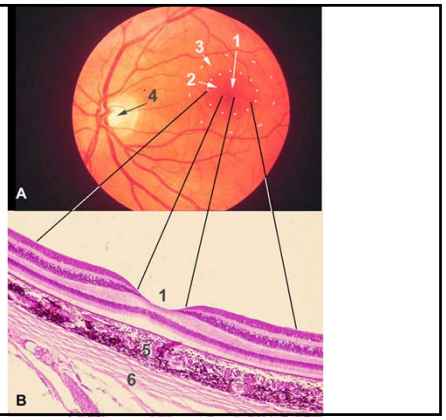
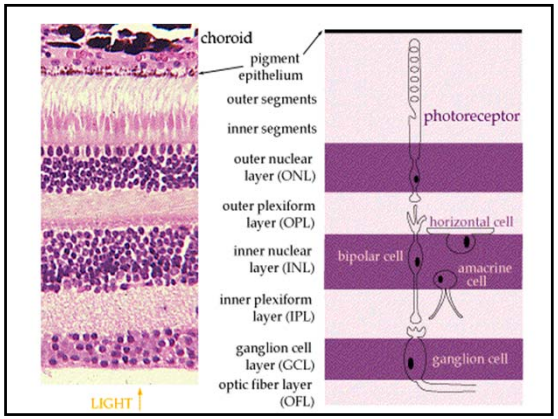
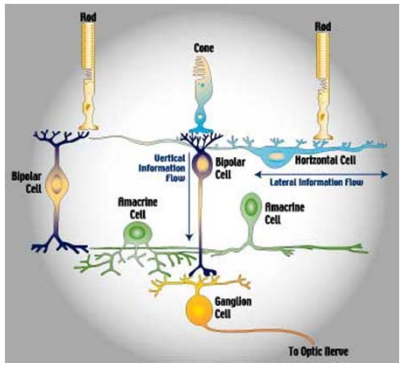
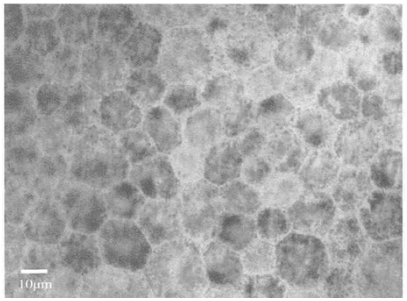
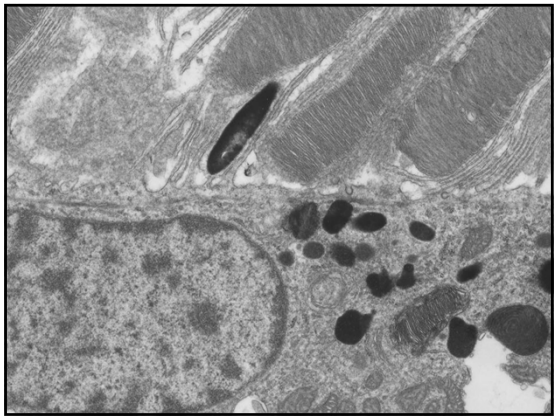




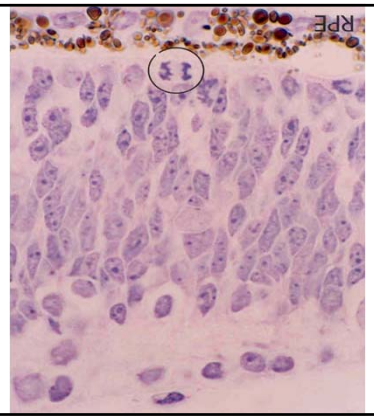


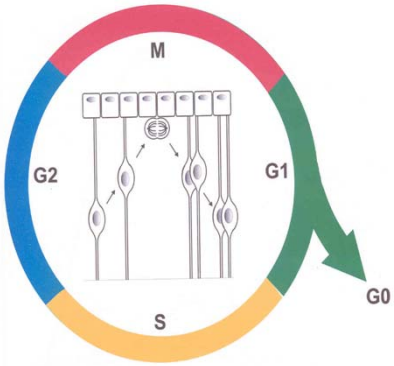
RPE is a monolayer of hexagonal shaped neural epithelial cells that have the same embryological origin as the neural retina. They mature before the neural retina and play a key role in metabolic support of outer retinal cells i.e. rods and cones.





