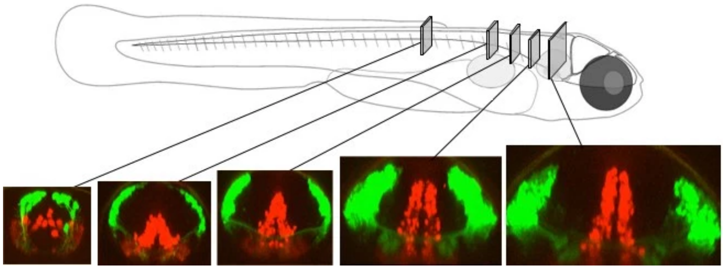

image courtesy of Prof. Joseph R. Fetcho

Columns in optical slices from a living zebrafish at different locations. The slice on the left is in the spinal cord; images to the right are in the brain.

FEATURED IN CATEGORY

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Left or Right? Researchers Study How Zebrafish Make Decisions

By **Jack Novak**

Imagine you are a larval zebrafish. You hear something: the sound of a predator racing towards you. You turn hard to your left. How did you decide to turn left instead of right?

Prof. Joseph R. Fetcho, neurobiology and behavior, and colleagues followed how this decision is made by mapping the circuit of neurons from the sensory input of the sound of a potential predator to the behavioral output of the actual muscle movement in their study: 'A circuit motif in the zebrafish hindbrain for a two alternative behavioral choice to turn left or right.'

Zebrafish turn rapidly to the left or right as an escape behavior when they perceive signs of predators.

"This escape behavior shows a circuit that collects sensory information from opposite sides of the body; sensory information comes in from the left and in from the right and what happens during an escape is that an animal has to weigh how strong is the information coming in from the right," Fetcho said.

During an escape, the animal has to weigh how strong the information coming from both sides is and then move, depending on which side has the strongest signal. The side with the strongest signal is the side where the attacking predator is present.

The circuit described in the study may be the general way in which different types of neurons are connected in the hindbrain. The escape behavior of larval zebrafish is a simple behavior. The circuit determining the behavioral choice of turning left or right involves fewer neurons than more complicated behavior, for which information is also collected over a longer period of time. The study showed how two alternative behavioral choices are competed against each other to make the appropriate decision. The competition occurs via inhibitory cells so that evidence for one alternative is also evidence against the other alternative.

Larval zebrafish are transparent and, according to Fetcho, this transparency comes in handy.

"We could use the transparency of the fish to visualize nerve cells, to record their activity with microelectrodes and map out a circuit," Fetcho said.

From this map, models were constructed of the circuit responsible for the physical reaction of turning to the left or the right or not turning at all. These models could predict the effect of eliminating certain cells, assuming the cell held a specific function. To test if these were, in fact, the functions of particular cell types, the predicted effect of the cells' absence on escape behavior was compared to the observed effect of destroying these cells. Destroying a specific type of cells in the brain of a model organism, whose behavior needs to be observed afterward, demands incredibly sensitive technique. Laser ablations — irradiating materials through lasers — were performed to test models of cell function.

Although the circuit appears to explain a highly specialized escape behavior, it may be a pattern. The circuit is located in the hindbrain, which, as Fetcho explained, controls movements.

"It's a region that controls all sorts of movements in animals [and] in us too, like eye movements, jaw movements, limb movements and body movements," Fetcho said.

Also columns of morphologically similar cells are found in this brain region across vertebrates. There is evidence that behavior is repeated laterally throughout these columns, with the activity of neurons at the relative bottom of the columns associated with faster behavior.

Referring to three-dimensional reconstructions of such a column, Fetcho said, "We can show that [in] these cells that are involved in swimming, when the fish swims fast, the cells that are active are down here [in the column], and as [the larval zebrafish] swims more slowly the active cells are higher and higher up [in the column]."

The circuit for escape behavior outlined in this study lies at the bottom of one such column. Thus, the general pattern of connectivity may be repeated along the column so that laterally higher circuits determine behaviors over a longer period of time.

Moreover, the study suggests a circuit motif. The pattern that is implicated is the competing of two alternatives via inhibitory cells; the basic framework of competing two alternative behaviors to come to an optimal decision may be repeated laterally. Although, the cells are not exactly the same in circuits higher up in the column, the pattern of sensory input acting as evidence for one response and also triggering inhibitory cells for the alternative response may exist as the basic framework for how decisions are made in this column and even across the hindbrain of other vertebrates.

Fetcho explained the potential of this circuit motif, saying, "basically you're building a circuit over and over again, but you're changing the actual electrical properties of the cells in ways that cause it to collect information over longer periods of time… So you can build [circuits with] neurons with different properties that allow them to operate over different time domains."

Fetcho and his lab are continuing this work and working on whole brain imaging: imaging every neuron in the brain of larval zebrafish. As Prof. Joseph R. Fetcho said, "if [the circuit motif] is repeated we should see predictable changes in the position and pattern of activity of cells at different places in the column as we vary the sensory stimulation."