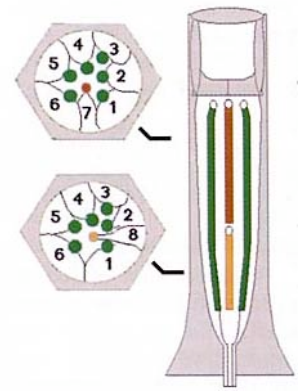
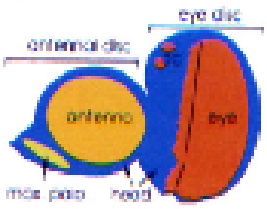
Eye development in vertebrates and *Drosophila*

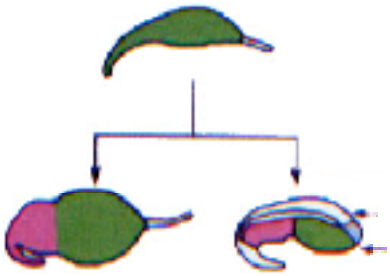
The compound eyes of insects have a radically different structure to that of the more familiar type of eye found in vertebrates. However both types of eye have common elements, including lenses, photoreceptors and pigmented cells. In this lecture I will show you that the development of these two very different structures also shares common elements in terms of developmental processes and genetics

Drosophila has a typical insect compound eye. Each eye is composed of several hundred simple units called ommatidia arranged in an extremely regular array. In the fly each ommatidium consists of a core of 8 photoreceptor cells (R1-R8) surrounded by 4 cone cells (equivalent to the vertebrate lens in function) pigment cells and a sensory bristle. The number of cells, their identities and functions within each ommatidium is invariant.



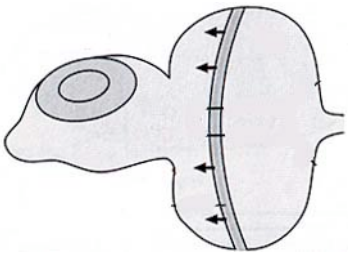
The adult *Drosophila* epidermis is derived from imaginal discs, cells set aside in the embryo, which proliferate in an undifferentiated state during larval life. The eye develops from the eye-antennal imaginal disc, different regions of which give rise to the eye, antetnna, head capsule and mouthparts.





In late third instar discs expression of the eye master control gene Pax6 (ey) is restricted to the eye primordium and if ectopically expressed in other discs or aother parts of the eye-antennal disc can induce the formation of ectopic eyes. Earlier in development Pax6 is expressed throughout the eye-antennal disc, only gradually becoming excluded from the antennal and other regions. The growth of the eye primordium at theses early stages depends on signals from the peripodial membrane, which is marked by expression of the transcription factor dMitf

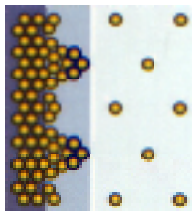
Not all ommatidia form at the same time. In late third instar eye antennal discs differentiation occurs in posterior to anterior sequence: the first ommatidia to differentiate do so at the posterior pole of the eye disc, the last at the anterior pole. The morphogenetic furrow marks the boundary between dividing, non-differentiating cells and differentiating ommatidia. The further posterior ommatidia are from the furrow the closer they are to having all cell types (R1-R8 cone cells and pigment cells) differentiated.



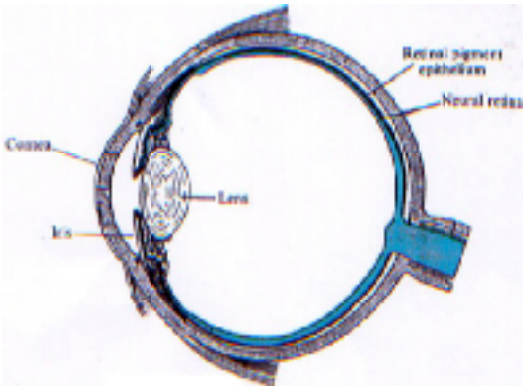
Cells anterior from the furrow divide asynchronously, while cells in the furrow are non-dividing. Immediately after leaving the furrow cells go through two last synchronous divisions. Photoreceptors differentiate in a fixed order starting with R8 and ending with R7.

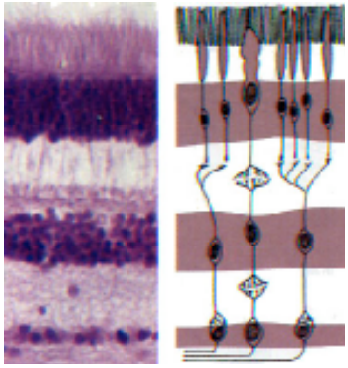
Although both this order and the cellular composition of each ommatidium are absolutely invariant the lineage of ommatidial cells varies both between ommatidia and between individuals in a way that suggests that lineage plays no part in determining ommatidial cell fate.

R8 differentiation is marked by a restriction in the expression of the atonal gene. Initially this is expressed in all cells anterior to the furrow but becomes gradually restricte to small regularily spaced clusters and then to single cells. Atonal mutants lack photoreceptors because R1-R7 require R8 to recruit them to the cluster and direct their development.



The gradual restriction of atonal expression to single, evenly spaced cells involves a process called lateral inhibition via an interaction of the Notch transmembrane receptor with its ligand Delta. Delta is also a transmembrane protein and can only interact with Notch recptors on neighbouring cells. Activation of Notch signaling when Delta bind to Notch causes increased expression of Delta and repression of R8 development. Initially all cells of a cluster have the same level of Notch signaling activity and express Deltal in equal amounts. Eventually (by chance) one cell will start to show higher levels of Notch activity and express higher levels of Delta than its neighbours. Ithe Delta mediated signal from this cell will repress R8 development in its neighbours setting up a positive feedback loop such that eventually all the cells of the cluster but one are prevented from expressing atonal and becoming an R8





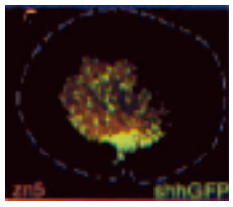
cell.

The vetebrate eye is a single structure with a lens that focuses light onto the retina. The pigmented retinal epithelium (RPE) provides trophic support for retinal calls. The outer laver of the retina (adjacent to the RPE) consists of photorecepteors (rods and

cones), the middle laver consists of various types of interneurons (amacrine cells) and the inner layer of retinal ganglion cells (RGCs), which extend axons to the brain via the optic nerve.

As in *Drosophila* Pax6 acts a master control gene for eye development. Unlike Drosophila the vertebrate eye is not entirely epidermal in origin. The lens originates in the surface ectoderm but both retina and RPE have their origins in an outgrowth of the brain, the optic vesicle. Pax6 is initially broadly expressed throughout the surface ectoderm and optic vesicle. Where the vesicle contacts the ectoderm a thickening or placed forms, which invaginates to form the lens. Pax 6 gradually becomes restricted to the lens and the retina and is excluded from the RPE. The RPE plays a similar trophic role to the peripodial membrane in *Drososphila* and is marked by expression of the vertebrate homologue of dMitf, Mitf.

Two further similarities between vertebrate and insect eye development lie in the lineage independence of cell type specification in the retina and the ommatidia and the role of atonal. As in *Drosophila* retinal neurons form in a strict temporal order, beginning with the RGCs. In zebrafish developing RGC cells transiently express the atonal homologue ath5 and the signaling molecule Shh before differentiating.



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