Cell division takes place next to the RPE. Neuroblastic cells have the capacity to differentiate into any of the cell types found in the mature retina



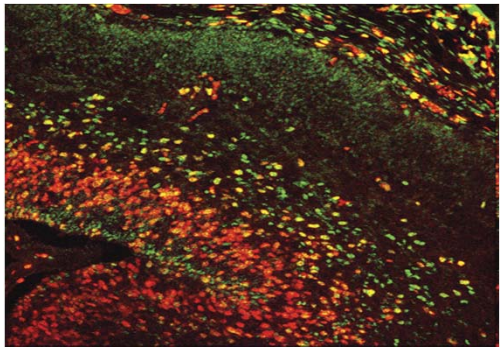


In the retina the nucleus of neuroblastic cells move between the ventricular and surface (RPE) and the margin of the inner retina during the cell cycle. This process slows with time as more cells leave the cell cycle.

Key question

- What determines what a dividing cell becomes? – issues of space and time

Markers of cell division



There are two waves of retinal neurogensis. The first produces ganglion cells and cones, the second produces rods and bipolar cells. Hence, time of cell cycle exit influences what a cell becomes. But the cell cycle changes with time, starting at ~9h and ending at ~36h in mice

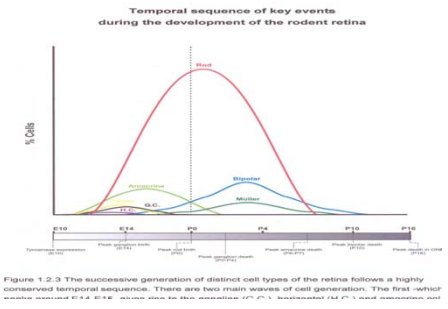
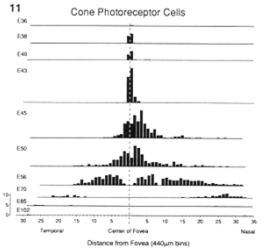
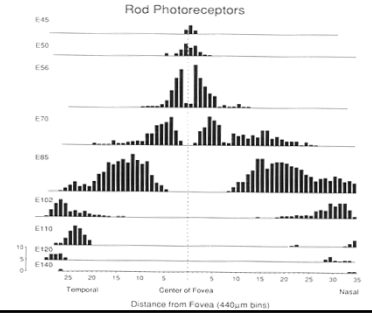


Figure 1.2.3 The successive generation of distinct cell types of the retina follows a highly conserved temporal sequence. There are two main waves of cell generation. The first -whic

All retinal cells are generated with a centre to periphery gradient emanating from the fovea with cones being generated before rods at any retinal location.



All retinal cells are generated with a centre to periphery gradient emanating from the fovea with cones being generated before rods at any retinal location.



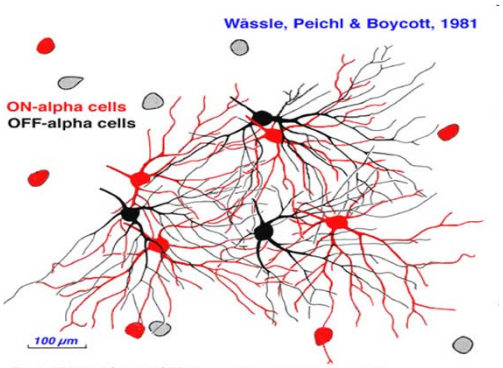
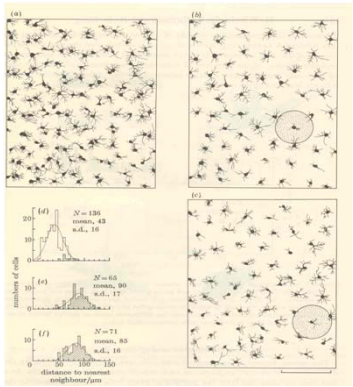


Fig. 7. HRP-filled ON- and OFF-center alpha cell mosaics in cat retina.



