The Visual System

Development

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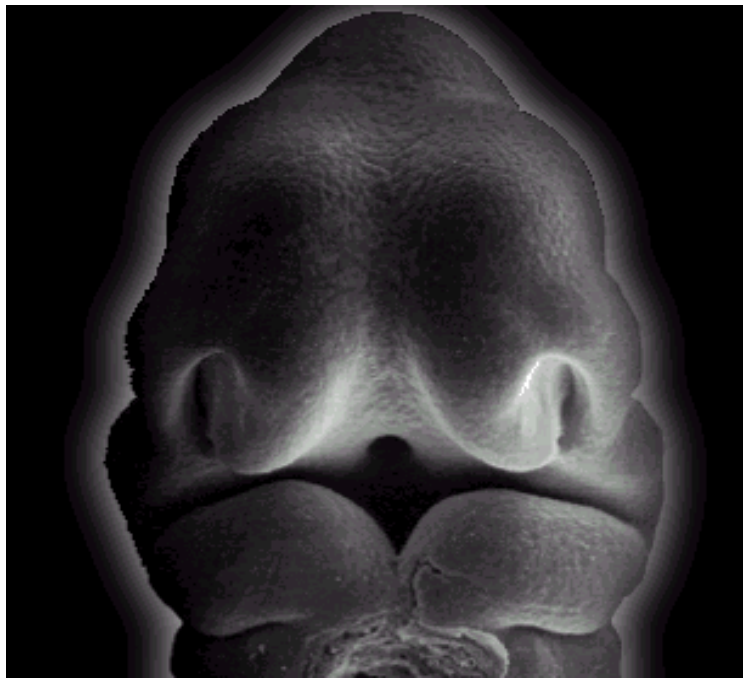

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Required Reading 3/5 & 3/15 Tovée Chapter 2, pp19-21 and Chapter 6; Mcllwain Chapter 2 and pp122-125

Useful information can also be found in the following books:
Norton et al., (2002) The Psychophysical Measurement of Visual Function, chap 9

Zigmond et al.,(1999) *Fundamental Neuroscience* Chaps 15-22, especially 15,17,19, 15,17,19, 21
Purves, D. et al. (Eds) (1997) *Neuroscience* Chapters 20-21.

Kandel et al., Principles of Neural Science, 4th edition (2000), chapters 52-58

Useful Web Sites:

http://www.med.unc.edu/embryo_images/

http://sdb.bio.purdue.edu/dbcinema/index.html

http://sdb.bio.purdue.edu/SDBEduca/QT_Embryos1.html

Did You Know That..

- Human genes important for eye development can be inserted into flies that then develop extra eyes?
- Some fish can re-grow all the cell layers in the retina even when the eye is damaged as an adult fish? Why can't we?
- Goldfish can be trained in a visual task, have their optic nerve cut and when it regenerates they remember the task?
- Visual Experience can influence the growth of your eyeball?
- Visual experience can influence the growth of LGN axons in early development?

Stages of Development

The development of the vertebrate nervous system can be divided into a series of overlapping stages. The earliest stages are likely to to be **neural activity independent** (1-4 on list below) while the later stages are **neural activity dependent** (5-7 on list below).

- i) induction and patterning
- ii) birth and generation of specific cell fates (phenotypes)
- iii) migration
- iv) axon path-finding and target selection
- **v) cell death**
- **vi) refinement of connections**
- **vii) continued synaptic plasticity**

