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Visual Cortex: More Wiggle Room for the Brain

Experiments in which one eye of a ferret is removed at birth show subtle effects on the development of visual cortex maps that are in agreement with those predicted by theory.

Nicholas V. Swindale

The philosopher John Locke was the first to argue that knowledge of the world can only be acquired empirically, through the operation of our sense organs. He proposed that, at birth, the human mind (and by implication the cerebral cortex) was a *tabula rasa* lacking information about the properties of the natural world. No one now accepts Locke's proposition completely, given the evidence, for example, that newborn babies can respond preferentially to faces, which implies that genes somehow contain information about faces and can translate it into appropriate kinds of neural connectivity. But questions concerning the influence of very early sensory experience and the extent to which brain structures are, or are not, genetically programmed continue to be of central importance to research on cortical development. The issues come into particularly clear focus in studies of visual cortex. Although the mechanisms of early cortical development are arguably best understood in this part of the brain, knowledge of what goes on in the time between the first migrations of neurons along radial glia to form cortical layers *in utero*, and the emergence of a functionally mature visual system some time after birth, is still very limited. Numerous studies have so far failed to determine whether basic aspects of visual cortex organization — neuronal receptive field properties and columns and maps — are determined by cues directly controlled by patterns of genetic expression, or whether development is a flexible, self-organizing process more likely to be influenced by neural activity and patterns of sensory stimulation. A recent study by Farley *et al.* [1] lends support to the latter proposition although, in my view, it does not unambiguously settle the debate.

Wiesel and Hubel [2] provided the first evidence that the early development of visual cortex could be altered by a change in sensory stimulation. In a classic experiment they closed one eye of a newborn kitten or a monkey. Ocular dominance columns — roughly half-millimetre wide regions of cortex running perpendicularly from *pia* to white matter (hence the term 'column'), containing cells that respond preferentially to one or the other eye — changed size [3]. Those connected to the seeing eye became wider and took over cortical territory made available by the shrinkage of columns connected to the closed eye. While this showed that altered visual experience could change the outcome of early visual development, it did not show whether visual experience was actively involved in setting up the columns to begin with. In fact, subsequent observations by Wiesel and Hubel [4] and others showed that visual experience does not play an active role in setting up columns. Thus, normal-looking ocular dominance columns and orientation columns — columns of cells having the same preference for stimulation

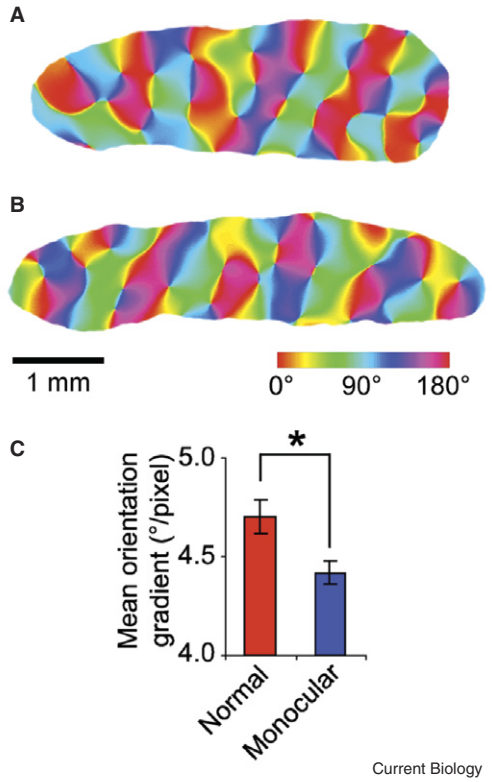

Figure 1. Perturbing orientation map development.
(A) Orientation map from a normal ferret with pixels colour-coded according to the orientation preferences of neurons at each location. (B) Orientation map from a ferret enucleated at birth. Differences in the periodicity of the patterns in (A) and (B) are not visually obvious but can be detected by Fourier analysis. (C) Mean orientation gradient values for normal (n = 10) and enucleated (monocular) (n = 12) ferrets. Error bars show the S.E.M. Gradient values are lower in the monocular ferrets, consistent with a lower spatial periodicity. (Adapted from [1].)

