EXPLORING THE JUNGLE OF THE EYE

This half of Dr Kit Pedler's polystyrene model of a small area of the retina shows the dendrites projecting like the pins of a fantastically complicated electrical plug.

The process of making a model begins with the delicate task—at which Mrs Tilly excels—of cutting a sample of the retina into slices one 200,000th of an inch thick.

LIGHT ENTERS OUR EYES from the outside world, and comes out along the optic nerve as a train of nerve impulses. Somewhere in the middle is an interpreter, translating light into a language our brains can understand. The magic is in the thin layer on the back of the eye called the retina. This is where the brain meets the outside world, so it is a fascinating piece of tissue for anyone who is interested in how our brains work. One of these people is Dr Christopher Pedler, who has been exploring the tangled jungle of cells in the retina for the past four years. He and his team have already shown that the retina is much more complex than used to be realised; with a rare combination of skill, imagination, and inventiveness they are developing techniques to map it even so. One of their aims is to produce a "circuit diagram," of the retina, like engineers drawings which describe electronic circuits. Their work could even lead eventually to an electronic version of the human eye.

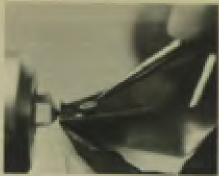
The team works in cramped quarters at the Institute of Ophthalmology, a dirty, redbrick building in Bloomsbury—and a much better candidate for demolition than St Pancras station near by. The accommodation is rather typical of what the biological sciences make do with in this country, but Kit Pedler is definitely not a typical scientist. An amateur sculptor, and formerly a racing-car driver, his latest enterprise is writing scripts for *Dr Who*, the children's television serial (watch out for "The Tenth Planet!"). The same love of form which led him to sculpture is carried over into his work. area, which has already led to discoveries that could not have been made in any other way. The prospects are exciting.

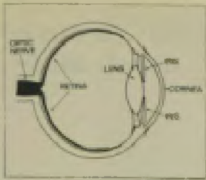
Scientists have been studying the retina ever since 1625, when Christopher Scheiner proved it is the screen on which the image of the outside world is projected. Even through an ordinary microscope it is possible to see that it consists of three major layers of cells, like three rows of pillars on top of each other. This simplification applies to most vertebrates as well as to man, so it is not usually human retinas which are used for experiments. The remarkable thing is that it is the bottommost of these three layers which consists of the receptor cells sensitive to light. After travelling across the eye, light has to pass almost right through the retina before being sensed by chemicals in these receptors. Then a signal travels back up the pillar of the receptor cell, through the middle layer containing the bipolar cells, to reach the top layer of nerve cells, which are really extensions of the brain. Finally, all the nerves of the retina come together in the optic nerve leading to the brain.

For a long time scientists thought that the signal from a receptor travelled more or less straight up through a bipolar cell on its journey to the brain, without any cross-connections between different columns of cells. But there are simply not enough cells in the retina for the eye to be as acute and adaptable as we know it is if this simple theory were true. There must be some more elaborate mechanism. Now Kit Pedler has shown there is an intricate the retina as an appallingly complex version of the electronic machines which process and transmit information according to the laws of the new science of cybernetics. Acting on this analogy, Kit Pedler and others are trying to work out the most likely "circuit diagram" of the retina—the plans of a paper-thin biological computer. On this view it is better to think of the dendrites as wires which all plug in to the sockets provided by the visual cells.

Working out where the wires go is an astonishingly difficult job. At this order of size, distances are measured in microns, and a micron is one millionth of a metre—there are about 25,000 microns in an inch. The complete thickness of a retina is typically about 200 microns—less than a hundredth of an inch—but the dendrites are only a fraction of a micron across. The tops of the receptors, called the pedicles, which take the dendrites like a wall socket takes a plug, are generally between five and ten microns in diameter. Light is too coarse for looking at this tiny world. An electron microscope can reveal it in detail, but only a thin slice at a time. A complete series of cross-sectional slices through the pedicle has to be assembled to show its three-dimensional structure—which is an essential first step in exploring the network of connections between the receptor and the bipolar cells.

