Fluorescent protein lets us read a fish's thoughts

17:00 31 January 2013 by Douglas Heaven

Video: Glowing protein lets us see into a fish's brain

The zebrafish spots its lunch. What goes through its brain? Now, for the first time, we can see exactly what it is thinking, thanks to a new way of studying single neurons that lets researchers track patterns of brain activity in a live animal.

A standard way to achieve detailed imaging of cellular activity is by genetically altering cells to express green fluorescent proteins (GFPs) which light up when calcium concentrations rise – such as occurs when neurons are activated.

To try to see activity in individual neurons, Koichi Kawakami at the National Institute of Genetics in Shizuoka, Japan, and colleagues created a super-sensitive GFP and tested it in zebrafish larvae between four and seven days old, when they are transparent.

The researchers focused on capturing activity in the zebrafish's tectum – a region of the brain that processes vision. They set up an LCD screen that displayed a blinking dot to one side of an immobilised zebrafish larva. As the dot appeared and disappeared, they saw corresponding flashes of light from the tectum, reflecting neural activity.

When the team moved the dot from left to right and top to bottom, they saw horizontal and vertical movement of brain signals in the tectum, revealing what is known as the visuotopic map. Visual information from each eye is processed in the opposite hemisphere of the brain, so movement seen by the right eye was replicated in the left side of the tectum and vice versa.

Magnification factor

The difference in scale between the brain map and the actual movement showed that the magnification factor was larger in the vertical direction than the horizontal, but why this should be is unclear. "I think fish eyes and our eyes could be better at finding differences in height rather than those in the horizontal direction," says Kawakami. "It's an interesting question."

The team then introduced a live paramecium – a tiny single-celled organism eaten by zebrafish – near the larva's head. There was no response when the paramecium was motionless, but when it started swimming, signals in the zebrafish brain matched the movement of its prey.

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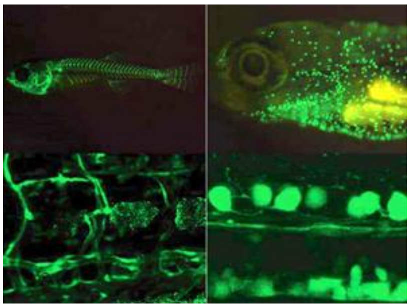

Fluorescent protein is a bright idea *(Image: The Kawakami Group/NIG)*

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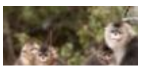

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Finally, the team observed brain signals while the zebrafish larva and prey both swam freely. Just before the larva caught its prey, the signals converged in the front of the tectum, suggesting that activation of this area could be connected with subsequent activation of the larva's motor pathways.

"This is very exciting work," says Martha Constantine-Paton, who studies brain development at the Massachusetts Institute of Technology. She hopes that it will soon be possible to watch how neural circuits grow as a zebrafish matures.

That will be the next big hurdle, she says, and since the fish are only transparent as larvae, it would require a cranial window or especially sensitive optical reagents. But we might not be far off. "The sensitivity resolution of this new green fluorescent protein is amazing," she says.

Kawakami and colleagues are now attempting to observe activity across the whole brain. "We will explore neurons that work while the fish learns and thinks," he says. "This will lead to an understanding of the fundamental neuronal circuits at work during human thought."

Journal reference: *Current Biology*, DOI: 10.1016/j.cub.2012.12.040

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