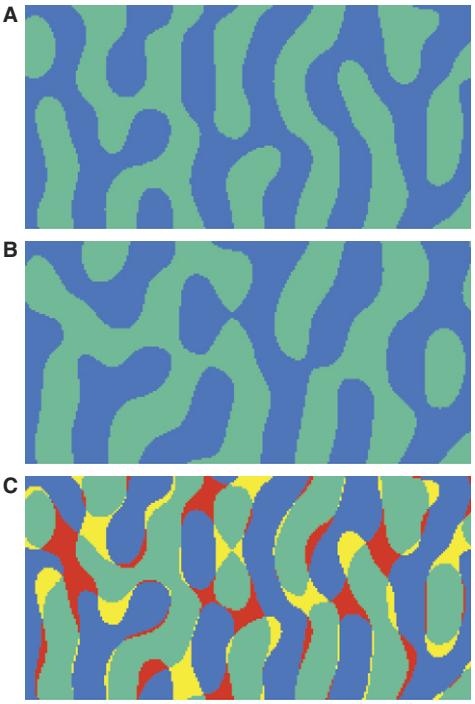

Figure 2. Demonstration of a periodicity change without major rearrangement of map features.

Simulated pattern of ocular dominance stripes in (A) has a periodicity, measured by Fourier analysis, of about 32 pixels (image is 110 × 220 pixels in size); the pattern in (B) has a periodicity of 35.5 pixels, about 10% greater than (A). (C) shows (A) and (B) superimposed with regions of change indicated by red and yellow. Note that most stripe positions remain relatively unchanged.

by lines or edges of a given orientation in the visual image — were found in newborn monkeys [4,5] and in kittens reared in darkness [6]. These observations of dependence and independence of visual inputs can be reconciled by supposing that innate, intrinsic mechanisms based on patterns of chemical labelling established by gene expression in the appropriate areas establish the positions of the centers of each type of column and thus their overall spacing, while at a later stage, the pattern is sculpted by spontaneous [7] or visually driven patterns of activity, fine-tuning it to the requirements of that particular individual and his or her environment.

Although it makes sense, this two-stage view is at odds with most models of the formation of columnar structures in the visual cortex, which are based on principles of self-organization, and do not treat early and late stages of development differently. Most also assume that neural activity, whether spontaneous or visually driven, and Hebbian synaptic plasticity drive the mechanism, although some are formulated in a sufficiently abstract way that they could be implemented by chemically based rather than neural-activity dependent processes [8]. The most successful models, based on a principle known as dimension reduction [9], are in fact these more abstract ones. They are based on the idea that the arrangement of columns is a compromise between two conflicting requirements: continuity and completeness. Continuity means that the nearer two columns are, the more similar their receptive field properties should be. This requirement can be satisfied by the trivial result that all neurons have the same receptive fields, and so is balanced by the opposing requirement of completeness. This specifies that, for each point in visual space (which is analysed by a roughly circular region of cortex about 1–2 millimetres in diameter), the possible permutations of receptive field properties, such as eye preference, preferred orientation, direction of motion and spatial frequency, should be represented as uniformly as possible. This requirement is sometimes referred to as coverage: satisfying it means that the cortex's ability to represent information about image properties is equally good for all positions in visual space.

