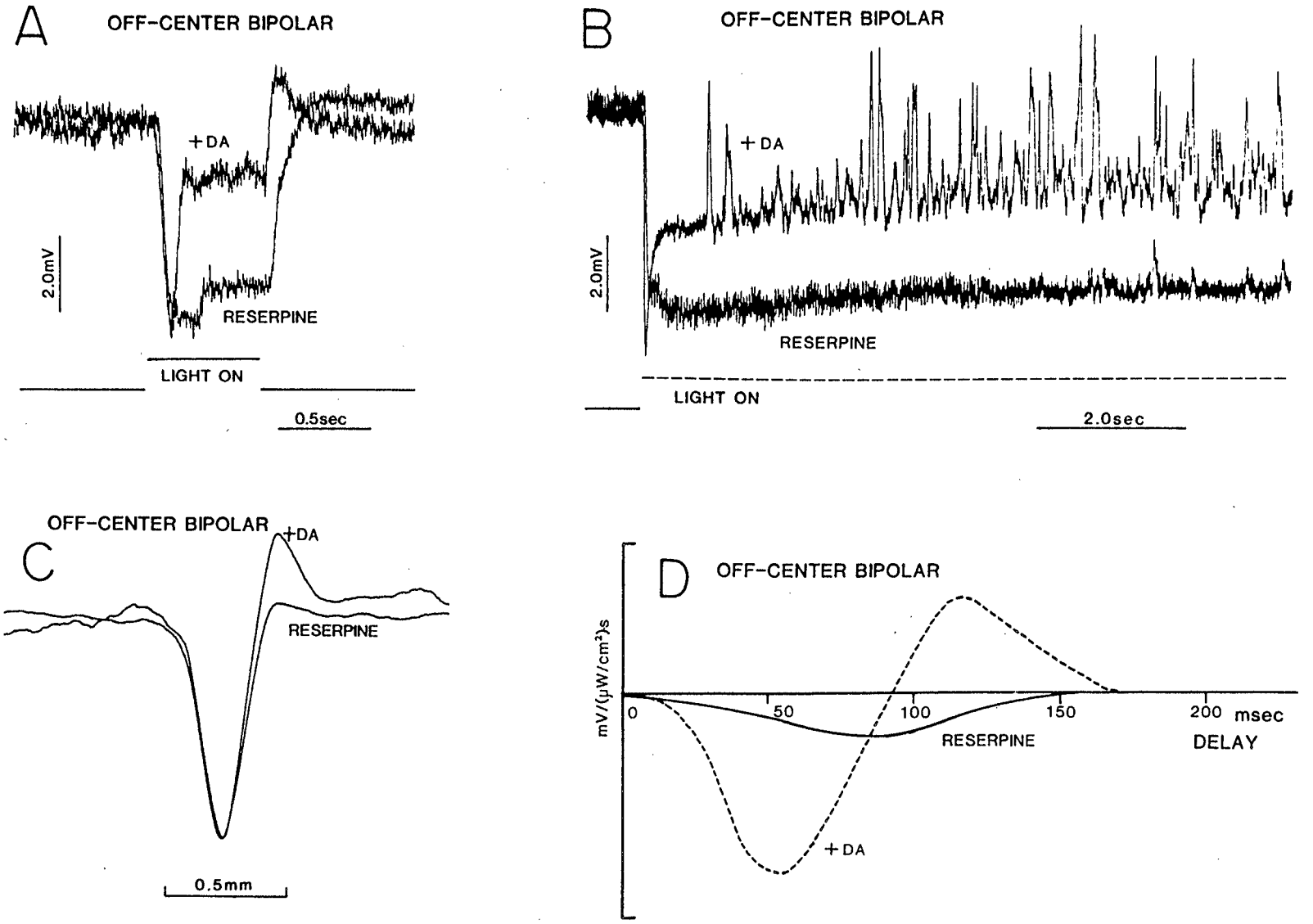

A
OFF-CENTER BIPOLAR
+DA
2.0mV
RESERPINE
LIGHT ON
0.5sec
B
OFF-CENTER BIPOLAR
+DA
2.0mV
RESERPINE
LIGHT ON
2.0sec
OFF-CENTER BIPOLAR
C
+DA
RESERPINE
0.5mm
D
OFF-CENTER BIPOLAR
mV/(μW/cm²)s
0
50
100
150
200 msec
DELAY
RESERPINE
+DA

