A big step along the visual pathway

David Hubel

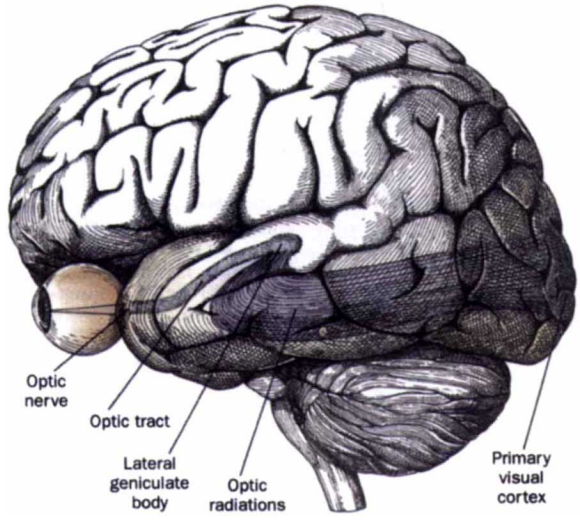
The results of some technically demanding experiments may resolve a long-standing debate — the cause underlying the orientation selectivity of cells in the primary visual cortex.

In their paper on page 249 of this issue[1], Ferster, Chung and Wheat come close to establishing the circuit that forms the basis of the simple cells of the cat primary visual cortex. The problem they have tackled — the mechanism whereby these cells show a phenomenon known as orientation selectivity — has been the subject of dispute for well over 30 years, but to my mind these new results provide the clearest-cut answer yet.

The visual system of mammals is organized as a series of neurally interconnected stages, beginning in the retina and continuing, in the brain, in the lateral geniculate body and then a succession of stages in the cerebral cortex (see figure). The first of these cortical stages is the primary visual cortex. The visual input to this cortical area is relayed from the retinas through the lateral geniculate bodies, and lateral geniculate cells respond best when the retina is illuminated by circular spots of light. Cortical simple cells, by contrast, respond to long narrow lines whose optimal orientations vary from cell to cell. The new work[1] is the latest in a series of studies pointing to the conclusion that this orientation selectivity is the result of direct excitatory convergence of inputs from the lateral geniculate cells, rather than of inhibition within the cortex itself.

Fibres of the optic nerves, and the retinal ganglion cells from which they arise, are already two steps removed from the retinal receptors, the rods and cones. Each ganglion cell receives connections, through one or two intermediate steps, from a close-spaced and roughly circular group of hundreds or thousands of receptors that make up the receptive field of that cell. In 1953 Kuffler observed[2] that in cats the ganglion-cell receptive field is not uniform, but consists of a small circular central region surrounded by an annulus. In about half the cells, the centre is excitatory: when illuminated it produced brisk machine-gun-like discharges from the cell; illuminating the surround caused a suppression of spontaneous firing. A large spot covering both centre and surround produced only a weak discharge or none at all. The other half of the ganglion cells ('off-centre cells') worked in just the opposite way, with an inhibitory centre and excitatory surround. Each ganglion cell was thus concerned not with general retinal illumination but with a comparison of the intensity of the light falling in one small region of retina with the intensity in the immediate surround.

This set of discoveries at once explained a number of perceptual phenomena, not least the fact that 'black' has little to do with the amount of light coming from an object, and everything to do with a comparison of that light with light from the immediate surroundings. It explains why a TV set when turned off looks white or grey but not black, whereas we see excellent deep blacks in a normal TV picture.



Visual pathway in the human brain, running from the retina through the optic nerve and tract to the lateral geniculate body (or nucleus) in the thalamus. The visual signal is then passed to the primary visual cortex at the back of the brain by optic radiations. It is there that cells are orientation selective — that is, individual cells respond to a line in some specific orientation but not to lines some 20–30° from the optimum — although the system is slightly different in humans and cats. (Adapted from ref. 11; artwork by Carol Donner.)

In the late 1950s, Torsten Wiesel and I began to use these techniques of visual stimulation and single-cell recording in the primary visual cortex of cats[3]. We soon discovered that most or all the cells in this area respond grudgingly or not at all to small spots of light, but respond with brisk repetitive firing to short lines — a bright line on a dark background, a dark line, or an edge boundary. A cell fires to a line in some specific orientation, vertical, horizontal or oblique, but not at all to orientations more than about 20–30° from the optimum. Cells in the lateral geniculate body, in contrast, had receptive fields that were at least qualitatively identical to Kuffler's ganglion cell fields, with no hint of orientation selectivity.

We found these results exciting because they were the first direct indication that cortical cells perform transformations on the incoming information — in short that the cortex actually does something interesting. Clearly, cells of the primary visual cortex were analysing a visual scene by asking whether any small region contained a light–dark contour and, if so, what its orientation was. That information was then presumably handed on to subsequent stages for further processing, locally and in other visual cortical areas.

It then gradually became clear that these orientation-selective cells were of several types[4], differing mainly in their complexity. The simplest, which we (imaginatively) called 'simple', had receptive fields that, like retinal ganglion and geniculate fields, were subdivided into excitatory and inhibitory regions, but the geometry was strikingly different. Most often the field consisted of a long, narrow excitatory region flanked on either side by an inhibitory region, so that a bright line confined to the excitatory region produced a brisk response. The width of such an excitatory region was generally about the same as the diameter of a geniculate receptive-field centre, so we proposed that the simple cell might be receiving direct excitatory input from a group of on-centre geniculate cells whose field centres fell along the excitatory region. The inhibitory flanks could be similarly the result of input from geniculate off-centre cells. Other circuits were clearly logically possible, but this seemed by far the simplest and it found support in the observation that simple cells are grouped together in the cortical layer (layer 4) that receives the geniculate inputs.