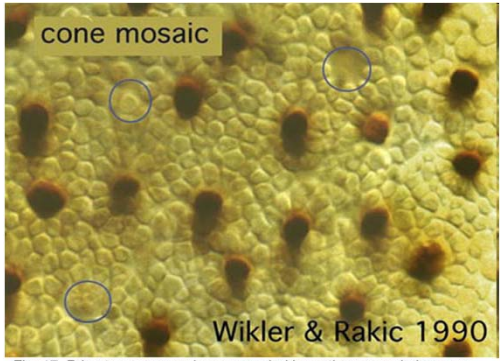
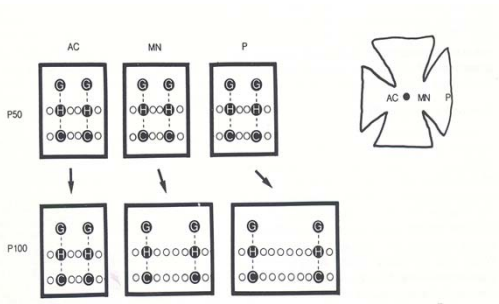
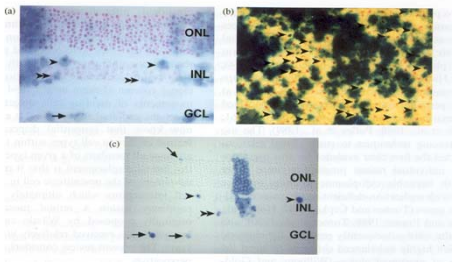


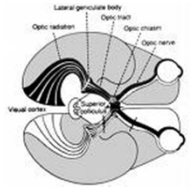
Fig. 17. Primate cone mosaic as revealed by anti-cone opsin immuno-staining. Cones that do not stain brown are blue cones (blue circles).



Phase 2 makes mosaics in phase 1 cells. Clonal populations remain closely associated only cells in a mosaic pattern disperse.

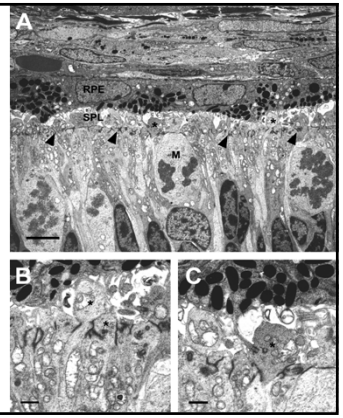


- **Spatial and temporal factors are both important during retinal development. A cells location in relation to a defined point in time will be a significant factor in determining what cell type it becomes.**
- **There are examples of the significance of these factors when the temporal element is disrupted both in terms of retinal development and its pattern of connections with the brain.**



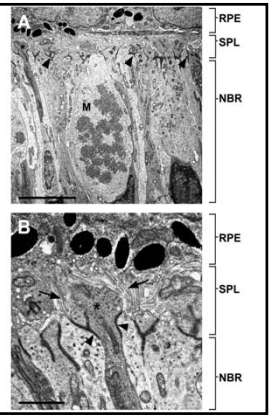
- The retina develops with a centre to periphery gradient
- Separate cell types are generated in different overlapping waves
- Cell division in the neural retina takes place next to the RPE, which plays a key role in development of retina. Pigment is important
- Differentiation of the retinal layers takes place after cell division is complete
- The RPE is developmentally advanced in relation to the neural retina. If it is removed experimentally the retina fails to develop. This happens in some cases of anophthalmia. If it lacks pigment the eye develops abnormally. Elements associated with pigment regulate cell cycle exit.