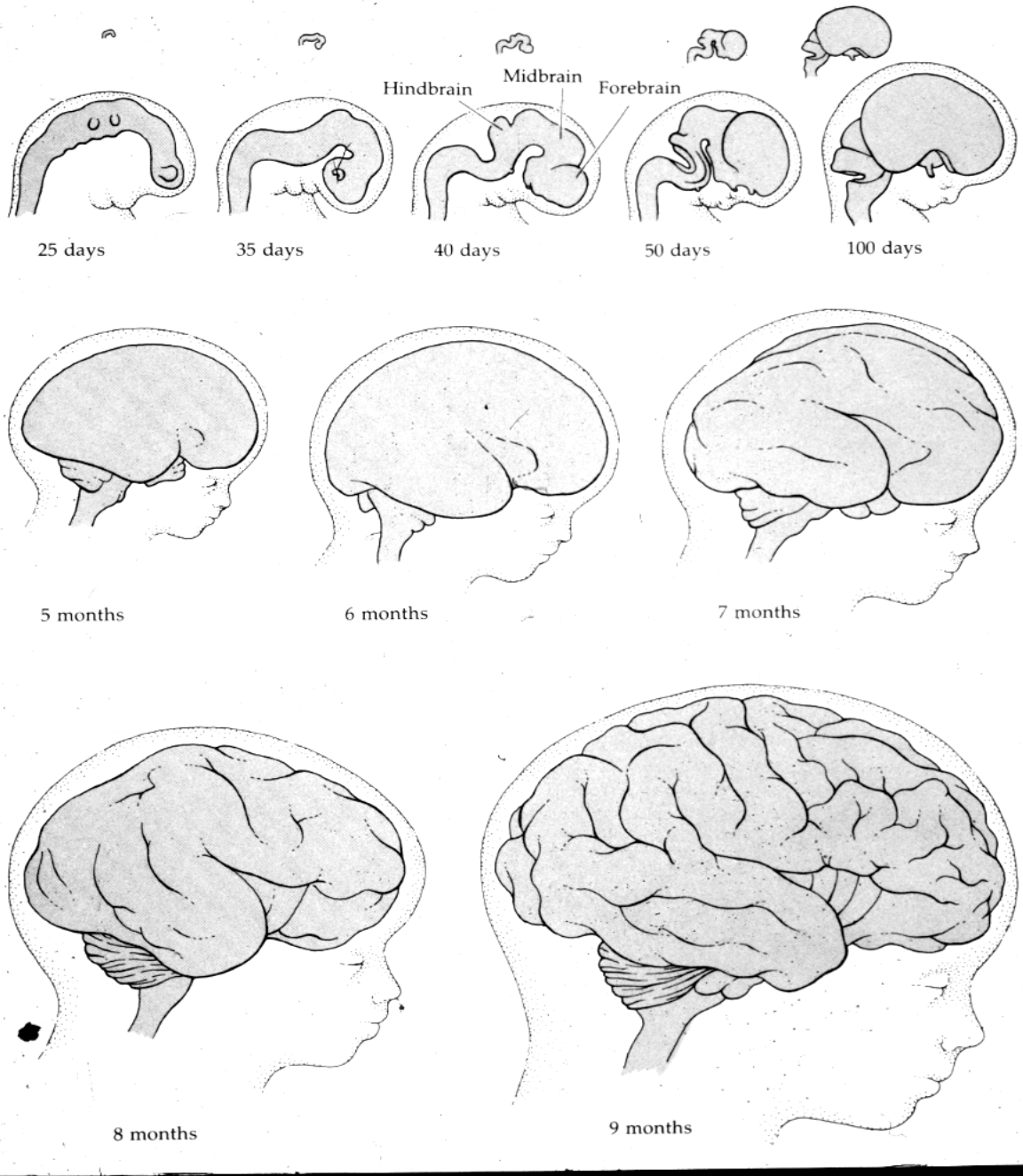
THE STAGE OF DEVELOPMENT AT BIRTH VARIES BETWEEN SPECIES

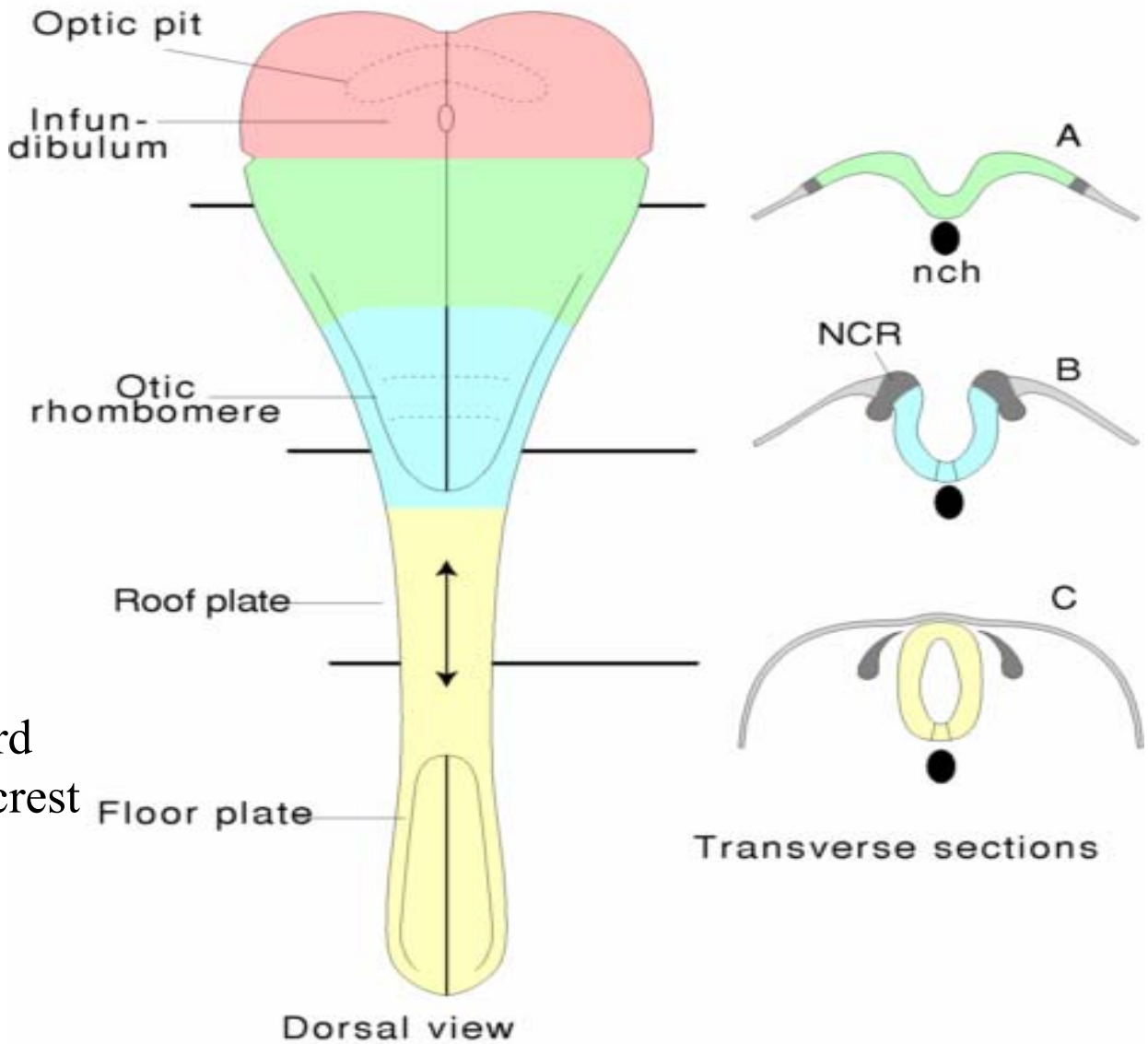
Primates are born with eyelids open, cats with lids fused. fused. Therefore, in primates much of the visual system develops without visual experience

FORMATION OF THE NERVOUS SYSTEM: early steps in the development

- The brain begins as a simple tube out of which form three brain vesicles.

- These three vesicles further differentiate through a a series of steps into the 5 main subdivisions of the the brain that further subdivide to become the adult brain.


Hindbrain
Midbrain
Forebrain
25 days
35 days
40 days
50 days
100 days
5 months
6 months
7 months
8 months
9 months