Soon, however, several alternative ideas sprang up concerning the circuit

underlying simple cells in cat cortex. Inhibitory synapses, employing the transmitter γ-amino butyric acid (GABA), are plentiful in the cortex, especially in layer 4, and much effort has been expended in trying to understand their function. One of the most popular notions, advanced by Blakemore and Tobin[5], was that a cell's orientation selectivity might be sharpened if it were to receive inhibitory inputs from other cortical cells with different orientations. This process would be analogous to events in the geniculate, where the power of the receptive field's surround to countermand the influence of the centre is enhanced, and seemed to be confirmed by Sillito[6] — he observed a loss of orientation selectivity of simple cells when the drug bicuculline, a GABA antagonist, was applied to the cortex.

On the other hand, evidence for the original idea of direct excitation came from Chapman, Zahs and Stryker[7]. They first determined the orientation selectivity of cells in a single orientation column in cat cortex. Then, by applying kainic acid or muscimol to the cortical surface, they eliminated all impulse responses in cortical cells but preserved the impulse activity of the geniculate afferent fibres. When they recorded receptive fields of a number of these fibres, all in the same orientation column, they found that they occupied a long narrow strip that paralleled the orientation of the cells they had previously recorded. Further support came from Tanaka[8], and from Reid and Alonso[9], in experiments in which impulses simultaneously recorded from a simple cortical cell and a geniculate cell were cross-correlated. Both studies found that in the two cells, receptive-field regions of the same sign — excitatory or inhibitory — were almost always superimposed.

Finally, two studies from Ferster's laboratory, one published in 1986 and the other in this issue, also point towards excitation from geniculate inputs as the cause of orientation selectivity. Both made use of intracellular recordings of cortical cells, and any reader must surely have wondered why no one had used these methods sooner: intracellular recording allows one to define the properties of a cell in terms of its impulse responses, and then to examine separately the summed excitatory and inhibitory inputs. The answer, of course, is that making such recordings requires consummate skill plus the patience and determination of Job. But if the recordings are successful they can give simple, decisive answers.

In the earlier paper[10], Ferster showed that, in response to visual stimulation, the summed inhibitory inputs to a simple cell, in the form of inhibitory postsynaptic potentials, showed the same orientation preference as the cell itself, with the same peak orientation and identical sharpness of tuning. If the function of the inhibition were that of sharpening the tuning, the orientation preference of the inhibition should have been different or at least broader.

In the second set of experiments[1], Ferster and his colleagues recorded intracellularly using the whole-cell patch technique, which is roughly equivalent to intracellular recording but more powerful — and still more difficult. They first determined the orientation selectivity of the cell and then suppressed the local impulse activity in that part of the cortex by surface cooling. This should abolish all visually evoked synaptic potentials except those arising from direct geniculate inputs — and indeed it did abolish all the inhibitory input and a fair proportion of excitatory inputs. The receptive fields of the remaining excitation had exactly the same orientation preference and sharpness of tuning as the cell itself before cooling. I find this compelling evidence that the orientation selectivity depends not on inhibitory inputs from neighbouring cortical cells (themselves activated by geniculate inputs, directly or over several stages), or indeed on excitatory polysynaptic inputs that might also serve to sharpen selectivity (by a previously proposed process that others have termed 'selective amplification'). As Ferster *et al.* point out, however, it is still possible that some excitatory input of cortical origin may have survived the cooling; layer 6, the furthest from the cooling element, is known to send excitatory input to layer 4.

Thirty-five years ago Wiesel and I would have been incredulous had anyone suggested that only now would our scheme for explaining simple cells be vindicated or disproved. At this rate we may expect to have a verdict on a similar proposal we made for complex cells by 2031. Extracellular recordings can tell us about the transformations the cortex makes in the information coming into it, but it is far harder to learn exactly how these transformations come about, in terms of the wiring and the excitatory and inhibitory connections. Ferster and his colleagues have shown that it is possible. □

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EVOLUTION

The games lizards play

John Maynard Smith

In evolutionary theory, an evolutionarily stable strategy (ESS) is a strategy, or phenotype, that is stable in the sense that, if most members of a population adopt that strategy, or have that phenotype, no alternative mutant strategy can invade the population. In simple models, there is usually either a 'pure' ESS (always do the same thing), or a 'mixed' ESS (sometimes do A, sometimes do B, with fixed probabilities). In the latter case, it may also be stable for some individuals always to do A, and others always to do B: that is, there may be a stable genetic polymorphism, instead of individuals adopting a mixed strategy. For some models, however, there is no ESS: the frequencies of different strategies in the population cycle indefinitely. It seems that Sinervo and Lively (page 240 of this issue[1]) have now found a real example of that phenomenon.

The logic of the case they describe is that of the 'rock–scissors–paper' game: rock beats scissors, scissors beat paper, and paper beats rock. In the side-blotched lizard, *Uta stansburiana*, males have one of three throat colours, each associated with a different behaviour. The difference between colour morphs is highly heritable. Orange-throated males establish large territories, within which live several females. A population of such males can be invaded by males with yellow-striped throats: these 'sneaker' males do not defend a territory, but steal copulations. The orange males cannot successfully defend all their females. However, a population of yellow-striped males can be invaded by blue-throated males, which defend territories large enough to hold one female, which they can defend against sneakers. Once sneakers become rare, it pays to defend a large territory with several females. Orange males invade, and we are back where we started from.

The empirical support for these conclusions is as follows. The frequencies of the three morphs were followed for a complete cycle, lasting six years. The fitness of individual males was estimated from the number of females they monopolized, or shared with neighbours. The regression of fitness on the type of neighbour was also estimated. These fitness values were of