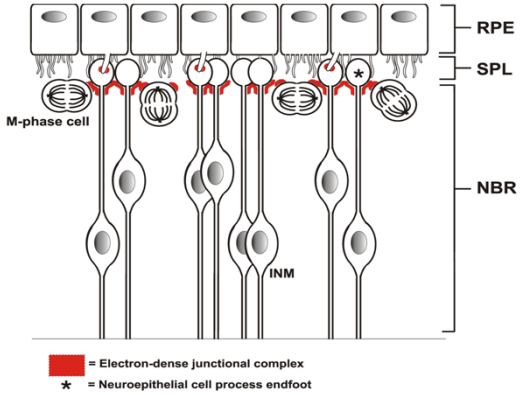
At the EM level retinal mitosis takes place away from the RPE and there is a junctional zone separating mitotic profiles from RPE cells. RPE cells have multiple and diverse processes reaching up and into dividing cells and the end-feet of cells in the cell cycle.

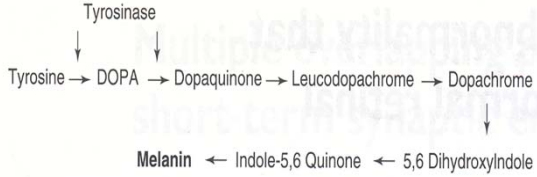


Long filament like fibres are commonly found rapping around the end-feet of neuroblastic cells. Melanin is often found in close association with these.

The Junctional zone contains large numbers of both tight junctions and gap junctions.

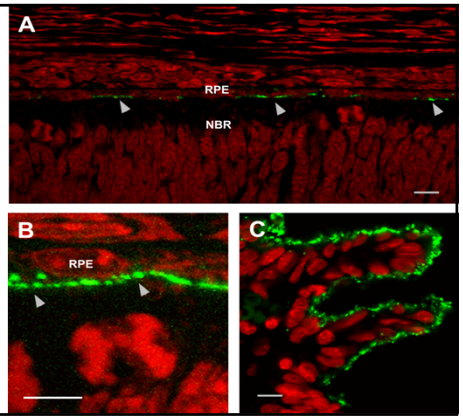




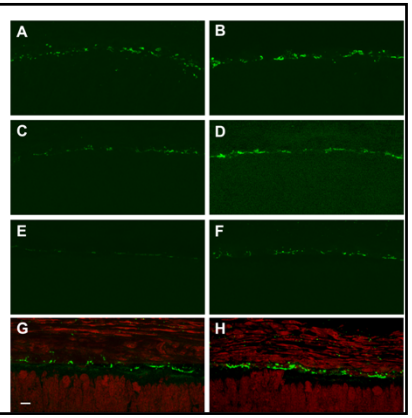


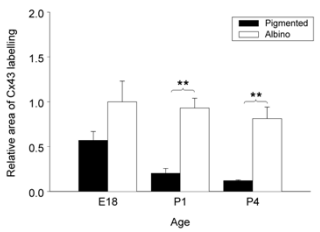
RPE talking to the retina

CX 43



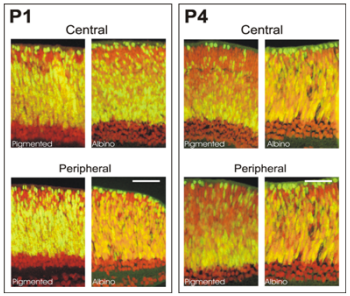
CX 43 is elevated in albinos across a range of ages





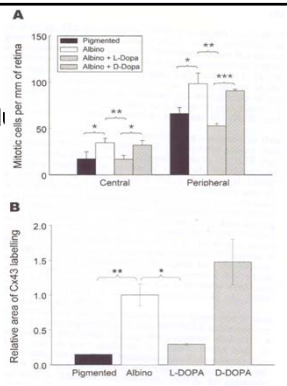
Connexin 43 levels in age matched pigmented and albino animals at progressive ages.

