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Charting the neural labyrinth

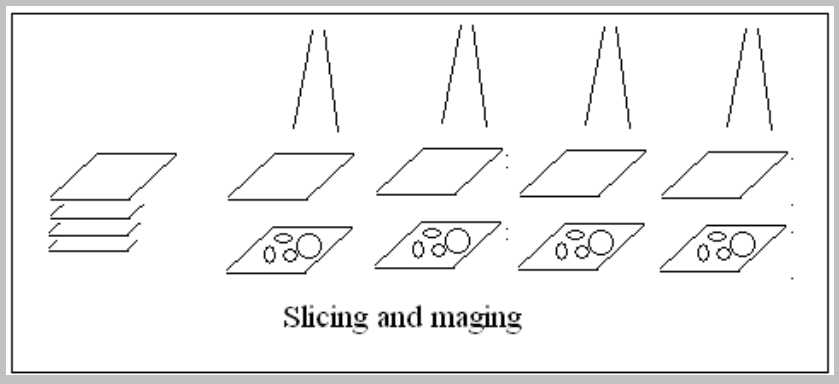
First steps have been taken to map brain pathways, says S.Ananthanarayanan.

The human brain consists of some 80 billion nerve cells and it works thanks to connections between cell and cell and stronger paths of some connections and weaker paths of others. Mapping such a mass of connections is still quite unimaginable. In fact, given the dimensions and complexity, even the connections of neurons within a small patch of brain matter has not been possible or attempted.

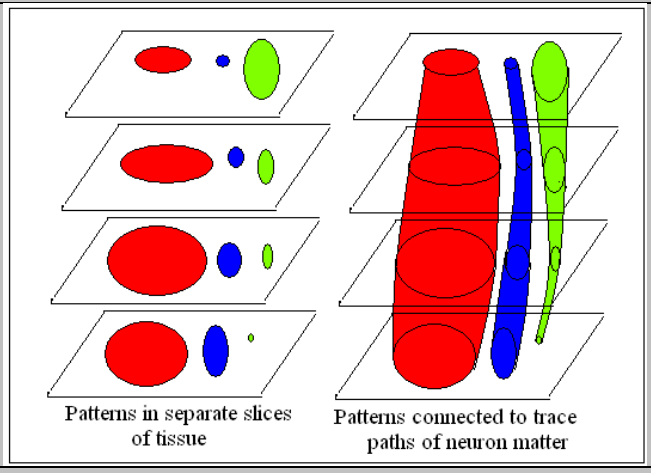
But scientists in Virginia, Halifax, Germany, Austria, Massachusetts, Maryland and London, working in three groups, report in three papers in the journal, *Nature*, the path breaking work they have done in modeling the connections between nerve cells in a small patch of mouse retina, which has revealed the working of different types of cells, closely matching the current understanding, which was based on molecular tracing and microscopy, of how these cells function. Two of the groups have built on the work of the first group, to identify the mechanism of the eye in detecting movement. There have been models of motion detection but the steps of neural events which bring about detection of motion have not been understood so far.

The retina, or the light sensitive material in the eye, is in fact a part of the brain itself, collecting information of light entering the eye and communicating with other parts of the brain via the optic nerve. Essentially, the retina is the layer of rods and cones, which are the cells that react when light falls on them, and then the layer of ganglion cells, which transmit visual data from groups of rods and cones to the brain. The eye could thus be considered to be a part processor of the visual data, before the data is interpreted as shapes or patterns, by the brain.

Nerve cells communicate by sending an electric signal through a path known as the axon, to the receptors, known as the dendrites, of other cells. The task at hand is essentially to trace the path – axon to dendrite to axon to dendrite, between different kinds of cells involved in the working of the retina, as a sample of brain tissue. But the task is complex, as there are 60 kinds of neurons, closely packed, and 20 kinds of ganglion cells. At the nanometer-scale of the cell-to-cell connections, these paths are not visible in ordinary microscopy. But in ultra thin slices, the structures of different cell material can be readily detected using electron beam microscopy



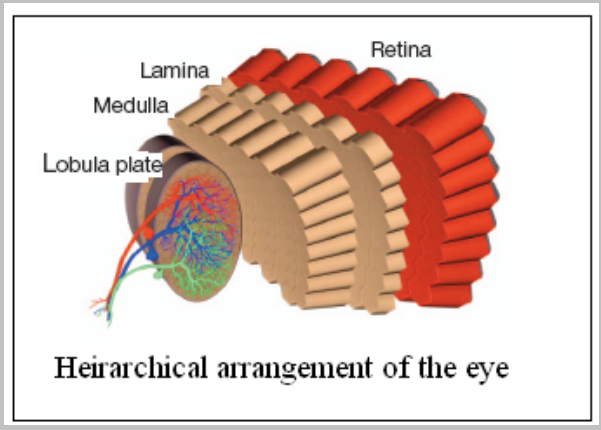
Helmstaedter and colleagues studied the path of nerve connection in a patch of 950 nerve cells in a 114 x 80 micrometer area (about a tenth of a millimeter across) of mouse retina using a manual and elaborate but very fine grained form of layer by layer scanning, or tomography.