Fig. 5.9

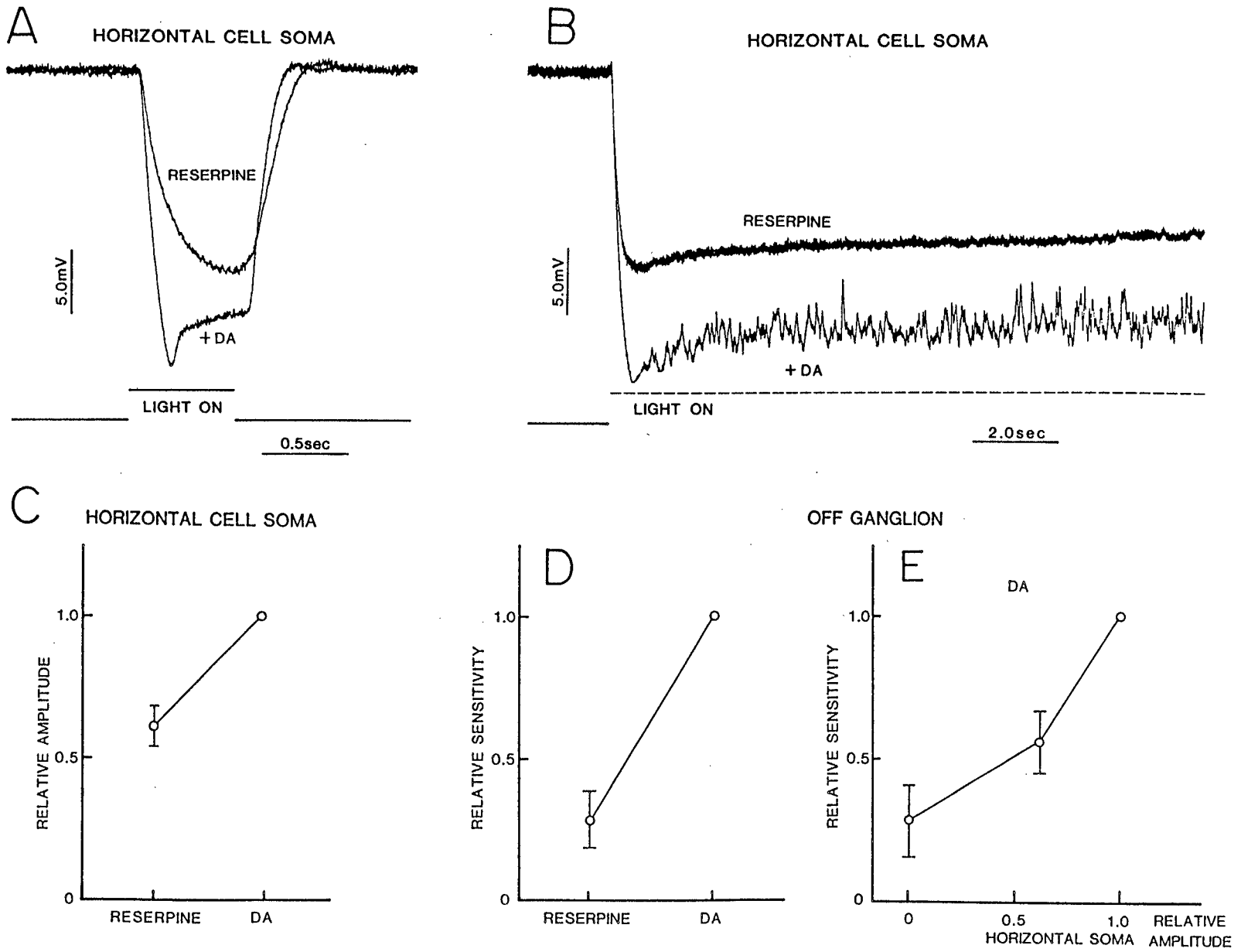

A
HORIZONTAL CELL SOMA
RESERPINE
+DA
5.0mV
LIGHT ON
0.5sec
B
HORIZONTAL CELL SOMA
RESERPINE
+DA
5.0mV
LIGHT ON
2.0sec
C
HORIZONTAL CELL SOMA
RELATIVE AMPLITUDE
1.0
0.5
0
RESERPINE
DA
D
OFF GANGLION
RELATIVE SENSITIVITY
1.0
0.5
0
RESERPINE
DA
E
DA
RELATIVE SENSITIVITY
1.0
0.5
0
0
0.5
1.0
HORIZONTAL SOMA
RELATIVE AMPLITUDE