Ki67 localisation



- We have examined the relationship between the developmental precocious RPE and dividing retinal precursors and found that mitosis is elevated in albinism.

- Introdu ems

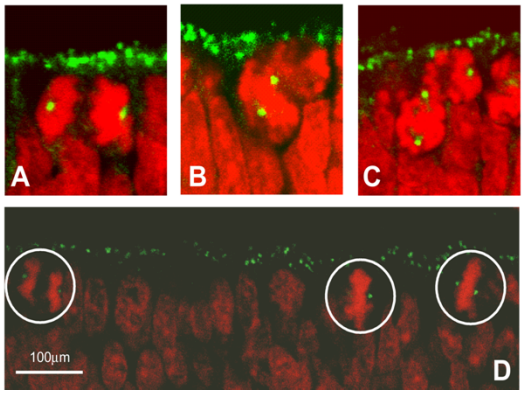


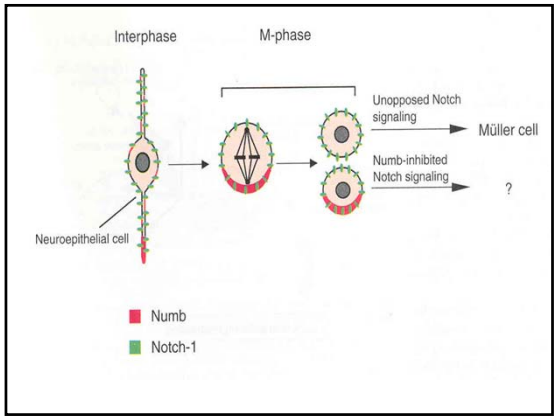
Retinal Features of albinism: an example of disrupted timing

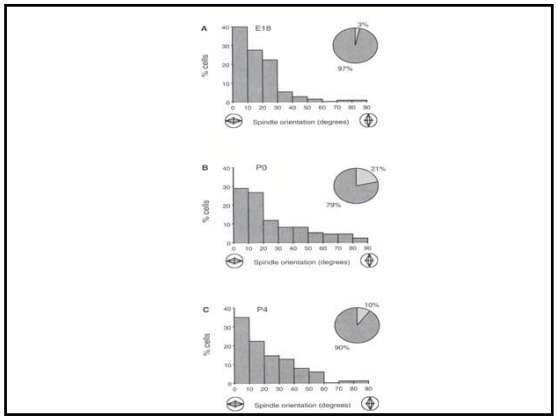
- **Absence of a fovea or underdeveloped area centralis**
- **Abnormal central blood vessels**
- **Reductions in specific cell types**
- **Abnormal pathways into the brain**

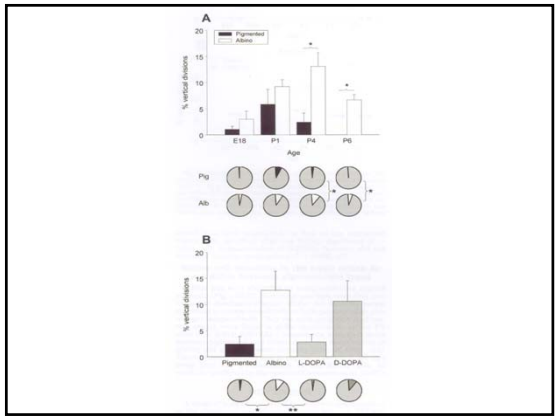
These abnormalities arise whenever pigment is reduced or absent irrespective of the genetic cause. Their diversity implies that there is a fundamental disruption in early retinal development in the absences of pigment.

A key feature of albino retinal development is that cells stay in the cell cycle too long. They miss their exit points.

