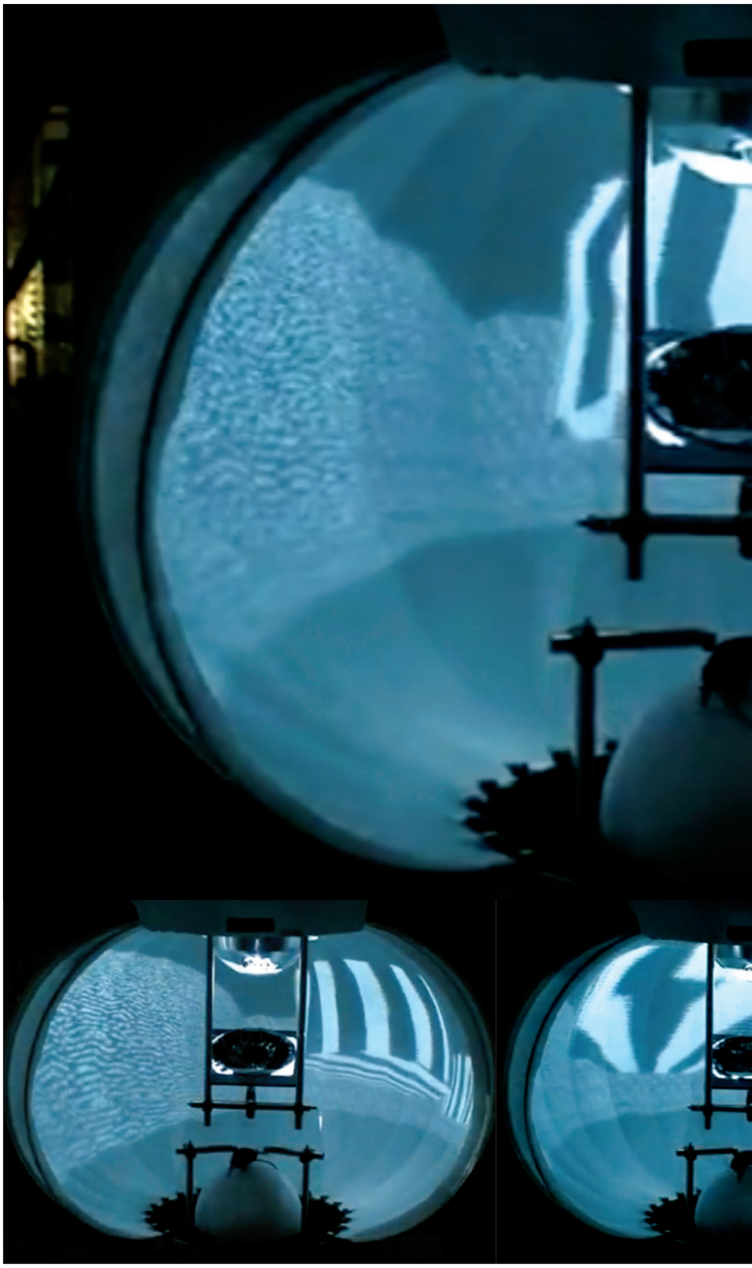
Virtual window on brains at work

Animals thinking inside a virtual world can help us understand what can go wrong in the brain


COURTESY OF DAVID TANK PRINCETOWN UNIVERSITY

Sujata Gupta

IT'S decision time. The mouse has scurried down the 3-metre-long corridor, and now faces a T-junction. It knows from experience that a reward of refreshing water lies at the end of one path. The other route leads to nothing. The mouse makes its choice and hurries off to the left.

Or so it thinks. In reality, the rodent is running on the spot, navigating a computer-generated world projected onto the inside of a spherical surface that fills its field of view. It is just one of many lab animals now living in a virtual world (see, "It's a simulated life...", opposite). Here, neuroscience meets animal behaviour to provide a powerful window into the workings of the brain and the underlying causes of neurological disorders.

We have always been able to watch how animals behave in the lab. More recently, new technologies have allowed us to see how single neurons fire as animals think. Put the two together and we can study how the activity of neurons affects the decisions that govern an animal's behaviour. "It's a whole new way to study the brain," says Bradly Alicea at Michigan State University in East Lansing.

There's just one problem: an instrument focused on a single neuron will be knocked out of alignment by the slightest shake. That means we can only study individual neurons in an animal that cannot move and is therefore unable to behave normally.