Nch = notochord
NCR = neural crest region

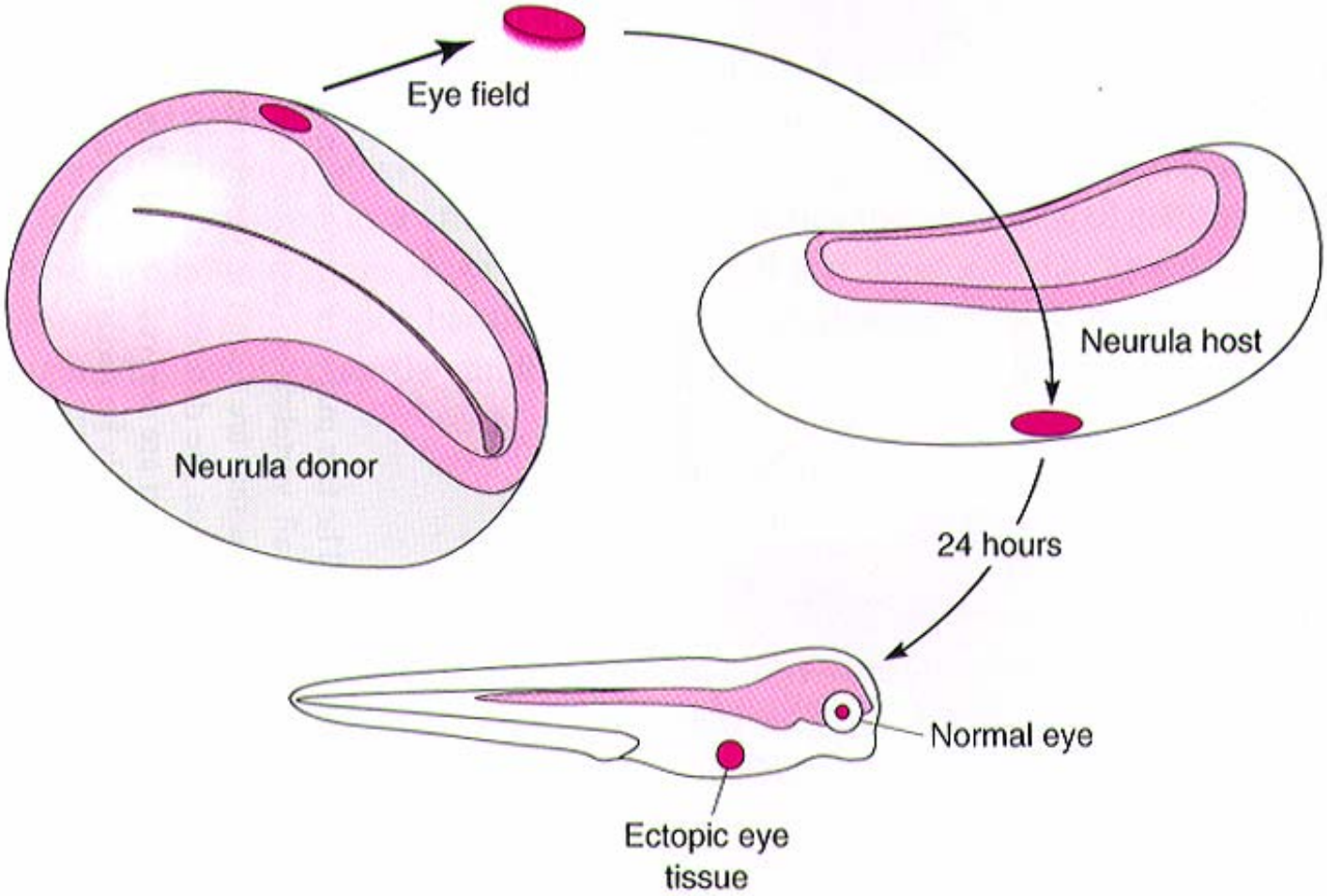


Figure 2.13 The cells of the neural plate take on a regional identity around the time of neurulation. For example, when the presumptive eye-forming region of the neural plate was transplanted to the flank of a different embryo, and the embryos were analyzed for the type of neural tissue that developed from the graft, it was found that an eye would develop from that tissue even in this ectopic location.

The eye develops as an out pocketing of the diencephalon.

i) The developing **optic vesicle** becomes the neural **retina** and **pigment epithelium**.

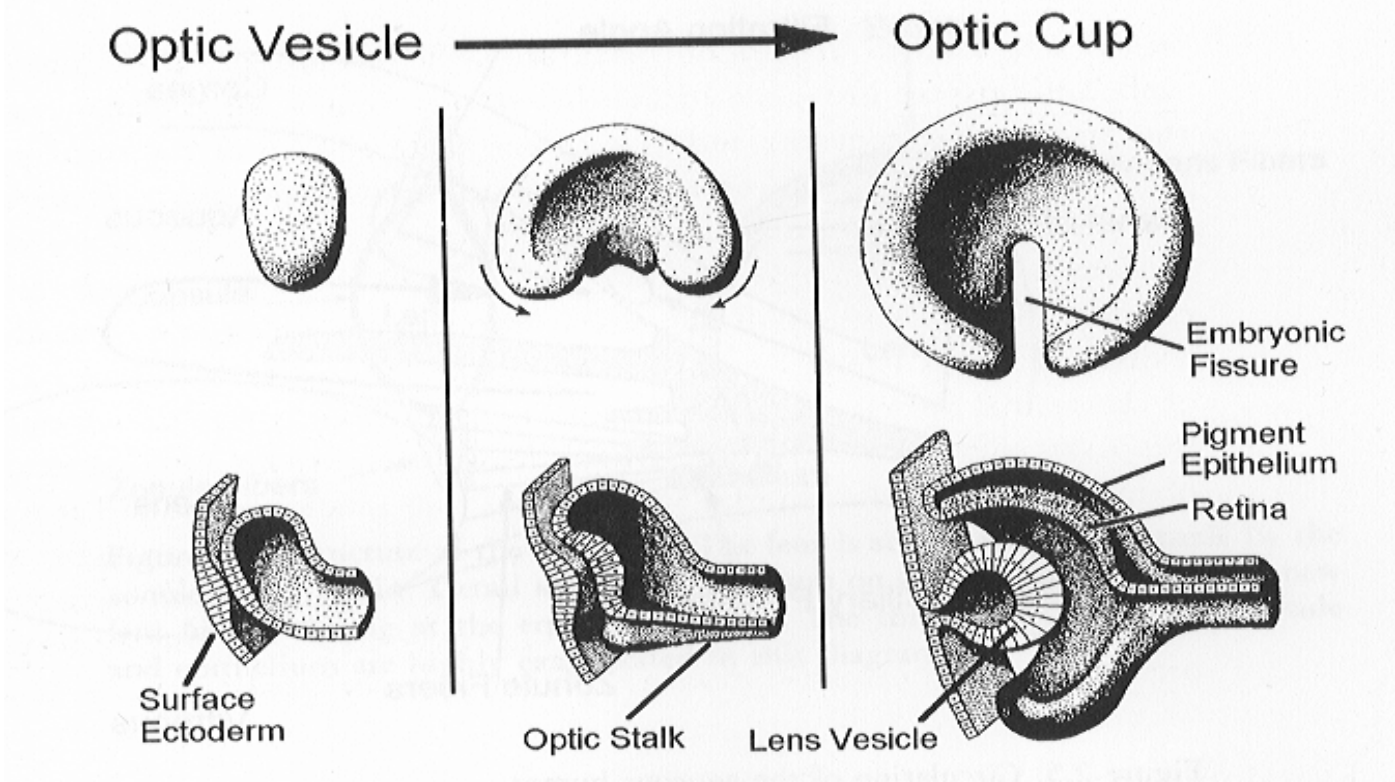
ii) The developing **optic stalk** will eventually contain the retinal vessels and the **optic nerve**.