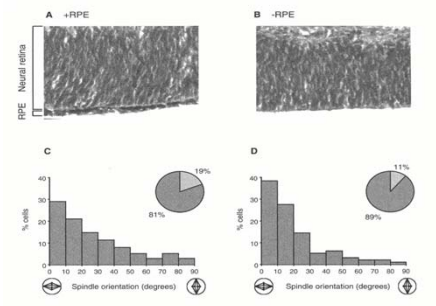




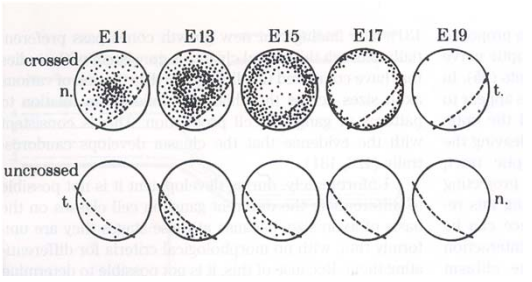


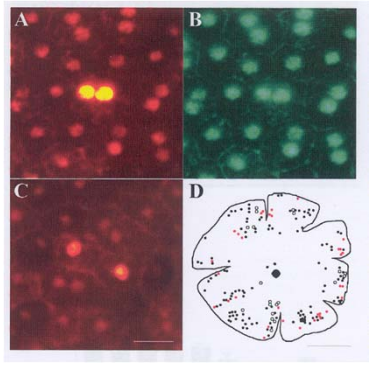


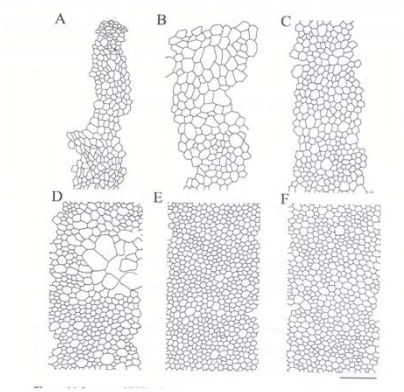
The RPE influences the orientation of dividing cells and hence possibly which cell type they differentiate into