Fig. 5.10

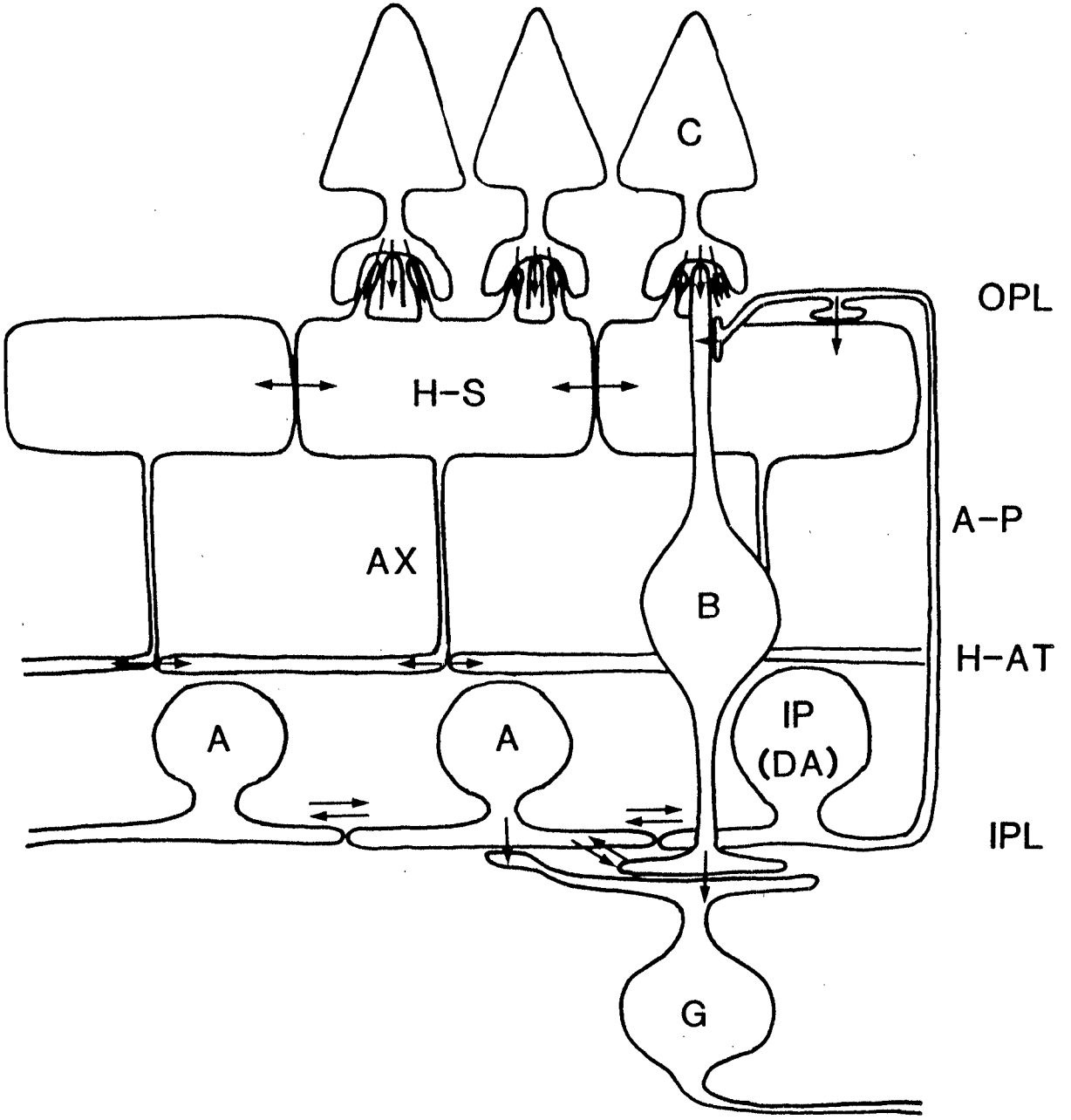


Fig. 5.11

CHAPTER 6

DYNAMICAL CHANGES OF SPATIO-TEMPORAL RECEPTIVE FIELDS OF RETINAL GANGLION CELLS DURING DEVELOPMENT FROM TADPOLE TO ADULT FROG

Introduction:

The vertebrate retina undergoes substantial changes in function and morphology during development. Especially, the development of the visual system in amphibians has recently received considerable attention. Autoradiographic studies on the developing retina in Xenopus have shown that cells are added continuously at the ciliary margin throughout larval life and until after metamorphosis (Straznicky and Gaze, 1971; Hollyfield, 1971). The steady increase in the number of retinal cells and optic nerve fibers during larval life is accompanied by a marked thickening of the retina and changes in the synaptic organization in the inner plexiform layer (Gaze and Peters, 1961; Wilson, 1971, Fisher, 1972; Grillo and Rosenbluth, 1972; Cima and Grant, 1980). Since the function of a neuron is intimately related to its structure and its connections with other neurons, morphological changes in the developing retina will result in accompanying modification of the receptive field properties of retinal ganglion cells. Pomeranz and Chung have noted that sustained edge detector cells absent in the tadpole retina appeared in the adult frog's, and that receptive field changes during metamorphosis appeared to be related to alterations in the shapes of ganglion cell dendritic trees (Pomeranz and Chung, 1970; Pomeranz, 1972).

In spite of several evidence showing functional changes of

ganglion cells (Fisher and Jacobson, 1970; Fisher, 1972), explicit parameters such as a latency or a receptive field size which characterize the spatio-temporal properties of ganglion cells in metamorphosis have not yet been comprehensively elucidated. The present study aims to clarify the fundamental parameters undergone appreciable changes accompanied by the reorganization of receptive field of ganglion cells during development of the retina. To achieve the end, spatio-temporal receptive fields of ganglion cells in both tadpole and adult frogs were examined by the use of TV snow noise. This approach dose not make a priori assumption about specific features the cell extracts (Rowe and Stone, 1980).