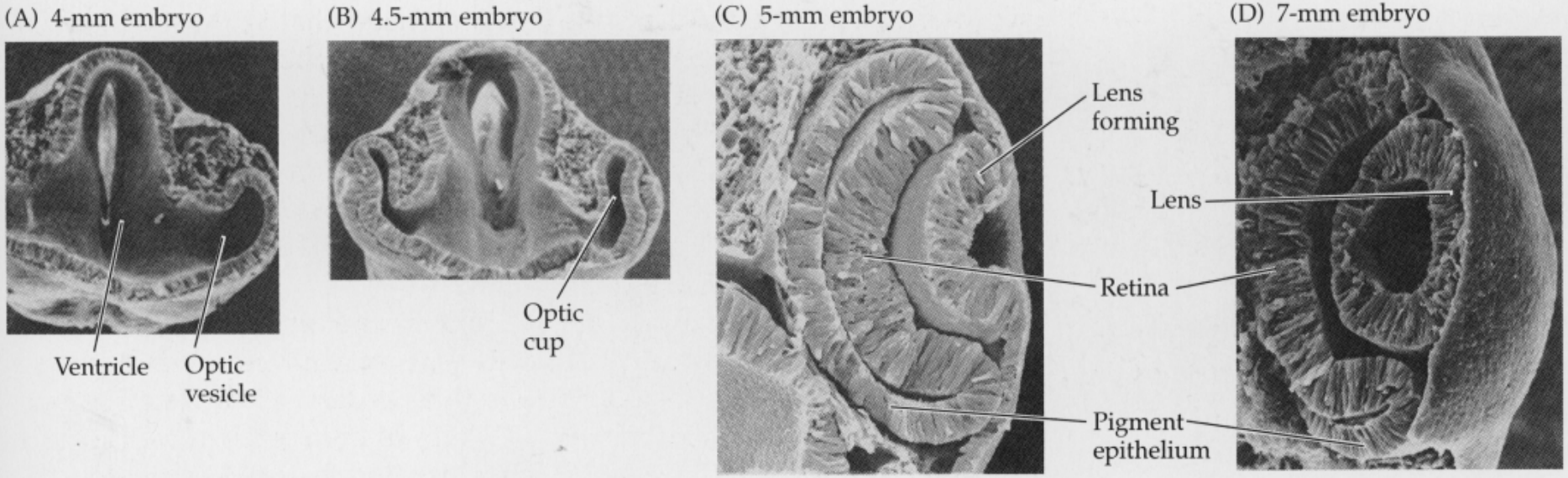
iii) The lens is INDUCED to form by molecular signals from the optic optic vesicle

(1) Lens **COMPETENCE within the ectoderm (layer of cells that will become the skin and nervous system)** is specified very early even before the neural tube has closed.

iv) During development the optic vesicle forms a half cup that folds to fuse into a whole cup at the ventral edge of the eye

v) After the lens has formed the cornea is INDUCED to form by CHEMICAL SIGNAL interactions with the lens tissue which, in turn, affects the final formation of the lens.


Optic Vesicle
Optic Cup
Embryonic Fissure
Pigment Epithelium
Retina
Surface Ectoderm
Optic Stalk
Lens Vesicle


(A) 4-mm embryo
(B) 4.5-mm embryo
(C) 5-mm embryo
(D) 7-mm embryo
Ventricle
Optic vesicle
Optic cup
Lens forming
Lens
Retina
Pigment epithelium

NEUROGENESIS: Cells divide and mature at different times

- Cells differentiate (develop into their mature phenotype) based upon an intrinsic genetic program and interactions with the local environment.