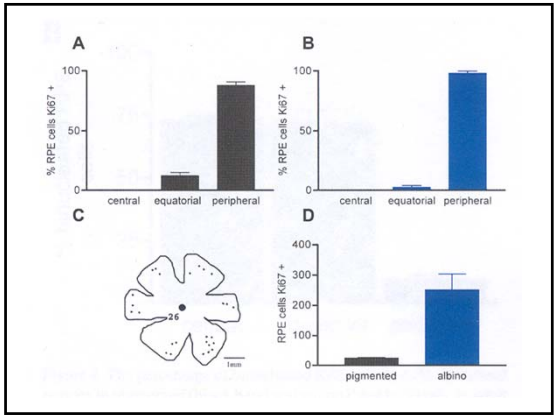


Ganglion cell birthdays

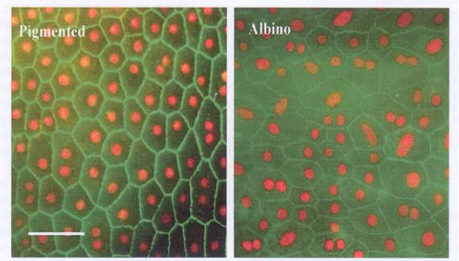






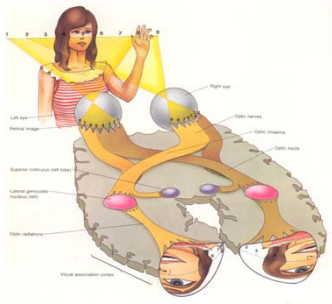


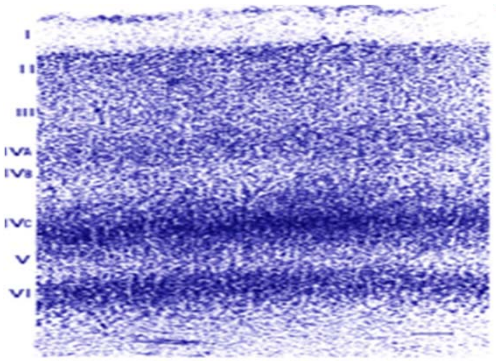
Arrested in the cell cycle

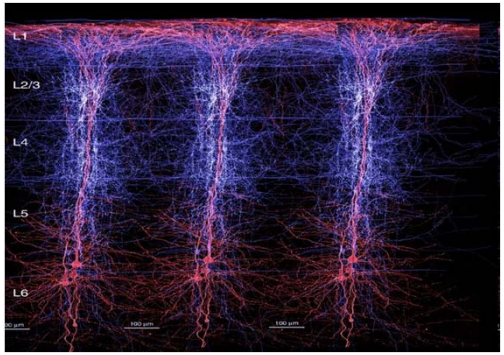


- **All of these events in the retina occur before birth in the human. At birth not only is the retina fully developed but its physical projections into the brain are established, and the environment has no influence over them.**
- **However the connections between the two eyes and the cortex are still plastic and here the early visual environment can be critical in sculpting the mature visual system**

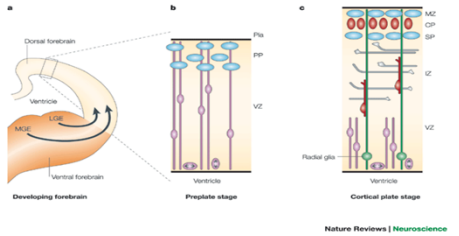
The central visual fields is seen by both eyes and represented as binocular in the cortex



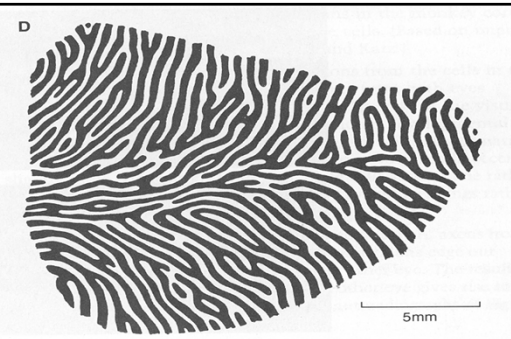




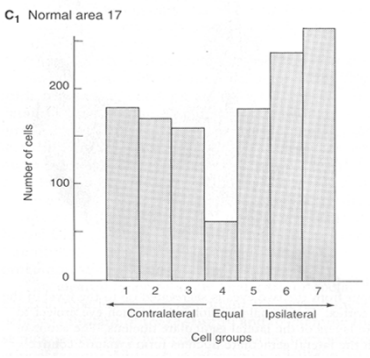
Cortex is not specified. You can make visual cortex motor and visa versa

