Healthcare industry BW

Motion sensor in the brain

Researchers from the Max Planck Institute for Medical Research have shown in zebrafish that visual movement stimuli are processed in the animals' visual system by two types of direction-sensitive neurons located in spatially separate circuits. Different directions of movement are represented in different layers.

Zebra fish larva, around 4 mm long.
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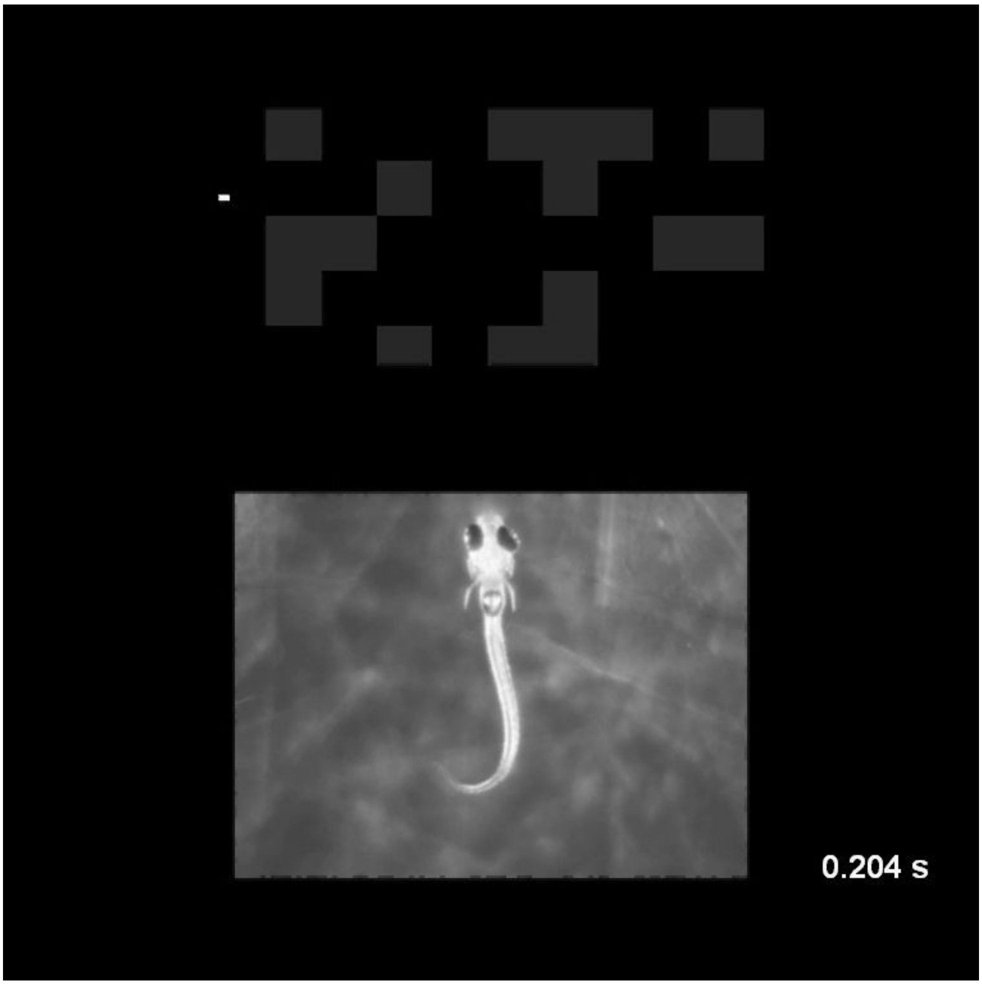
The zebrafish (Danio rerio) is one of the most popular model organisms in biological research: it is small, robust, has a short generation time and can be kept and bred in large quantities and at relatively low cost. The zebrafish genome has already been decoded, and efficient methods for producing and screening for mutations have been established. As a vertebrate, the zebrafish is much closer to humans than flies or threadworms, and many genetic, developmental and physiological findings gained from zebrafish research can be transferred to the situation in humans. The fact that embryonic development takes place outside the female body, alongside the possibility to investigate the transparent embryos and early larval stages under the light microscope, is an enormous advantage in experimental terms.

Phantom hunting of zebrafish larvae



Partly embedded larva observing virtual prey on a small screen.
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Scientists at the Max Planck Institute for Medical Research (MPImF) in Heidelberg make use of the favourable properties of zebrafish larvae for neurobiological research. They are aiming to achieve an understanding of what happens in the eyes and the visual centre of the zebrafish brain as the animals perceive movements. When they are seven days old, zebrafish larvae are around four millimeters long and their brain is less than 0.5 mm thick.