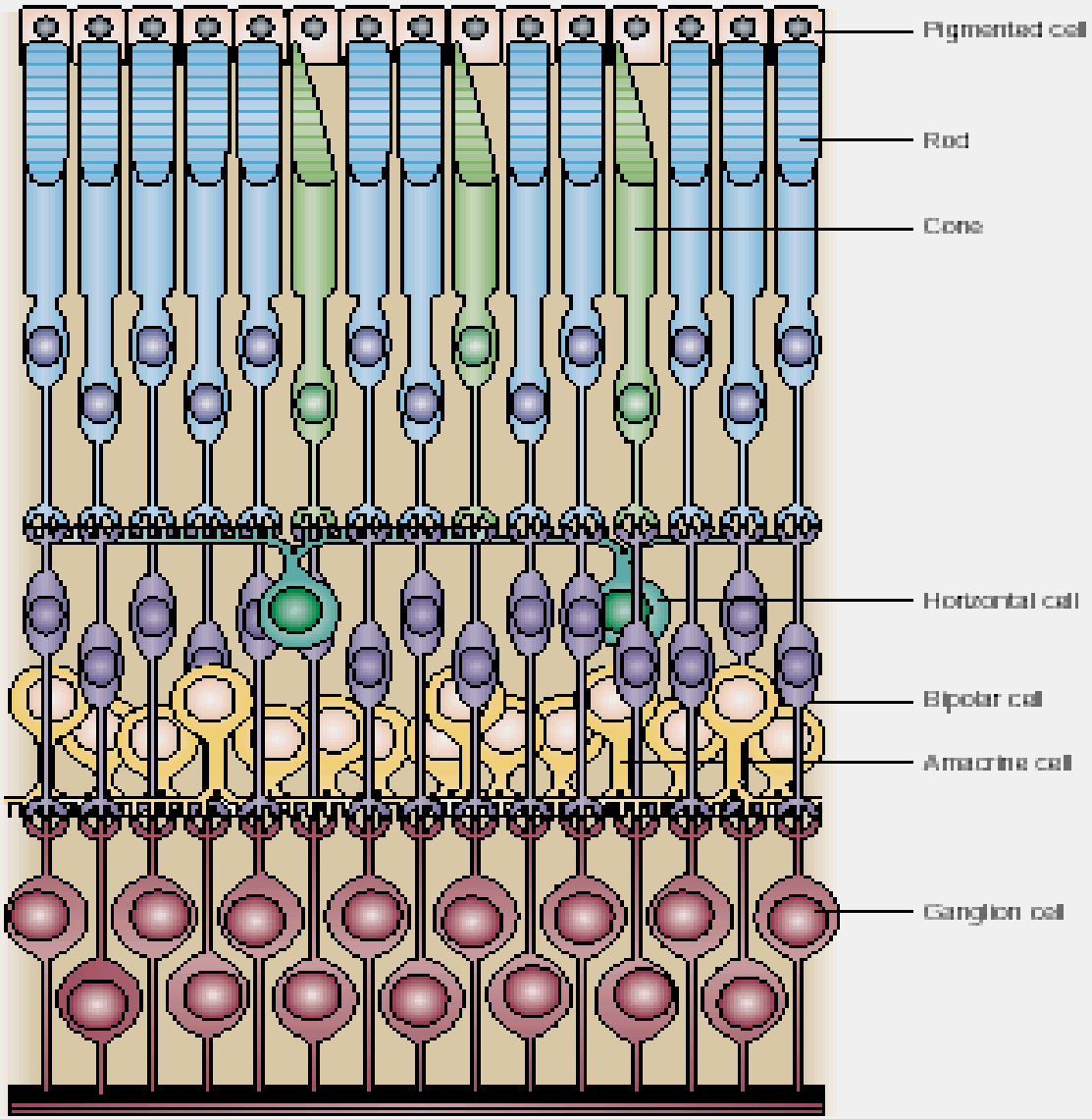
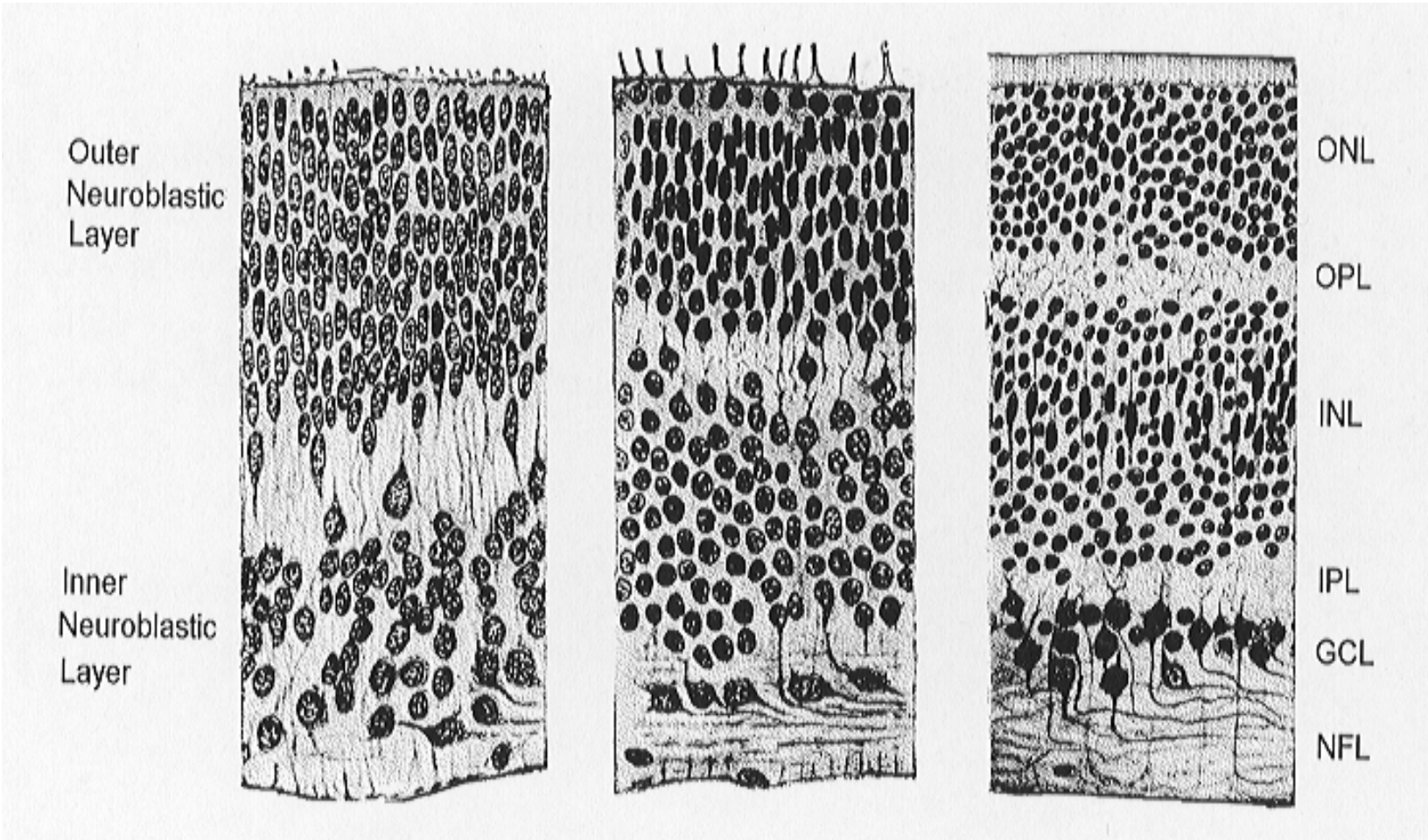


Figure 1 | **Histology of the adult mammalian retina.** The seven main cell types are shown, but it should be noted that in many species there are many distinct subtypes within each class of neuron[85]. For example, there are at least 22 subtypes of amacrine cell in the rabbit retina[86].

Cells in the different layers Of the retina develop at different times. **Ganglion cells** are "born" (undergo their final mitotic division) **first**. **Rods** are born **last**.

Stages of the developing retina



Cells are generated nearest the original venticular zone in an outside out pattern.

Cell Fate in the Retina

- Cells both acquire and lose the ability to make specific retinal cell types depending upon their state of competence and environmental signals (e.g., negative feedback signals from cells already generated).

- If, for example, a progenitor cell that would normally produce ganglion cells is confronted with molecular signals that suggest lots of ganglion cells are already present it will go on to produce a bipolar cell.