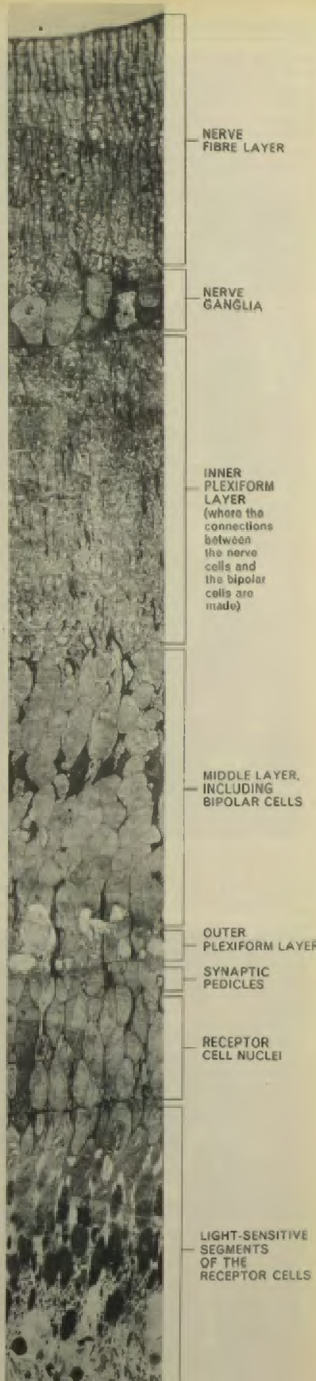
But first the pedicle has to be cut up into slices, each less than a tenth of a micron thick, and mounted on copper grids to be photographed in the electron microscope. Pedler would never have discovered so much as he has without the help of his technical





The strip on the right is a cross-section through a retina, magnified roughly 1,500 times. The area where the dendrites of the outer plexiform layer plug into the synaptic pedicles is the one Dr Pedler is particularly interested in. The diagram on the left shows the position of the retina at the back of the eye, and the photograph shows the slicing process in close-up. The slices are picked up on a grid for photography.

When the slices of retina have been photographed in the electron microscope, the surface of the pedicles is traced out using a " hot wire " pantograph which cuts a sheet of polystyrene foam into the corresponding shapes.



managed a perfect run of more than about 50 of these serial sections, they are keeping quiet about it, but Mrs Tilly can cut and mount 200 slices of the retina—a good material for the purpose—as a matter of routine. Exceptionally she has managed 350. " It's more than we need really," she admits, " but I hate to stop when I'm winning."

Once the serial sections are mounted, photographing them in the electron microscope is straightforward enough, although it is a slow business. The next step is to try and make some sense out of a series of about 100 pictures. At first Pedler traced the main features of each one on to a sheet of transparent plastic, and assembled the sheets to give a three-dimensional picture. This method revealed a lot about the surface of pedicles—it showed that there are more than 200 dendrites making contact with a single receptor in some cases—but it took a long time and it was still very difficult to visualise the surface as a whole. Then Pedler had the idea of using sheets of polystyrene foam instead of transparent plastic, and cutting out each cross-section of the pedicle from the polystyrene instead of tracing it. When all the cross-sections were assembled in the correct order they would provide a complete topographic model of the surface of the pedicle; assembling the other halves of the cut-outs in the same way would produce a model of the projecting dendrites. A specially made pantograph, such as draughtsmen use for making an enlargement direct from a drawing, but fitted with a hot wire to cut the polystyrene, would be used to trace the cross-sections from the photographs. " It worked first time—we all went off and had a drink," Pedler remembers with pleasure.

That first model showed features which could never have been spotted from single sections. For example, it showed that one of the dendrites ran in a complete ring right round the pedicle, and the same thing has since been found in others. Later models show that some pedicles form siamese twins, a complication that had not been suspected before.

But there is a long way to go yet before anyone can produce a circuit diagram of the connections between the receptors and the bipolar cells. Imagine the complexity of the connections to a plug which has 200 pins, and you will have some idea of the difficulty of the problem. The multitude of cross-connections means that the signal from each receptor is processed by a large number of bipolar cells—probably to sort out information about different factors such as shape, movement, brightness, and colour. Then the bipolar cells pass on the information to the nerve cells in a form they can understand. There is no room here to go into all the additional complications. But from the models, and other ways of studying the retina, it should be possible to describe its circuitry much more exactly and hence find out how it works—and more about how the brain works as well. One day it may even be possible to build an electronic machine which could see in the same way as human beings—the so-called electronic eye we have today is only sensitive to light and darkness—and if this could be done it would extend the scope of automation tremendously.

Unfortunately, Dr Pedler has recently been ill. His exploration of the retina has been held up and is only just beginning to get under way again. To speed it up he wants to build a mechanised version of the pantograph which could trace the cross-sections direct from the electron microscope screen and cut out time-consuming photography. However, his original invention will not be forgotten. The Institute has secured a patent on it and it could have many uses—for example, making relief models from contour maps. TIMOTHY JOHNSON