Virtual reality (VR) technology offers a solution – a way for animals to explore a simulated world while remaining rooted to the spot. David Tank at Princeton University and colleagues were among the first to put the idea into practice. By 2009 they had developed a harness that kept the head of a mouse stable enough for them to study neurons via electrodes inserted into its brain. Its legs were left free so the rodent could run on top of a styrofoam trackball that controlled movement through a virtual scene projected onto a screen surrounding the mouse. It had the job of running up and down a simulated corridor (*New Scientist*, 17 October 2009, p 18).

"The mice navigate a virtual maze, offering a chance to peer into the brain as decisions are made"

The experiment showed for the first time how a class of neurons called place cells fire during navigation – a step towards understanding how these cells misfire in people with Alzheimer's.

This week, Tank and colleagues announced the latest results from their VR studies. The technology has improved so that mice can navigate a T-shaped maze rather than simply scampering along one corridor, offering an opportunity to peer into the brain as decisions are made.

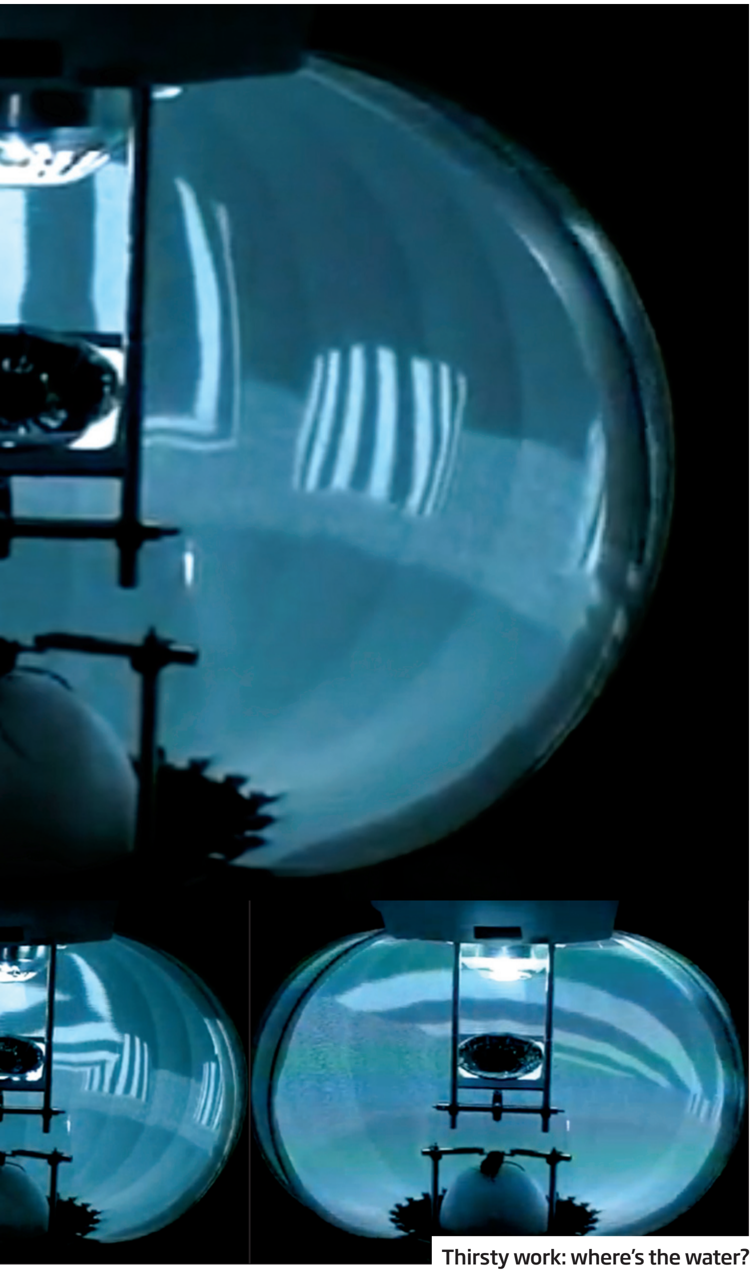
Rather than studying individual neurons with electrodes, this time Tank's team cut a window into the mouse's skull and used a microscope to view all of the neurons within the posterior parietal cortex, a brain region thought to control short-term memory. This region is implicated in neuropsychiatric disorders such as schizophrenia.