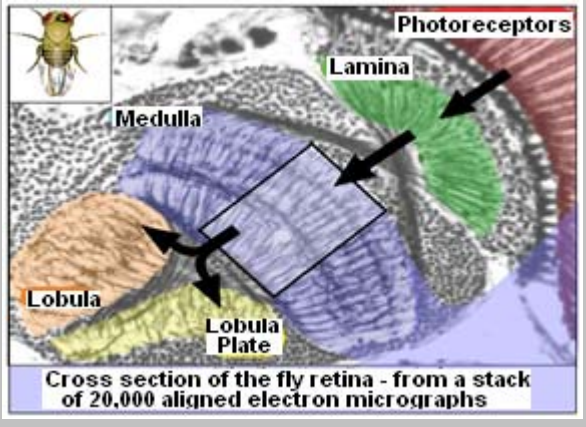


The patch of retina was first sliced into very fine layers. Each slice was then scanned by an electron beam microscope. Once the pattern of cells material in the different layers was identified, the layer images were put together and the original material reconstituted, using computers.

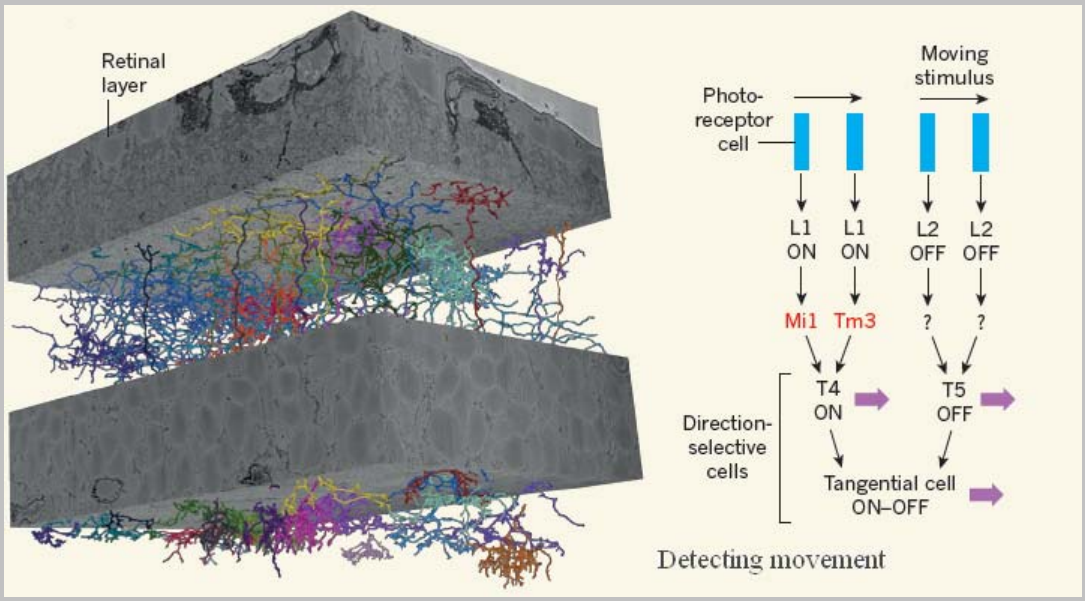
The computers first assigned a different colour to each structure in the images of each slice. The computers then connected the successive slices to identify the progress of the structures through the depth of the sample, and the computers could identify the connections between cells, the ***synapses***, along the scan. But to recreate the long branches of the cells, in 3 dimensions, the computers did not have the required ***pattern recognition*** capacity. To help out, the experiment used 300 trained students, for 100 hours each, 30,000 hours in all, to trace the paths of the neurons, and with this input, the computer could join up the coloured patches and create a 3 dimensional model of the neuron paths, from rods and cones to ganglion cells, in the tiny bit of mouse retina

The other groups, of Takemura and colleagues and Maisak and colleagues, studied the detection of motion in the eye of the fruitfly. The fruitfly, which is celebrated for how fast it can detect movement, to avoid attack (or being swatted), has the classic ***compound eye***, divided into hundreds or even thousands of separate units, called ***ommatidia***. The eye is arranged in arrays of six ommatidia, each group of six passing signals, which correspond to one part of the visual field, down to the ***lamina***, and a series of nerve bodies, in a ***column***.





For detection of motion, what is needed is the change of the image, or signal, coming down in two adjacent columns. Given the complexity of tracing neuronal connections, the study hence looked at a sample of just one column, surrounded by six others. It is known that although photo-detector cells by themselves cannot make out motion, somewhere down the line, there are cells that clearly indicate motion, up-down or right-left. The directional discrimination is created by neurons called ***T4*** and ***T5***, but they are too small for study of their electrical activity. Maisak and colleagues got around this by genetically coding T4 and T5 cells to change colour when they fired. It was found that the cells form four groups, which respond to movement up, down, front to back and back to front. And further that the cells can discriminate between images with bright edges and those with dark edges, breaking visual data a total of eight ways.



And how do the T4 and T5 cells do all this? Takemura and colleagues find that in the case of T4, just upstream of the cells, there is a pair of neurons, ***Mi1*** and ***Tm3***, which pass down information about points that are narrowly separated in space. Given the nature and timing of the signals, T4 is able to make out the direction of the movement being reported. There is still work to be done, but the Maisak technique of genetically coding Mi1 and Tm3 to respond by glowing in different colours could help discover the last details of how the eye detects direction of movement.

But whether the progress made would be able to chart the pathways of the brain itself is an open question. The extent and level of complexity is way above what has been overcome. Even modest targets would need huge manpower and spending. It is proposed that the work of identifying neural paths through the images of successive slices could be put on the Internet as a game, to make use of public manpower and computing resources. This would create a huge database of basic brain topography and would leave it in the public domain.