Materials and Methods:

All the experiments were performed in retinas of the tadpoles and adult frogs of Rana catesbeiana. Tadpoles used in this study were between stage 25 when limb buds were beginning to appear and stage 29 just before the development of feet(Iwasawa and Morita, 1980). The table made by Iwasawa and Morita describes the normal stages of development of Rana brevipoda, a close relation to Rana catesbeiana. As no table is acquired concerning the normal development of Rana catesbeiana, this table was consulted at the suggestion of Prof. Iwasawa. Daily observations over two years indicated that the stages of development for Rana catesbeiana are similar to those described in the table of Iwasawa and Morirta. Adult frogs were of more than three years old with the eye ball of the diameter of exceeding 1.0cm. The results reported here were obtained from 36 tadpoles and 14 adult

frogs. The eye ball of the tadpole or the frog was removed, hemisected, and vitreous fluid was carefully drained by filter paper. Extracellular action potentials were recorded from ganglion cells located in the center-dorsal region of the retina. Impedance of the tungsten electrodes was about 200kΩ at 1kHz. The method for measuring spatio-temporal receptive field was identical with that employed in chapter 3. The mean intensity of TV snow noise was about 0.1 $\mu W/cm^2$. STRFs of ganglion cells in tadpole and adult frog were measured at successive steps of 30 or 40 msec from 0 to 450 msec(tadpole) or from 0 to 300 msec(adult frog) to explore entire spatio-temporal properties of the cell.

Results:

Two examples of STRF from tadpole cells are shown in Fig. 6.1 in which each picture shows averaged(accumulated) TV snow frames which produced spike discharges at the delay indicated in the frame. These figures indicate that the size and magnitude of the receptive field changed with time. The cell shown in the upper row had a receptive field with a bright center and dark surround. The size and magnitude of the center reached a maximal value at a delay of 140 msec and then monotonically decayed. The faint but still discernible receptive field was seen at a delay of 260 msec. This was the entire time course of the receptive field and the four frames in an imaginary three-dimensional domain would comprise the STRF of the cell. The lower row shows STRF of the cell which had a dark center with bright surround. Both center and surround reached their maximal magnitude at a delay of 100 msec and then monotonically decayed. At a delay of

260 msec, clear receptive field was still seen. Although entire records are not shown, both center and surround components disappeared within a time span of 400 msec.

Tadpole ganglion cells could be classified into two types from the spatial configurations of STRF. One has center-brightening receptive field organization, and is abbreviated as type A. Another type has center-dimming receptive field with small surround, and is abbreviated as type B. Type A cells responded tonically during field illumination, whereas type B cells showed off-discharges at the termination of field illumination. The receptive field of both types of cells was composed of center region with a diameter of 600 μm in average and appreciable surround area with a diameter of 1 to 2 mm. Exact estimation of the surround was difficult because of the noisy receptive field profiles. The tadpole STRF had a monophasic time course and polarity reversal of the receptive field was rarely seen. Only six cells among sixty-eight cells showed polarity change at around 400 msec delay.

Fig. 6.2 shows STRFs from three adult ganglion cells. Row A was from a cell with center-brightening receptive field. The center reached its maximal size and magnitude at a delay of 60 msec, and then disappeared together with the surround at a delay of 100 msec. Receptive field center with reversed polarity reappeared at a delay of 210 msec. The cell in row B had a center-dimming receptive field configuration with clear surround. The cells shown in row A and B were classified into type A or type B cells, respectively. The cell shown in row C had a complex

three-phase STRF which could not be classified into type A or B cells. The receptive field showed initially center-dimming pattern at a delay of 30 to 60 msec and then changed the polarity, and reappeared with center-dimming configuration at delays of 100 and 210 msec. A cell with the reversed polarity of row C(i.e. brightening-dimming-brightening center in the order of delays) was also found in the adult frog. These three-phase cells were classified as type C cells. The shapes of receptive fields of types A, B, and C cells in the adult frog retina were almost circular except for some cells with distorted center.

Figs. 6.1 and 6.2 clearly indicate that the STRFs in both tadpoles and adult frogs had similar spatial extents, but response time course was much faster in the frogs. The results are summarized in Table 6.1 in which STRF characteristics from 68 tadpole cells and 71 adult frog cells are shown. All tadpole cells could be classified into type A or type B. Almost of the cells(95%) analysed belonged to type B cells. In the frog, 87% of the ganglion cells could be classified into type A or type B, and there were more B's than A's. The population of A's increased from 4% in the tadpole to 14% in the adult frog. In both frog and tadpole, no noticeable difference in center size was found between type A and type B cells. There was, however, a class of cells which produced complex STRFs classified as type C. This class of cells was not found in the tadpole. The latency to the peak response was defined as the shortest delay-time when the receptive field center reached its maximal size and magnitude. With respect to the latency in frogs or in tadpoles, there was no

major difference between type A and type B cells. But the latency to the peak response in the tadpole was about twice as that in the frog. Moreover, the time course of STRFs of tadpole cells was considerably longer compared with that of frog cells. About 45% of tadpole ganglion cells showed discernible STRFs at 400 msec delay, whereas STRFs of frog ganglion cells disappeared within 260 msec delay. These results strongly suggest that tadpole ganglion cells cannot easily follow rapid changes of light intensity. The three-phase type C cells had relatively fast time-courses. In the frog, the delay to the second peak response of three-phase cells was about 110 msec, whereas the latency to polarity reversal of both type A and type B cells was about 200 msec.

