ERM 2023

17 - 20 September, 2023
Tübingen, Germany






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European Retina Meeting 2023

17 – 20 September, 2023 in Tübingen, Germany

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Direction selectivity in the fish retinotectal system: Review and new aspects

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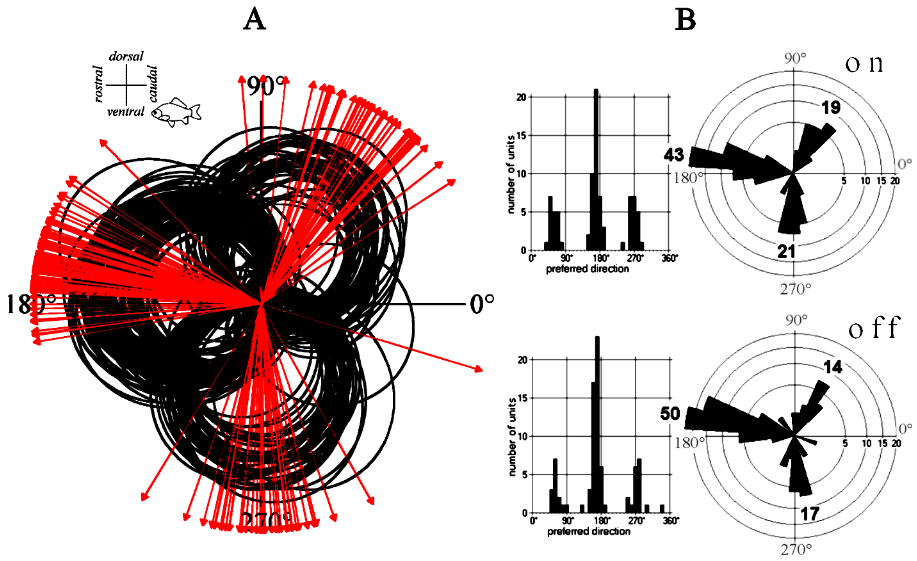
The retinal ganglion cells (GCs) are the output units of the retina. They send highly processed information about visual environment to tectum opticum (TO) - the main primary visual center of the fish brain. The aim of this report is to summarize the main electrophysiological data about direction selectivity in the fish retinotectal system, accumulated in our laboratory for many years of research. Single unit responses of the retinal direction selective (DS) GCs were recorded extracellularly from their axon terminals in the superficial sublaminae of TO (about 50μm from tectal surface) in living fish. The DS GCs projecting to TO were shown to comprise three physiological types according to their preferred directions separated by 120° - caudo-rostral, ventro-dorsal and dorso-ventral. They are also selective to the sign of stimulus contrast – they are either ON or OFF units, which makes six types in total unlike to four types of ON-OFF DS GCs in mammals. It was shown that direction selectivity in fish DS GCs is mediated by asymmetric null-side inhibition. They are characterized by relatively small receptive fields (4°) and remarkable spatial resolution. We have also recorded responses of direction-selective tectal neurons (DS TNs). Their responses differ from the responses of DS GCs by their spike form and the profile of spike discharge. These TNs are ON-OFF type units, they have large receptive fields (up to 60°) and were shown to select four preferred directions, three of which are similar to those already selected on the retinal level. Match of three preferred directions of ON and OFF DS GCs and ON-OFF DS TNs allows us to hypothesize that retinal DS units are input neurons for corresponding types of DS TNs. The responses of DS TNs of these three types may be recorded at a depth of about 100μm and deeper about 300μm from the tectal surface. The fourth DS TN type with rostro-caudal preference (lacking in the fish retina) has been revealed in TO. These units are recorded exclusively in deep TO layers. The direction selectivity of these DS neurons is built de novo at the tectal level by unknown cellular mechanism that remains to be clarified. DS TNs (all four types), as DS GCs, have high and “acute” contrast sensitivity and high spatial resolution. It was proved that fish retinal DS units and their putative tectal targets DS TNs are nonlinear integrators, with the visual acuity close to the limit determined by the density of the cones.

Acknowledgments: Institute for Information Transmission Problems of Russian Academy of Sciences, Moscow, Russian Federation


A
B
dorsal
rostral
caudal
ventral
90°
180°
0°
270°
on
off
19
43
21
14
50
17
number of units
preferred direction

Direction selectivity in the fish retinotectal system: Review nad new aspects *

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* Dedicated to Dr Vadim V. Maximov who was a chief of our group over a long period of time. His scientific attitudes, as well as meticulous experiment planning and data analysis are behind all the research findings.