Back to our mouse at the junction – it guessed correctly by turning left. This isn't surprising since it had received a tip-off: as it ran towards the junction it spotted a tall wall on its left and it has learned that the water is always on the same side as the wall. The challenge? The mouse passes the tall wall long before it reaches the T so it must store the information in its short-term memory long enough to make the correct turn when the time comes.

"It's like driving or walking down the street, seeing a street sign and deciding whether to turn left or right at the intersection," says team member Chris Harvey at Harvard University.

While researchers suspected

In this section
■ Thank worms for our complex brains, page 10
■ Video games are officially hard, page 12
■ Were we taken in by LulzSec hacker Sabu? page 22



Thirsty work: where's the water?

IT'S A SIMULATED LIFE...

Studying the brains of mice and fish as they engage in different behaviours is useful (see main story) but the vertebrate brain is more complex. Nematode worms have just 302 neurons and about 5000 synapses, making them ideal for basic investigation.

Last year Serge Faumont at the University of Oregon, Eugene, and colleagues created a virtual world for worms in which they moved forwards and backwards as the team studied their brains. The same neurons governed both sets of behaviours – an unexpected finding that provides basic information on the workings of the brain (*PLoS One*, DOI: 10.1371/journal.pone.0024666).

Neuroscientists aren't the sole beneficiaries of VR studies. In 2010, Andrew Straw, now at the Research Institute of Molecular Pathology in Vienna, Austria, created a VR world for flies. He wanted to know how flies set their cruising altitude, work which could help design more dexterous tiny flying robots.

Previous research had suggested that flies use their speed to inform altitude. That is, when the floor beneath them races past, they rise up – when the floor slows down, they descend. When Straw changed ground speed in his virtual world, however, the flies didn't change altitude at all.

Instead, his work suggests that flies adjust their altitude by taking into account the location of horizontal edges in their environment (*Current Biology*, DOI: 10.1016/j.cub.2010.07.025).

The next generation of robot fliers may use visual information to navigate in a similar way.

that normal function in the posterior parietal cortex required neighbouring neurons to fire together, the new study shows they actually fire in an out-of-sync sequence (*Nature*, DOI: 10.1038/nature10918).

This suggests that the problems with short-term memory and decision-making sometimes seen in schizophrenia may arise from disruption to this normal sequence, says Christos Constantinidis, a neuroscientist at Wake Forest School of Medicine in Winston-Salem, North Carolina.

"Virtual reality will become the industry standard for studying animal behaviour within a decade"

Do virtual worlds really deceive animals? The emphasis is on fooling their visual sense. Mice are nocturnal, though, and often navigate using their vestibular senses, which detect motion and balance. Head-fixing technology deprives them of these senses, says Daniel Dombeck at Northwestern University in Evanston, Illinois, an author on Tank's initial study. He is trying to artificially stimulate the vestibular sense to build even more effective virtual worlds.

"We've found a minimum of what's required," Dombeck says. "Now how good can we make the simulation?"

Florian Engert at Harvard University has an inkling of what's involved. He has built one of the most sophisticated VR systems to date and his zebrafish larvae have spent all of their lives inside it.

Engert's fish control their VR world with their thoughts, which strengthens the illusion. They are paralysed, but Engert works out how the fish would move by reading the pattern of electrical activity in the motor neurons that normally control fin movement. He then moves a virtual sandy substrate projected beneath the fish in time with the expected fin strokes – all in real time.

There's another advantage to studying the tiny fish: their heads are translucent, making it possible to focus a microscope on any, or all, of the neurons in its brain without a surgical window.

In a study scheduled for publication later this year, Engert changed the ambient conditions in this VR environment – making the larvae's virtual swim strokes unexpectedly strong or weak, for instance – to see how the fish adjusted. He found that some neurons light up only in response to such surprises, implicating specific cells in learning and adaptation. Finding out more about these neurons could lead to better methods to help people who are paralysed adapt to a neuroprosthesis controlled through thought alone.

As the field gains momentum, Michael Reiser at Janelia Farm Research Lab in Ashburn, Virginia, suspects that VR will become the standard for studying animal behaviour within a decade. "It's no longer acceptable to do neuroscience research without incorporating behaviour." ■