Spatial profiles of the STRF from tadpoles and adult frogs when its center had maximal magnitude, are shown in Fig. 6.3. Each trace is from a different ganglion cell. The figure demonstrates that the half-width of profiles was comparable in both tadpole and frog cells, but frog cells had a larger variety of diameters than tadpole cells (see SD of the second column of Table 6.1).

Discussion:

Development of the visual system is a challenging problem which can be studied with an advantage in the amphibians. These animals are readily available and the stages of development can be readily distinguished. The complexity of the receptive field of the frog ganglion cells is well-documented (Maturana et al., 1960; Lettvin et al., 1961; Keating and Gaze, 1970; Nye and Naka,

1971; Grüsser and Grüsser-Cornehls, 1976). The present study investigated the spatio-temporal properties of both frog and tadpole ganglion cells by transforming complex receptive fields to simple ones. The method employed here is to extract linear STRF from complex response properties. Although complex functions inherent in the cell might have been missed, this approach provides basic data concerning the development of receptive field organization.

The analysed STRFs indicates that the majority of the cells in both tadpole and frog retinas had a linear receptive field component which was mostly circular with concentric organization. These cells were classified into type A or B cells. Besides the appearance of complex types in the adult frog, the main features of the STRFs in the frog and tadpole were twofold: (1) the time course of the tadpole STRF was much slower than that of the frog's. Indeed, the delay to the peak of STRF in tadples was about twice that in frogs. Slow time course of response in tadpole ganglion cells may result from sluggish phototransduction process in photoreceptors or slow synaptic transmission among signal pathways from photoreceptor to ganglion cells. (2) STRFs of frog cells showed clear polarity reversal, whereas those of tadpole cells did not change their polarity. This property indicates that frog ganglion cells responded better to changes of light than tadpole's. Such high sensitivity to the changing patterns in adult frog cells may result from synaptic reorganization in the inner plexiform layer (Fisher, 1972) which yields highly pattern-sensitive function such as a moving

detection or edge detection(Lettvin et al., 1959; Maturana et al., 1960; Gaze and Jacobson, 1963). (3) The size of both tadpole and frog STRFs was not much different although the diameter of the tadpole eyeball was about 2 mm, whereas that of the adult frog was about 20 mm. If the spatial resolution is directly proportional to the eyeball's diameter(or the size of the retina), the spatial resolution of the adult frog retina is 10 times finer than that of the tadpole's. This is analogous to two cameras with films of different size but of the same graininess.

Consistent approach using TV snow noise to several types of cells with distinct response properties unequivocally revealed fundamental parameters to characterize cell's dynamics such as a latency, span of temporal dynamics, size, shape, and polarity of the receptive field. It is, however, difficult to find the straightforward connection of STRFs of frog ganglion cells with their trigger features revealed by feature extraction analysis. This fact suggests the limitation laid on first-order cross-correlation analysis using spatio-temporal random noise. Higher-order cross-correlation analysis (Citron et al., 1981) may provide a partial clue to overcome the difficulty. Close link between spatio-temporal receptive field analysis using random noise and trigger features analysis, may be facilitated by comparing receptive field properties revealed by spatio-temporal random noise with those explored by cell-specific natural stimuli.

Figure Legends:

Fig. 6.1: STRFs from two tadpole cells at delays of 60, 100, 140, and 260 msec. The upper photographs show a center-brightening cell and the lower row a center-dimming cell. Both STRFs have surrounds. Calibration: 0.5mm.

Fig. 6.2: STRFs from three frog cells at delays of 30, 60, 100, and 210 msec. The upper and middle rows are from a center-brightening and center-dimming cell, respectively. The lower row shows a three-phase STRF. The center changes dark-bright-dark. Time courses are much faster than those of the tadpole. Note that the time scale is different from Fig. 6.1. Calibration: 0.5mm.

Fig. 6.3: Each trace is the digitized representation through the STRF center from different ganglion cells at the peak response. Upward represents bright areas and downward shaded areas of the 35 mm frame. The STRF size was estimated by measuring the width of the trace at its half amplitude. (A) and (B) are from tadpole cells and (C) and (D) are from frog cells. (A) and (C) are from center-brightening cells and (B) and (D) from center-dimming cells. Each trace was normalized to the maximum response.