Our main articles on the topic

Maximov VV, Maximova EM, Maximov PV. 2005. Direction selectivity in the goldfish tectum revisited. Ann NY Acad Sci. **1048**:198-205. https://doi.org/10.1196/annals.1342.018

Damjanović I, Maximova EM, Maximov VV. 2009. Receptive field sizes of direction-selective units in the fish tectum. J Integr Neurosci. **8**:77-93. https://doi.org/10.1142/S021963520900206X

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Damjanović I, Maximov PV, Aliper AT, Zaichikova AA, Gačić Z, Maximova EM. 2019. Putative targets of direction-selective retinal ganglion cells in the tectum opticum of cyprinid fish. Brain Res. **708**:20-6. https://doi.org/10.1016/j.brainres.2018.12.006

Direction selective units of the fish retina

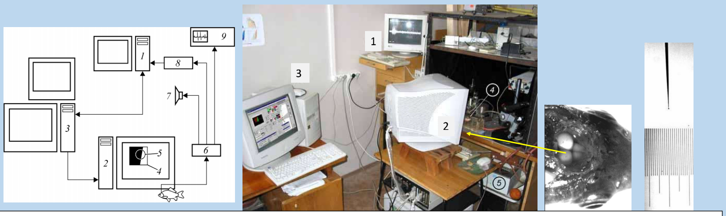

Fig.1. Method of recording. A scheme and photo of the experimental setup. Immobilized fish (d-tubocurarine, *i.m.)* were placed in their natural position in a transparent Plexiglas tank, with perfusion of aerated water through the gills, the eyes remained under water. Visual stimuli were presented on the computer-controlled CRT monitor to the right eye. An opening was made in the skull over the *tectum opticum*. Responses of direction selective ganglion cells were recorded extracellularly from their axon terminals in the left tectal lobe with the aid of the metal-in-glass microelectrode (ME) with a platinum tip (2-5μm). Scheme of the experimental setup (left panel): 1 – recording module; 2 – stimulating module; 3 – controlling module; 4 – stimulation area on the monitor screen; 5 – receptive field of the recorded cell; 6 – AC preamplifier; 7 – loudspeaker; 8 – A/D converter; 9 – oscilloscope. Photo: 1 – recording module; 2 – stimulating module; 3 – controlling module; 4 – experimental fish; 5 – water pump.

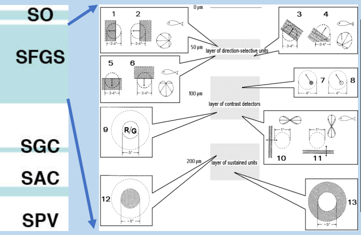

Fig.2. A schematic view of retinal projections in the retinorecipient layer of the goldfish tectum. Left: layers of the fish *tectum opticum*. Retinal afferents predominantly terminate in the retinorecipient layer - *stratum fibrosum et griseum superficiale* (SFGS). Right: segregation of retinotectal projections as derived from extracellular recording (thickness of SFGS in adult goldfish is 150μm approximately): 1,2 – ON- and OFF- DS GCs of caudo-rostral preferred direction; 3,4 – ON- and OFF- DS GCs of ventro-dorsal preferred direction; 5,6 – ON- and OFF- DS GCs of dorso-ventral preferred direction; 7,8 – black spot and white spot detectors; 9 – color-opponent units (R/G type); 10,11 – detectors of horizontal and vertical line; 12,13 – dark sustained and light sustained units.