Dyer and Cepko, 2001

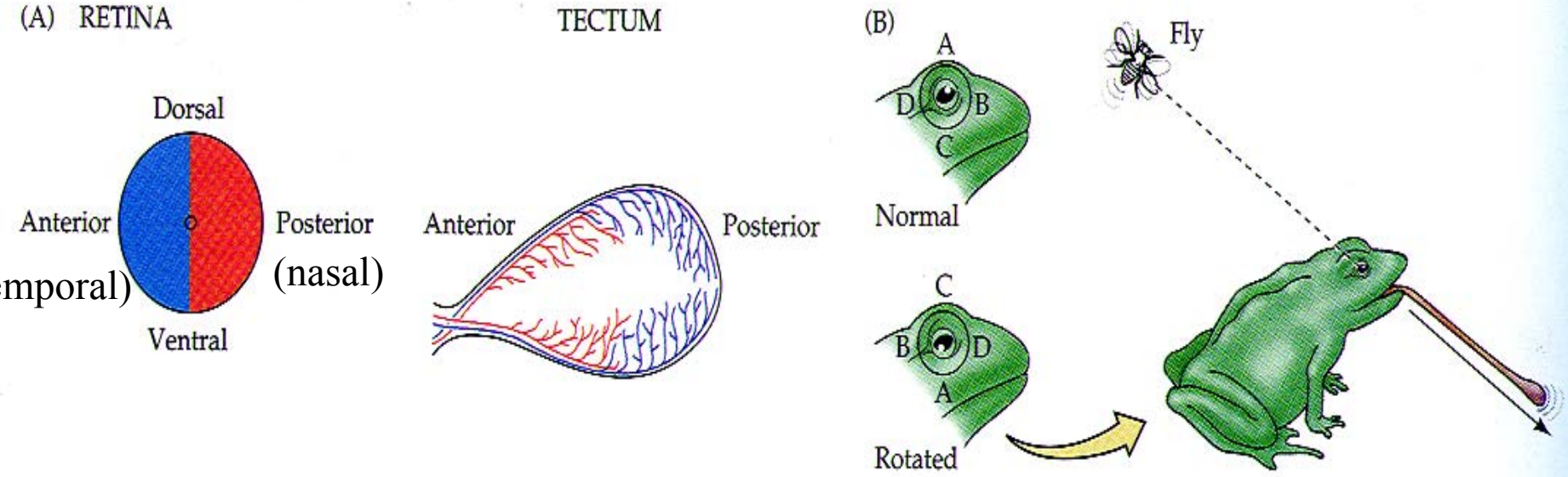


Figure 21.6 The axons of the retinal ganglion cells project to appropriate positions in the optic tectum during both development and regeneration in frogs and other "lower" vertebrates. (A) Posterior retinal axons project to the anterior tectum and anterior retinal axons to the posterior tectum. When the optic nerve of a frog is surgically interrupted, the axons regenerate with the appropriate specificity. (B) Even if the eye is rotated after severing the optic nerve, the axons regenerate to their original position in the tectum. That the topographical visual map in the tectum remains unchanged is evident from the frog's behavior: when a fly is presented above, the frog consistently strikes downward, and vice versa. This outcome indicates a specific matching of retinal neurons to their target cells in the tectum, a phenomenon taken to explain topographical mapping in the mammalian brain as well. (After Sperry, 1963.)

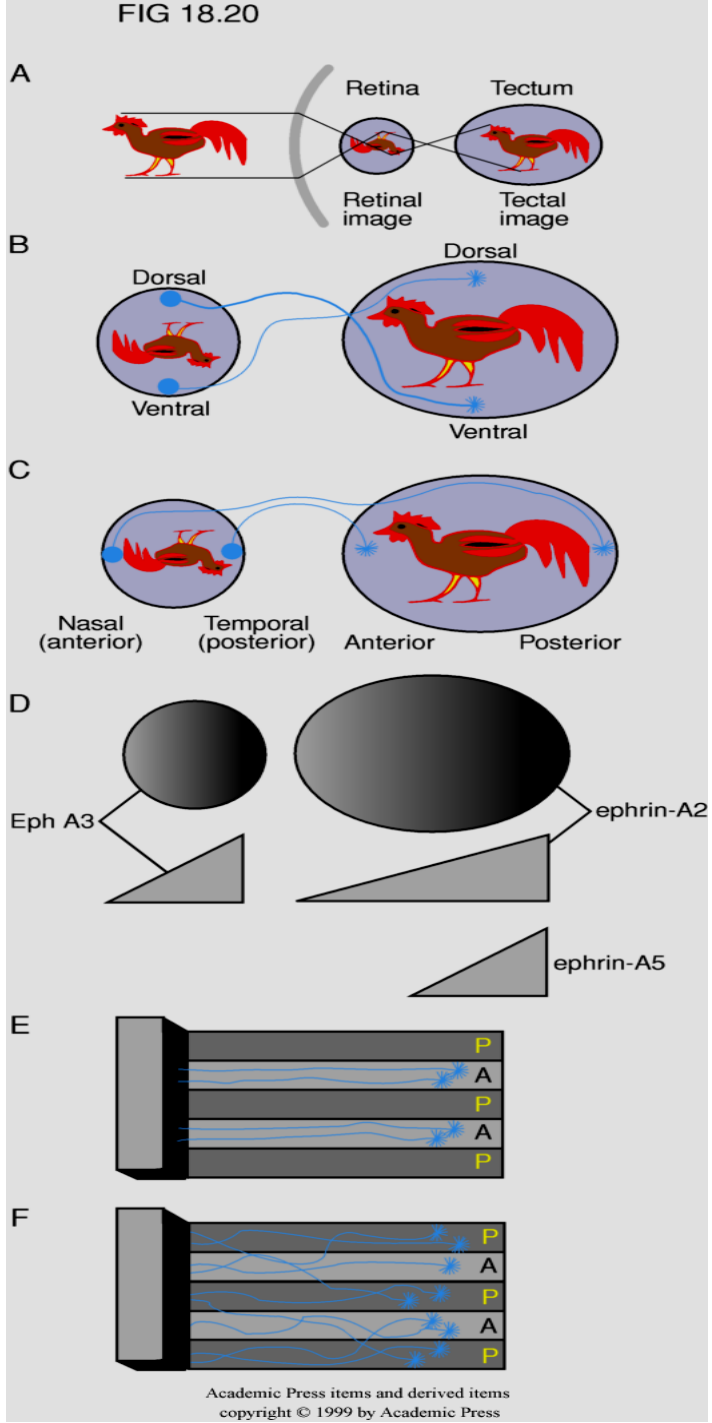
Roger Sperry proposed that topography developed correctly due to **chemospecificity**.

Chemospecificity: How rigid?

Experiments by Roger Sperry showed that retinotectal projections regenerate with precision in frogs.

Subsequent experiments have demonstrated that coordinates are only roughly specified during development by chemical gradients which are either attractive or repulsive to axons. Refinements of topography require neural action potential activity.