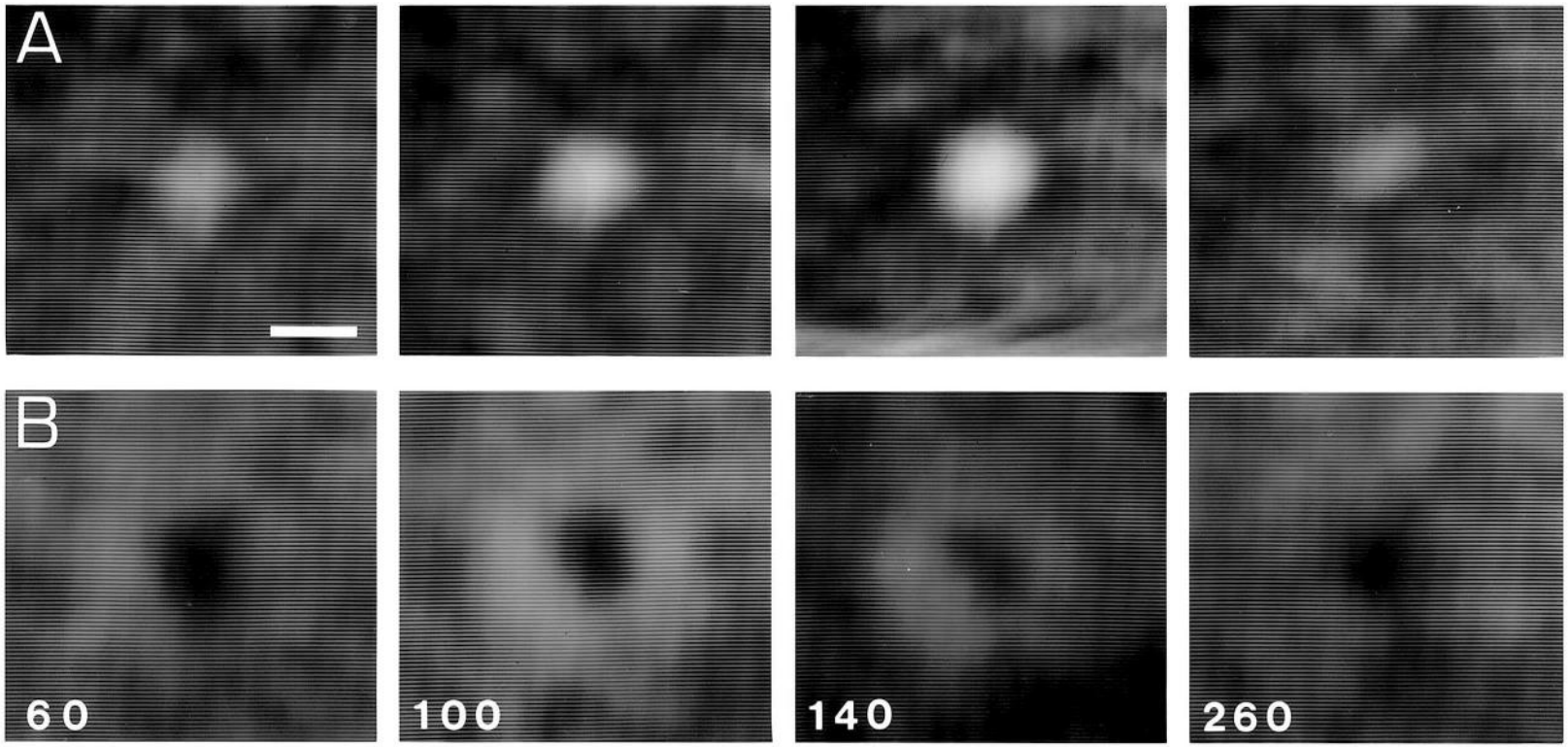


Fig. 6.1

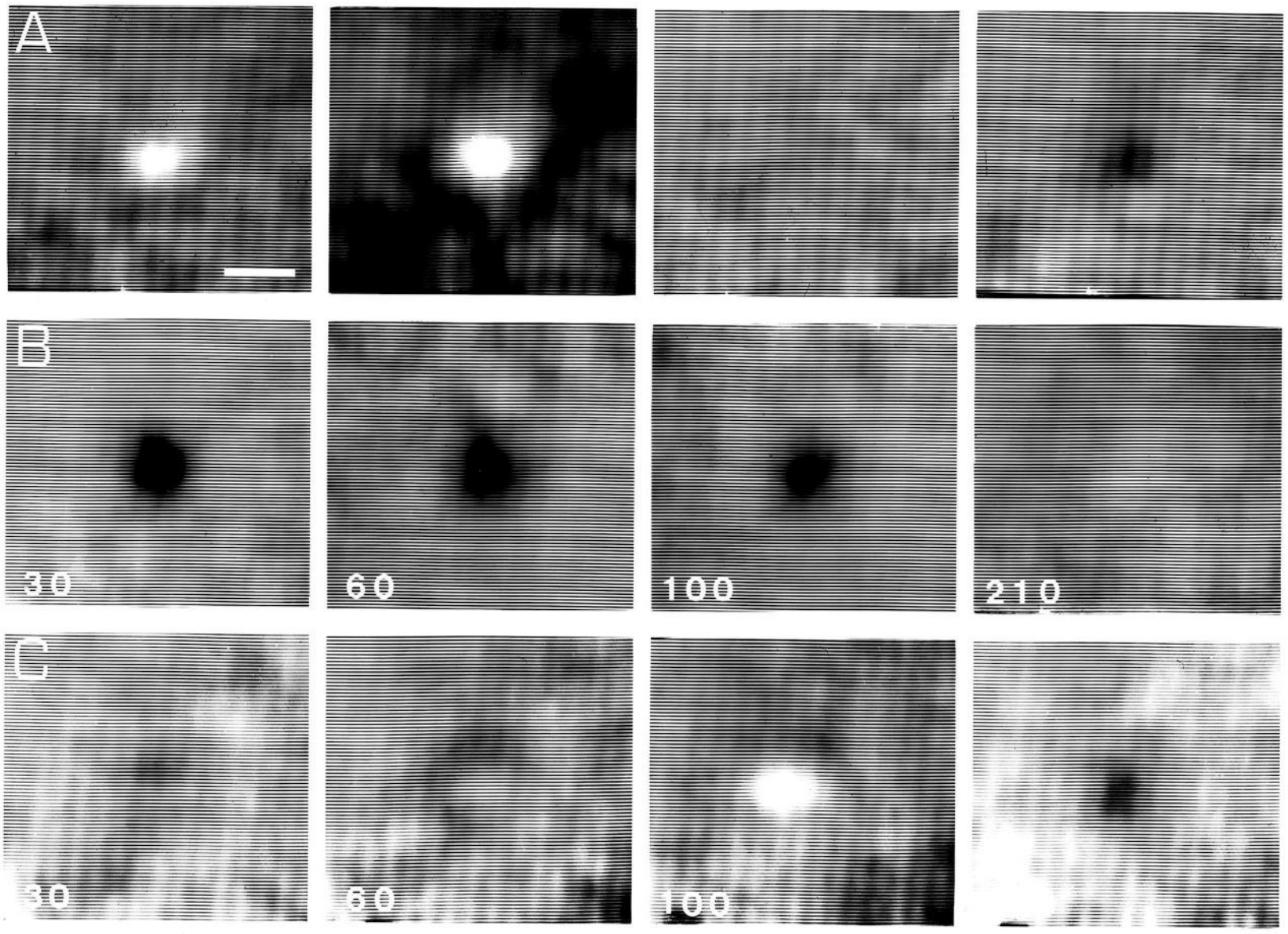


Fig. 6.2

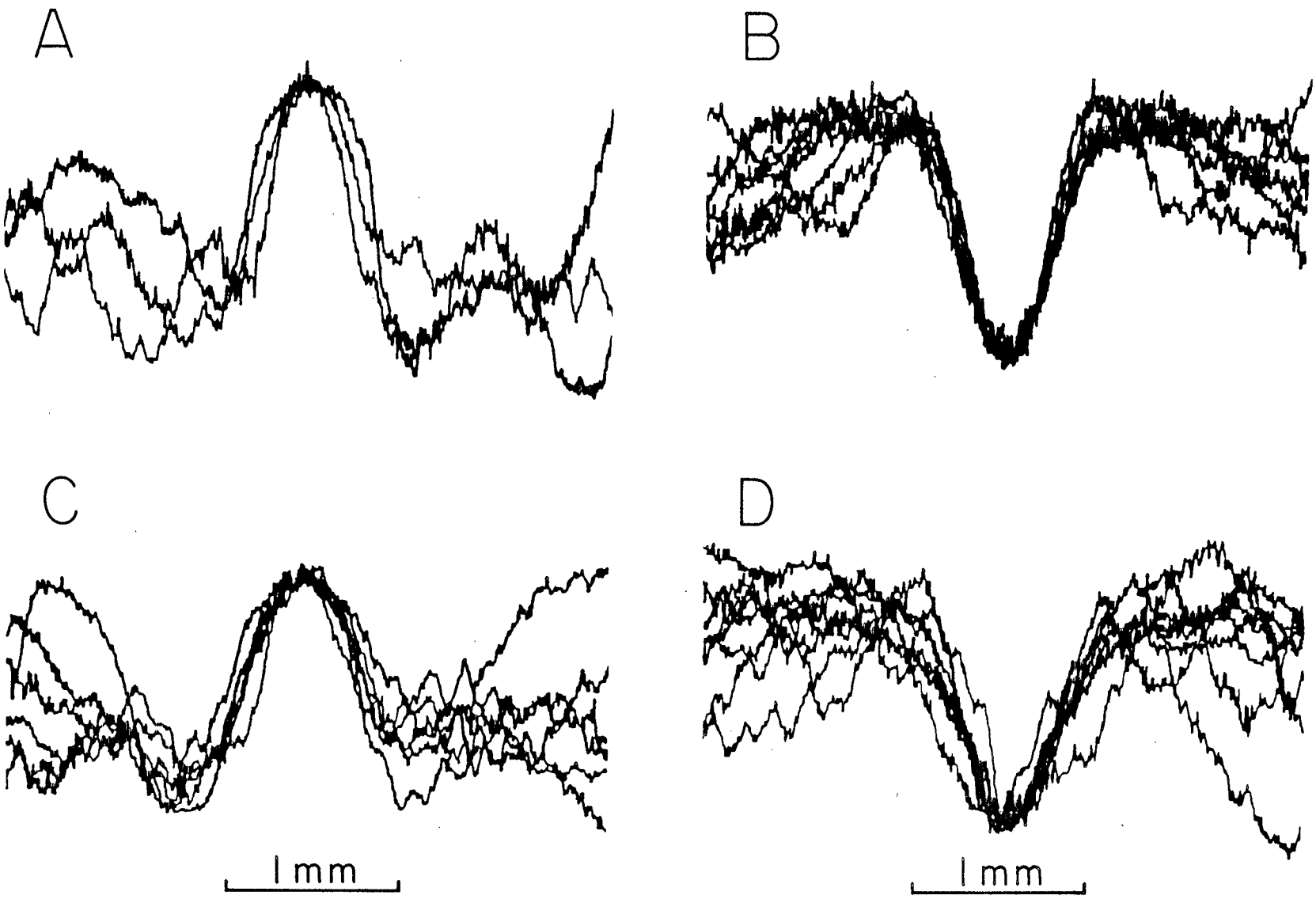


Fig. 6.3

STRF characteristics of tadpole and frog ganglion cells

	Latency to peak response(msec)	Diameter of receptive field center(um)	Number of cells
Tadpole			
Type A	130 ± 20	680 ± 78	3(4.4%)
Type B	130 ± 50	580 ± 83	65(95.6%)
Frog			
Type A	70 ± 10	710 ± 210	11(14.1%)
Type B	60 ± 30	680 ± 150	53(76.0%)
Type C	not determined	not determined	7(9.9%)

Diameter of the receptive field center was defined as the half-width of the receptive field profiles with maximal magnitude.

Table 6.1

CHAPTER 7

PERSPECTIVE

The present study has shown that receptive field center of bipolar and ganglion cells in the catfish retina detects and transmits local brightening or dimming of incident light. Receptive field surround has been shown to play a very important role in regulating center response. Based on the present study, three lines of exploration may be required to elucidate the visual information processing mechanism in the retina.

First, a new type of stimulus is needed to investigate more elaborate regulatory mechanisms which have not yet been fully ravealed by the stimuli used so far. For example, a random noise whose intensity distribution is unsymmetrical around the mean is suitable for probing the regulatory mechanism by use of third-order moment of incident light. Such mechanism would