Models which achieve trade-offs between these two constraints do a remarkably good job in showing how retinotopic maps from the two eyes can be combined while keeping the information from each eye separate (in the form of ocular dominance columns) together with other properties such as orientation preference. Computer simulations show that these good solutions resemble the maps found in the brain: they are characterised by periodic foldings or spatial oscillations in the layout of each property across the brain surface. There is also a tendency for the maps to have orthogonal gradient relations with one another: this means that the direction of the steepest rate of change in one map property at a given location is more often orthogonal to the gradient directions of other maps at the same location than it would be by chance. As more properties (or stimulus dimensions) are squeezed in, these gradient relationships become weaker and the spatial rate of change and oscillation of each property becomes more rapid [10,11]. This is probably because better coverage can be obtained with faster oscillations, albeit at the expense of continuity — which is less because the rate of change is faster.

Farley *et al.* [1] have now demonstrated these predicted effects in ferrets by removing one eye at birth. Some weeks later, when the cortex has matured, the remaining eye now projects uniformly across contralateral cortex and ocular dominance columns are absent. As a result of one less property being present, gradient relationships become more strongly orthogonal, and other map properties, in particular preferred orientation, are found to change less rapidly with position in the cortex and have a slightly greater spacing than they would otherwise have had (Figure 1). These effects are quite small, although they are based on reasonably large numbers of animals (10 normal and 12 experimental for one of the comparisons) and are statistically robust. The statistics and large numbers are important because it is known that ocular dominance column spacing varies significantly from individual to individual [12] and this variation may have

a hereditary component [13]. Thus even quite large differences between small groups of animals may be accidental.

The results of Farley *et al.* [1] suggest two particular conclusions. First, it has always seemed possible that the mechanics of dimension reduction models might have little to do with real visual cortex development, even though the models predict the end result of it well enough. Thus, prenatal development — as optimised by evolution — might have contrived to come up with columnar arrangements that satisfy completeness and continuity constraints, without optimising them explicitly, or being able to adaptively optimize them in the face of perturbations. Farley *et al.*'s [1] results suggest the opposite and that developmental mechanisms act, like the models, to adaptively optimize coverage at the expense of continuity. Second, because eye removal was performed before thalamic inputs had arrived at the cortex, and most likely before any kind of columnar structures, or precursors of them, would have been present, it could plausibly have resulted in a remodelling of the entire system of columns, not just a sculpting of a pre-existing pattern. This would further support the view of developing cortex as a plastic, self-organizing system, relatively independent of genetic control. This is not an inescapable conclusion however. Removal of an eye might alter chemical, or genetically mediated cues, in addition to neural activity. A change in pattern periodicity might at first sight imply a wholescale remodelling of columnar structures, but in fact changes of the magnitude seen by Farley *et al.* [1] (around 10%) can be accomplished by relatively small alterations in structural detail. Figure 2 shows how this can be so.

If these experiments do not conclusively resolve the issue of the innate determination of columnar structures, what kinds of experiments might? Comparison of the patterns of gene expression in different columns might give clues and is now technically feasible, although changes in gene expression could be linked to changes in neural activity, making the two hard to disentangle. A more decisive test would be to compare columnar patterns in cloned animals. If these turned out to be different (as are coat patterns [14]), it would strongly support the self-organizing view of columnar development. But while the answers to these questions remain unknown, visual cortex modellers can, for the moment, chalk up another success.

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Centriole Assembly: The Origin of Nine-ness

Recent studies of the *Chlamydomonas bld10* mutant have revealed that the ninefold symmetry of the centriole is set by the length of the cartwheel spokes, which fixes the diameter, and thereby the circumference, of the centriole.

Wallace F. Marshall

The centriole is a cylindrical structure found in the core of the centrosome. Centrioles possess a remarkable ninefold symmetry, consisting of nine parallel microtubule triplets arranged like the blades of a turbine. At the proximal end of the centriole, where the minus-ends of the microtubule blades are located, is a structure called the 'cartwheel' consisting of a central hub joined to the blades by nine spokes. So, how does the ninefold symmetry of the centriole arise?

One possible model is that assembly is templated from a single molecule or complex that is located in the cartwheel hub and itself has a ninefold symmetrical repeat structure. This central template would then produce an