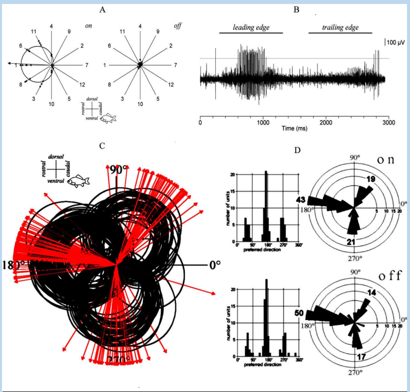

Fig.3. Response pattern and preferred directions of fish DS GCs. (A) Polar plots of a roach ON DS GC to the leading and trailing edges of moving white broad stripes. Stimuli moved in 12 directions across gray background in a random order into the unit receptive field. The plot marked with the label "on" was built from the responses to the movement of bright edges, while that marked with label "off" - to the movement of dark edges. **(B)** The response of the same unit to the leading and the trailing edges of the white broad stripe moving in the preferred direction. **(C)** Clustering of polar plots diagrams calculated for 164 goldfish DS GCs (preferred directions calculated for directional tuning curves are marked by red arrows). **(D)** ON- and OFF-type DS GCs were presented in practically equal quantities (in the tested units). Histograms of preferred directions for both types of DS units are presented. Results of our experiments on several marine and cyprinid fishes have shown that the properties of their DS GCs did not differ from each other (see recent review paper of Damjanović et al., 2023; https://doi.org/10.2298/ABS221216003D). Our findings were additionally confirmed in a calcium imaging study of the retinal DS GCs innervating the tectum of zebrafish larvae (Nikolaou et al., 2012; https://doi.org/10.1016/j.neuron.2012.08.040).

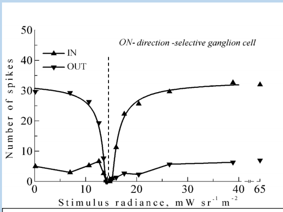

Fig. 4. Intensity-response profiles of a goldfish ON-type DS GC. The ordinate indicates number of spikes in the cell discharge in response to the movement of achromatic wide stripes of various brightness over a fixed gray background (GB) through the DS GC receptive field in the preferred direction. Two branches of the curve correspond to responses to the leading (in) and trailing (out) edges of the stimulus.

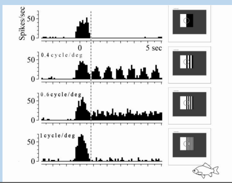

Fig. 5. Spatial properties of a goldfish OFF DS GC. Stimuli - square-wave gratings of various spatial frequencies (shown on the right) moving over the DS GC receptive field in the preferred direction were presented to fish in the square area. Peristimulus histograms of the recorded responses are shown on the left, each near the corresponding stimulus. The first discharge evoked by the leading edge of the grating was discarded (dashed vertical line) and the remaining response was analyzed. DS unit finally ceased to respond to grating of high spatial frequency (1 cycle/degree).

Receptive field organization of retinal direction selective units

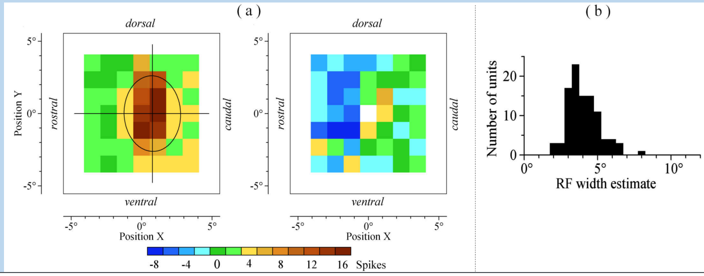

Fig.6. Receptive field (RF) mapping of goldfish OFF DS unit (random checkerboard method). (a) – Left panel: unit responsiveness across the stimulation area, recorded by RF mapping with one flashing black spot against a light background. Unit responses over the entire stimulation area measured by this method are represented in the form of a topographic map (see the scale at the bottom of the figure). The major and minor axes of the RF were evaluated according to the two-dimensional equivalent of the standard deviation for this data set. The ellipse built based on the evaluated RF axes, presents an estimate of the RF area. Right panel: lateral interactions in the RF of the same OFF caudo-rostral DS unit measured by two flashing spots. The influence of the second spot (flashed at different positions in the stimulation area) on the response of the central one was determined by the difference between the mean number of spikes in response to simultaneous stimulation of the two spots and the mean number of spikes in response to the central stimulus alone. The differences were mapped considering the position of the second spot. **(b)** – Distribution of the RF sizes evaluated by a random checkerboard for 99 DS GCs (mean value 4.3°±1.1°).