induce adjustment of operating range of both on- and off-center cells according to the properties of intensity distribution. The regulation relating with third-order moment of incoming light cannot be revealed by symmetrically distributed stimulus pattern as used in the present study. One candidate for the cells which participate in such higher-order regulation, is a sustained amacrine cell whose functional role is little known. Whether the amplitude of DC shift caused by light illumination represents mean illuminance of stimulus, is not fully understood in sustained amacrine cells. Furthermore, sustained amacrine cells show very complex responses to spatio-temporal random noise(cf. Chapter 3 of this thesis). Therefore, the analysis of response to

unsymmetrical stimuli is very important to unveil the function of sustained amacrine cells.

Second, the estimation of spatio-temporal resolution diagram of both bipolar and ganglion cells is prerequisite to clarify the spatio-temporal dynamical interaction in the retina. Besides the spatio-temporal random noise, sinusoidal gratings may be convenient test stimuli for this end.

In the final section, presumable close relationship between cell types and their dynamic range is discussed. As briefly described in general introduction, on- and off-center cells may serve as a range fractionation in the retina. The scheme I propose is that on-center cells handle lower intensity range, whereas off-center ones handle higher one to cover entire dynamic range in cooporation with two types of units. This speculative scheme has supporting reasons when considering the visual information processing task. Under a very low ambient light, detection of a brightening pattern against the dark background has very important meaning for animals. Such detection is conducted by on-center cells. In a very bright environment, on the other hand, the detection of a dimming pattern is rather important than the extraction of a brightening object. If so is the case, on-center cells are thought to be dominant in rod-dominant retinas. Conversely, off-center cells are expected to be more abundant than on-center cells in cone-dominant retinas. In fact, it has been reported in rod-dominant dogfish retina that 95% of the bipolar cells sampled in the electrophysiological study are on-center type (Ashmore and Falk, 1980). In cone-

dominant catfish retina, sampling population of off-center cells was about four times of that of on-center cells (Naka, 1977;, Chapter 3 of this thesis). The validity of this scheme has to be assessed by electrophysiological examination in several species of retinas with different rod-cone ratio. Furthermore, knowledge about how response properties of both on- and off-center cells change with adaptational level, would help to understand adaptation mechanisms in the retina.

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