As the larvae have transparent skin, “virtually all brain areas can be examined using multiphoton fluorescence microscopy that enables us to study live cells,” said Dr. Johann Bollmann of the research group "Neural Circuits and Behaviour" in the MPImF's Department of Biomedical Optics. As tiny as they are, the principle structure of the eyes and visual centre in the mid-brain of zebrafish larvae is extremely similar to that of mammals. Zebrafish larvae, which display a very clear prey capture behaviour, use this well-developed visual system to hunt for ciliates and other single-celled organisms in the water. The Max Planck scientists hope that the analysis of the larvae’s targeted movements and the electrical signals that are produced in the brain will provide them with better insights into how neurons interact in intact brains.

Eyes and a projection running from the retina to the tectum (dorsal region of the mid-brain) in a 3-day-old zebrafish. The structures are stained with an anti-ath5-GDP antibody.
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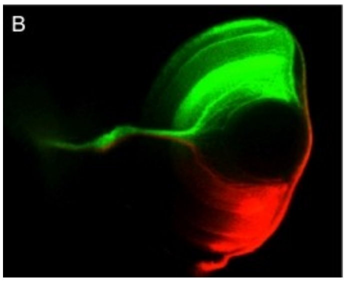
The scientists used high-speed video recordings to study the natural swimming behaviour of the larvae and derive information in order to create a “virtual reality” where the small fish were presented virtual prey consisting of computer-controlled images that were projected onto a small screen. As the larvae were temporarily fixed onto a small gel strip they were able to execute typical prey capture sequences with their eyes and tails without actually moving. Bollmann and his team were therefore able to specifically alter the movements of the virtual paramecia and study the reactions of the animals’ visual system and the resulting movements in relation to the processing of visual stimuli. Optophysiological approaches involving transgenic fish larvae and fluorescence microscopes enabled the scientists to study the resulting electrical signals in the brain.

Identification of direction-sensitive neurons

The scientists from Heidelberg used zebrafish larvae in which the molecular marker GFP (green fluorescent protein) was expressed in a specific cell type in the dorsal region (tectum) of the mid-brain. Working with the MPImF’s “Developmental Genetics of the Nervous System” research group headed up by Soojin Ryu, the researchers also introduced the calcium-sensitive GCaMP3 gene into the animals in such a way that it was only expressed in specific neurons and made them glow only when in the presence of calcium.



Dual staining of the retina of a zebrafish larva. Green: temporal retina with a projection that runs (to the left) towards the tectum. Red: nasal retina.
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Special neurons, which react specifically to visual motion, are involved in the perception of movement stimuli and their processing in the visual system of vertebrates. Such direction-sensitive neurons (DS neurons), which react specifically to opposing directions of movement, are found in the retina of eyes as well as in the brain cortex and the mid-brain tectum. The retina is directly connected with the tectum by way of projection neurons whose inputs are arranged such that spatially adjacent optical stimuli activate spatially adjacent regions on the surface of the tectum. The sensory neurons are connected in circuits with motor neurons located in deeper tectum layers that can trigger eye and head movements. The existence of these circuits has principally been shown in experiments involving other animal models in which individual neurons were activated and visualised using fine electrodes.

Spatial arrangement of the movement circuits

Using new fluorescence microscopy techniques such as multiphoton microscopy, it is possible to study the spatial and temporal distribution of neural activity patterns. Using these techniques, the Max Planck researchers from Heidelberg have discovered a circuit in the tectum of zebrafish larvae that is involved in the processing of movement directions in the visual system. Multiphoton microscopy was also used to determine the direction sensitivity of neurons containing the GCaMP3 gene. Using very fine glass pipettes, the scientists injected a red fluorescent dye into the cell body of these neurons, which then spread into the finely branched dendrites within a few minutes. These experiments enabled the scientists to identify two types of DS neurons that react specifically to opposing directions of movement. The scientists made the unexpected discovery that the dendrites of the two different types of neurons were located in different layers of the tectum.

Further experiments revealed that the direction-sensitive signals of the projection neurons that come from the retina also arrived in specific tectum layers. It appears that different directions of motion are processed in different layers of the tectum. With this discovery, the scientists from Heidelberg were the first to localise the circuits that are responsible for the processing of visual motion signals in the brain. Bollmann highlighted that these new findings are basically due to the favourable properties of zebrafish larvae that make them particularly suitable for such types of investigations: the larvae are transparent, have a compact build, can be easily manipulated genetically and they use information from the visual system for the execution of movements when reacting to the movements

Dr. Johann H. Bollmann, Biomedical Optics, Max Planck Institute for Medical Research.
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of prey.

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