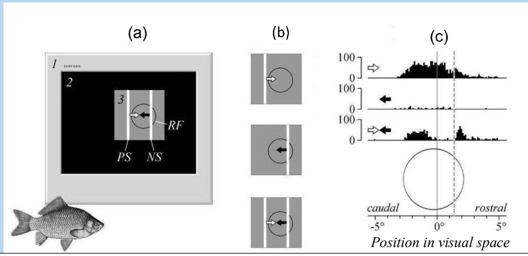

Fig.7. Stimulation procedure with two stripes moving in opposing directions. (a) – Schematic presentation of the experimental paradigm. 1 – stimulating monitor; 2 – monitor screen; 3 – gray stimulation area; RF – rough estimation of the receptive field of the recorded unit with regard to the stimulation area; PS – preferred-side stripe; NS – null-side stripe. Two stripes (PS and NS) move simultaneously in opposing directions – one stripe enters the cell RF from the preferred direction and the other one from the null direction (marked by a white and black arrow, respectively). **(b)** – An example of the experimental procedure performed on a goldfish ON-type DS GC. The unit was stimulated by white stripes. The stimuli were presented on the screen within a square area of stimulation with angular dimensions of 11×11°. Modes of stimulation: top panel – single stripe moving in the preferred direction; middle panel – single stripe moving in the null direction; bottom panel – paired stripes moving simultaneously in opposing directions (paired stimuli cross in the middle of the square area and afterwards move away from each other). **(c)** – Eighteen consecutive presentations of stimuli were performed at each step of stimulation. Averaged peristimulus histograms of single-unit responses, calculated for all 3 modes of stimulation are presented in the same order as in (b). Spatial coordinates of the stimulation area are presented at the bottom of the diagram in the coordinates of visual space (degrees; 0° marks the center of the stimulation area). The rounded area represents a rough estimation of the unit RF. The inhibitory effect mediated from the null direction lasted during the approach of stimuli. After the stripes crossed each other in the center of the stimulation area the response of the unit restored. Dashed vertical line marks the position of the preferred stripe (PS) when the unit response to paired stimuli started to recover.

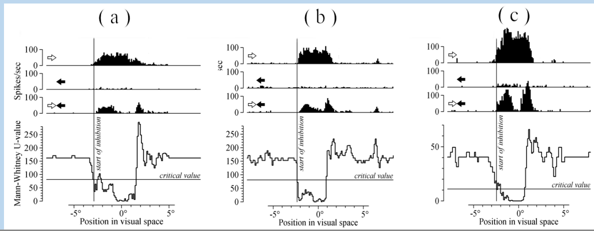

Fig. 8. Statistical analysis (Mann-Whitney test) of null-side inhibitory influences in goldfish DS GCs. Mann-Whitney U-values presented on bottom panels were calculated in three goldfish DS GCs at different positions of the preferred side stripe for two data sets - single stripe moving in the preferred direction and two stimuli moving in opposing directions. U-values were calculated over narrow intervals occupying 20' of the fish visual field. When the U-values fell below the critical level it was considered that the inhibitory effect from the null side was initiated at that point (position of the preferred side stripe at that moment is marked by the solid vertical line signed as "start of inhibition"; criterion U-value was fixed at α= 0.05). **(a)** – ON-type DS GC selective to caudo-rostral movement. **(b)** – ON-type DS GC selective to ventro-dorsal movement. **(c)** – ON-type DS GC selective to dorso-ventral movement. Stimuli – white stripes. Width of stimuli: 30' (a,b), and 10' (c). Eighteen (a, b) or nine (c) consecutive presentations of stimuli were performed at each step of the stimulation. Other conventions are same as in Fig. 7.

Direction selective neurons of the fish tectum

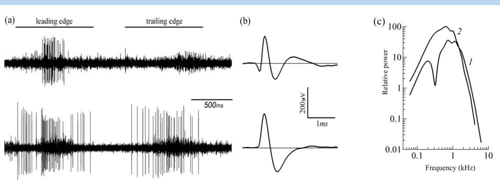

Fig. 9. Response patterns of two goldfish DS units in response to the movement of leading and trailing edges of the broad stripe ("edge stimulus"). (a) The first unit (upper trace) is a retinal OFF-type DS GC stimulated by the caudo-rostral movement of a broad black stripe on a neutral gray background; the second (lower trace) is a tectal DS neuron (ON-OFF unit) stimulated by downward movement of the broad white stripe. **(b)** Averaged spike forms for retinal DS GC (upper trace; N=42), and tectal DS neuron (lower trace; N=61) shown in an expanded time scale. **(c)** Power spectra for spikes of DS GC (1) and tectal DS neuron (2).

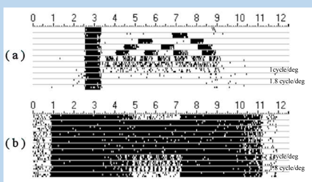

Fig. 10. Spatial resolution of DS TNs. Raster plots of the responses of a caudo-rostral ON-type DS GC **(a)** and a caudo-rostral DS TN **(b)** to gratings of different spatial frequencies (both units recorded in goldfish). The retinal DS unit ceased to respond to gratings with spatial frequencies exceeding 1cycle/degree, while the tectal DS neuron continued to respond to high-frequency stimuli. Experimental method was same as in Fig. 5.