Axons from the nasal and and temporal retina have been shown to prefer either the anterior or posterior optic tectum (tectum = superior colliculus) based upon gradients of molecules.



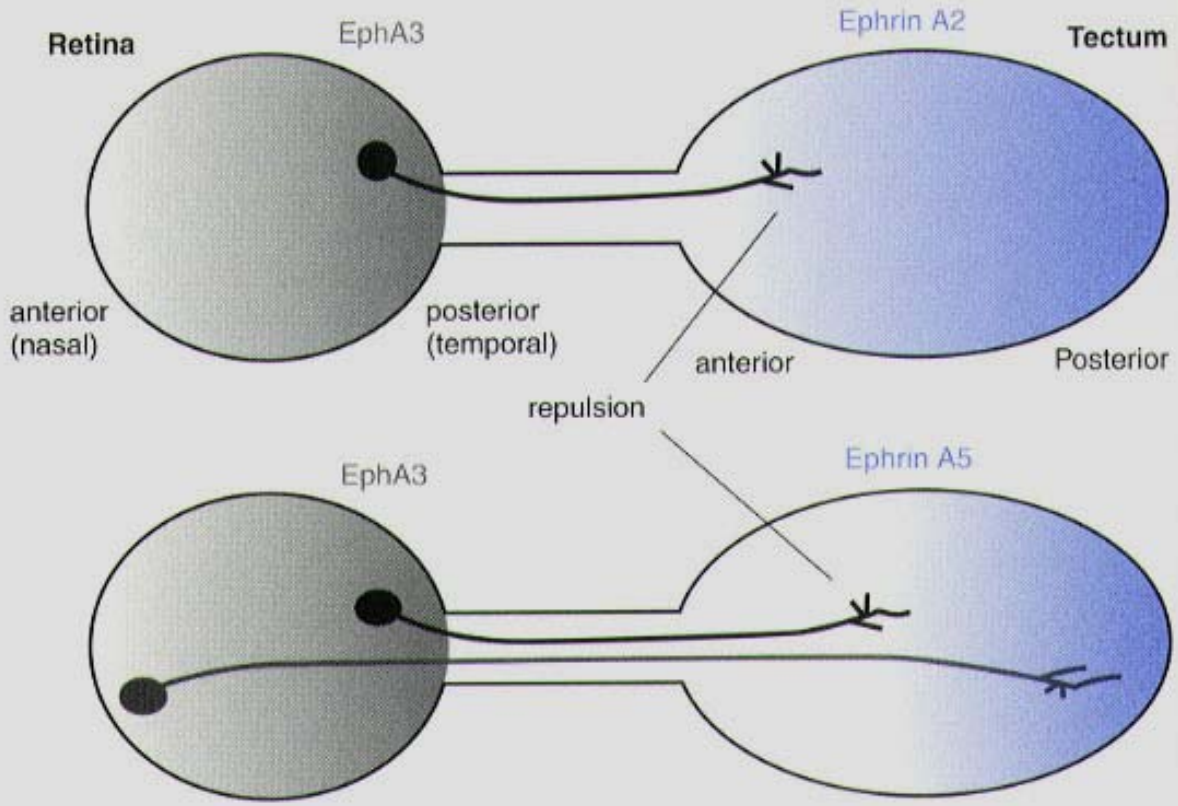


Figure 18–6. Gradients of ephrins in the tectum. Ephrins A2 and A5 in cells of the posterior tectum repel axons of neurons from posterior retina, which contain the EphA3 receptor.

Neural Activity is important to stabilizing synapses
Cells that are active receive more nutrient materials (neurotrophic molecules) from potential postsynaptic targets)

Cells that are near neighbors in the retina tend to be active at the same time synapse close together in their targets where near by cells also tend to be active at the same. Cells that **fire together tend to wire together.**

Mistakes in wiring are eliminated by cell loss or cell death or pruning of inappropriate connections.

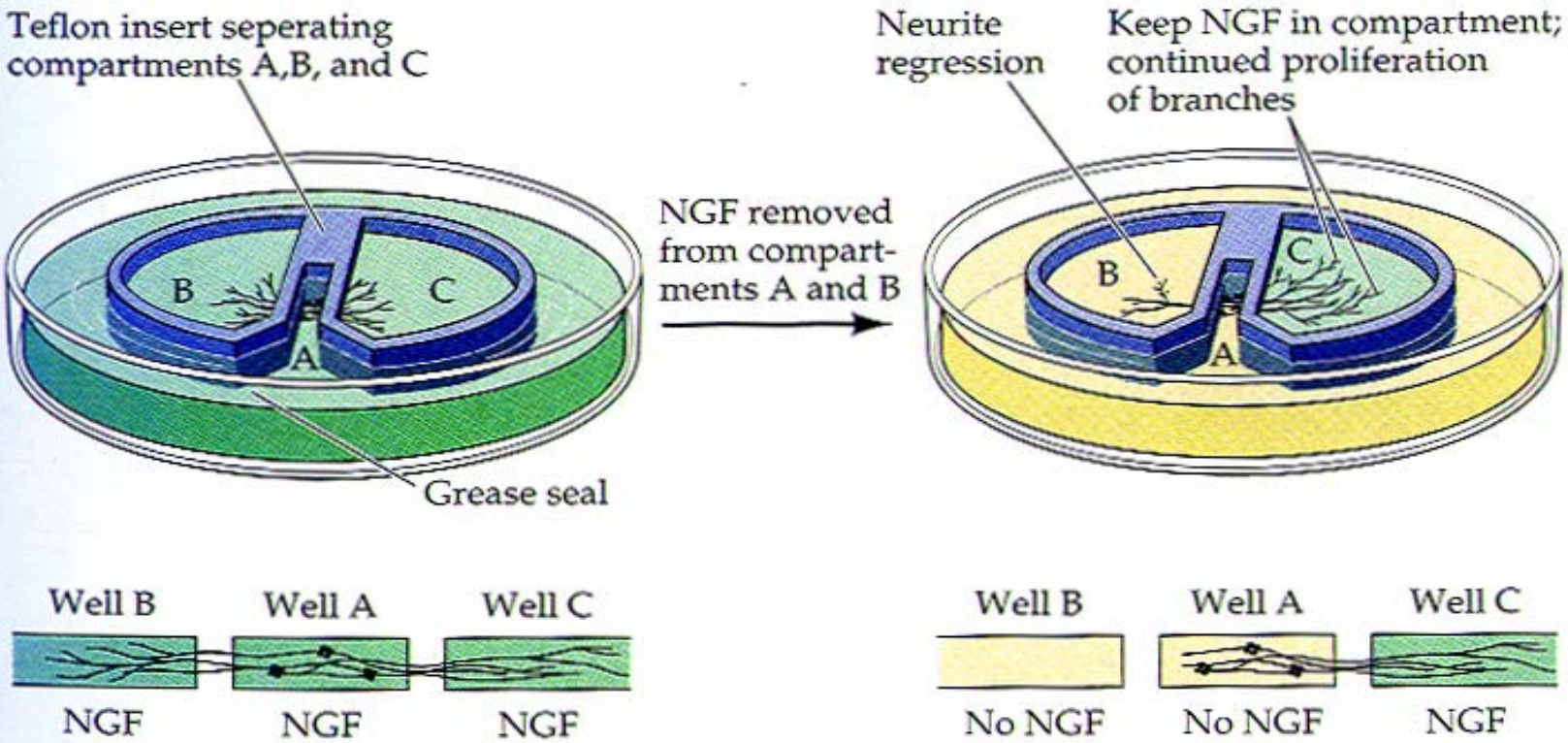
Together dorsal/ventral and nasal/temporal gradients in the retina and tectum (or LGN) and the activity rule is enough information to organize topographic connections.