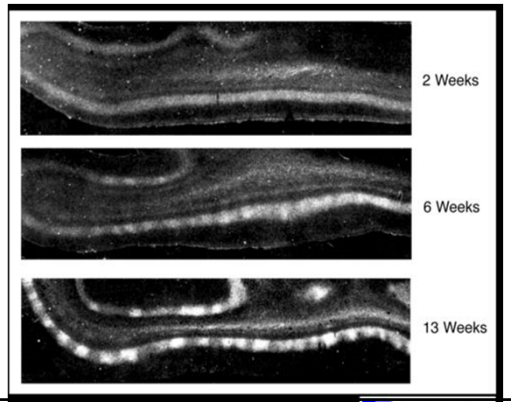


Large binocular cortex with both eyes seeing similar views

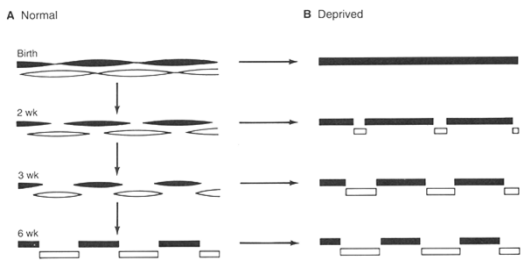


Cells are often driven by both eyes

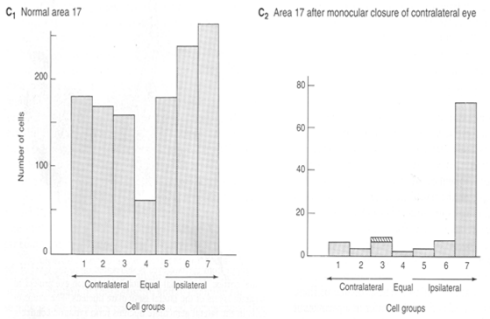




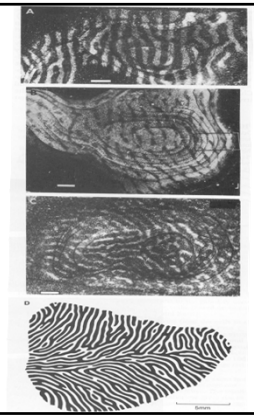
Schematic representation of plastic changes in cat cortex visual cortex in response to eye closure

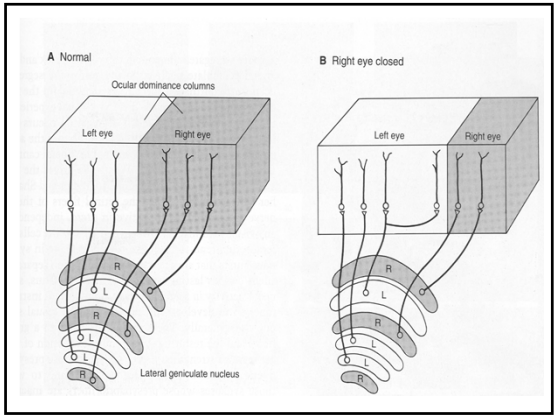


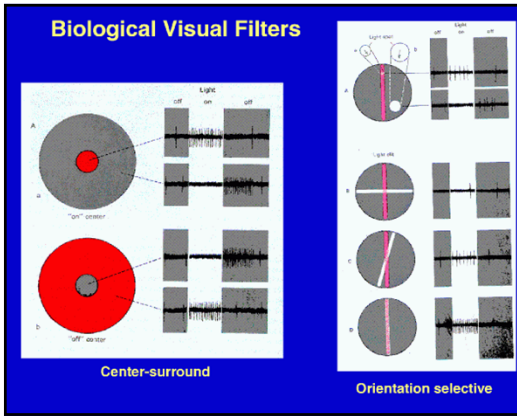
Ocular dominance columns in normal cortex and cortex where the contralateral eye has been closed



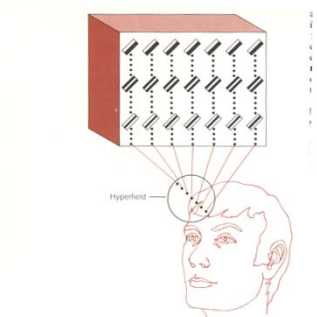
Closing one eye Shifts the balance of the two projection in favour of the open eye, but this change remains plastic for the first 4-6 years and can be partly reversed





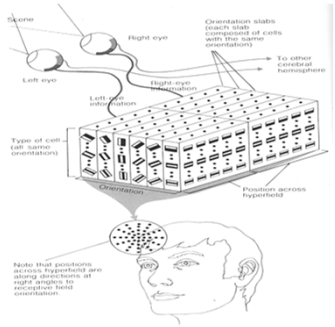


Cells in the visual cortex have receptive fields designed to detect orientation



60 A slab of obliquely tuned columns within the same hypercolumn as

These orientation tuned cells are organised into units that change their orientation as you move across the cortex between the ocular dominate columns



The orientation tuning of the cells is directly influenced by the visual environment