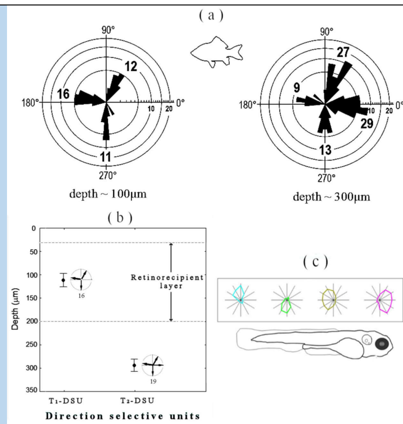

Fig.11. Preferred directions of fish DS TNs. (a) The distribution of preferred directions calculated in 117 DS TNs (98 goldfish and 19 carp units). Distributions of preferred directions for two groups of fish DS TNs recorded at different tectal levels are shown: at the tectal depth of about 100 μm (left histogram; 39 units) and at the tectal depth of about 300 μm (right panel; 78 units). **(b)** Relative depth distribution of DS TNs in the fish tectum. Closed circles: averaged depths in "μm" for two groups of recorded units. They were recorded at two tectal levels: in the retinorecipient layer (T_1-DSU) and in deep tectal zones (T_2-DSU). Vertical bars denote 0.95 confidence intervals. Direction preferences of tectal DS units are given near the corresponding plotted data (the number of analyzed units is shown). The fourth rostro-caudal preference emerges in a deep group of tectal DS units exclusively. Clear segregation of two groups of DS units (T_1-DSU and T_2-DSU) was statistically proven (one-way ANOVA). The data were collected in goldfish and carps. **(c)** The results consistent with our data were presented in zebrafish by calcium imaging study (see the paper of Hunter et al., 2013; https://doi.org/10.1523/JNEUROSCI.1493-13.2013). It was shown that DS neurons of *Danio* tectum comprise four preferred directions, three of them compatible with those already described for the retinal DS GCs.

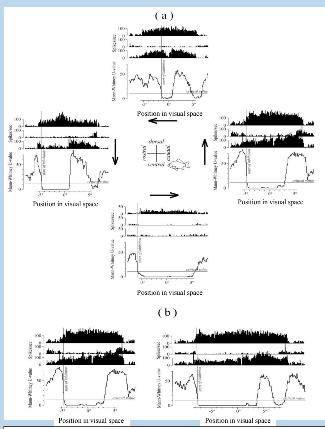

Fig. 12. Null-side inhibition in goldfish DS TNs. (a) Null-side inhibitory effects during opposing motion recorded in four types of tectal DS neurons. Preferred directions for presented neurons are marked by arrows. Top panel – width of stimuli 10'; middle panels –width of stimuli 1° for both neurons; bottom panel –width of stimuli 30'. Other conventions are same as in Fig. 8. **(b)** Null-side inhibitory effects during opposing motion recorded in a ventro-dorsal DS neuron in stimulation areas of different widths - 11° (left) and 16.5°(right).

Conclusions

1. Direction selective ganglion cells (DS GCs) of the fish retina projecting to the superficial sublamina of tectum opticum (TO) use separate ON and OFF channels and are characterized by small receptive fields (RFs).
2. Direction selective tectal neurons (DS TNs) have large RFs and ON-OFF type responses. Latter indicates (at least for DS TNs with caudo-rostral, dorso-ventral and ventro-dorsal preferences) that DS GCs of both ON and OFF types converge as excitatory inputs to tectal DS neurons.
3. The fourth DS TN type with rostro-caudal preference (lacking in the retina) emerges in TO. Their responses are recorded in TO deep zones exclusively, whereas responses of DS TNs of other three types may be encountered in retino-recipient layer too.
4. Asymmetric null-side inhibition as a mechanism underlying direction selectivity of DSGCs as well as DS TNs in fish has been demonstrated by stimulation procedure with two stripes moving across unit RF in opposing directions .
5. Both, S GCs and DS TNs are characterized by finest contrast sensitivity and high spatial resolution.
6. The spatial resolution of DS TN is higher than that of retinal DS GCs.