COMPETITION AND CELL DEATH

- Neurons require trophic support in form of secreted molecules (e.g., growth factors) from target cells in order to survive. If they don't get these factors they may die or attempt to connect (synapse) with other cells that provide these "nutrients". Since the trophic molecules exist in limited quantities neurons are said to "compete" with each other to make connections with other cells that can supply the appropriate nutrient.

- Almost 50% of cells born and connections made during development are eliminated via **cell death** or removal of connections before maturity.

Nerve Growth factors support cell growth



NGF = nerve growth factor

Key Points

Cell phenotype is genetically specified early but depends upon correct chemical signals from the environment to be expressed.

The optic vesicle induces the lens to form which, in turn induces the cornea to to form.

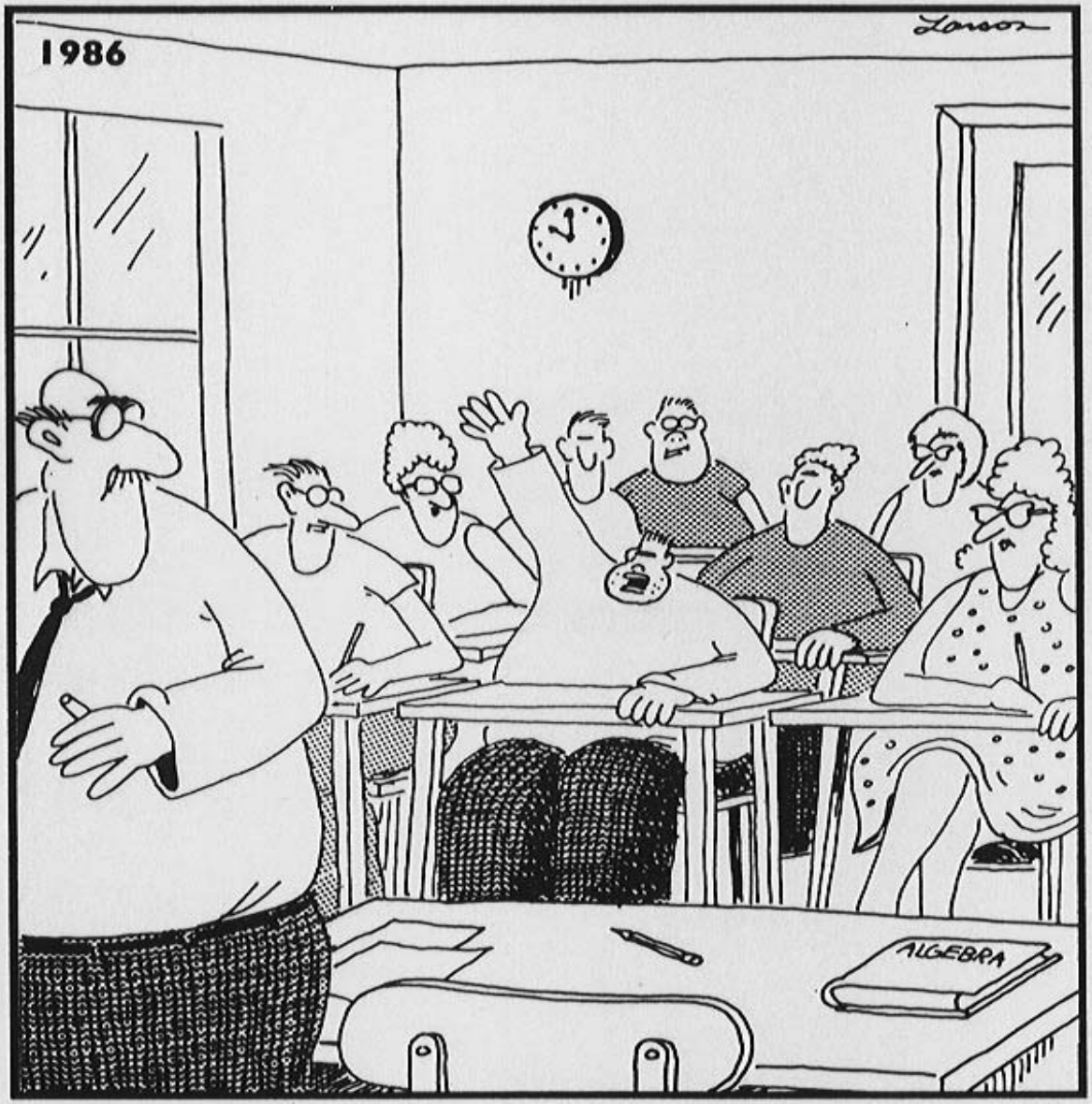
Cells often must migrate distances to their proper location (e.g. in visual cortical development cells migrate from where they are first generated).

Axons are guided to their proper places initially by growing towards chemicals chemicals that attract them and moving away from chemicals that repel them.

More cells are born then will survive. The survivors obtain the correct "nutrients" from growth factors.

Connections are refined by neural activity. "Cells that fire together wire together"

Visual experience influences synapse formation and axon wiring in development.



"Mr. Osborne, may I be excused? My brain is full."