Refinement of Connections I

Steven McLoon
Department of Neuroscience
University of Minnesota

Course News

Graduate School Discussion

Wednesday, Nov 28
11:00am (right after lecture)
In Mayo 3-100

with Dr. Paul Mermelstein
(invite your friends)

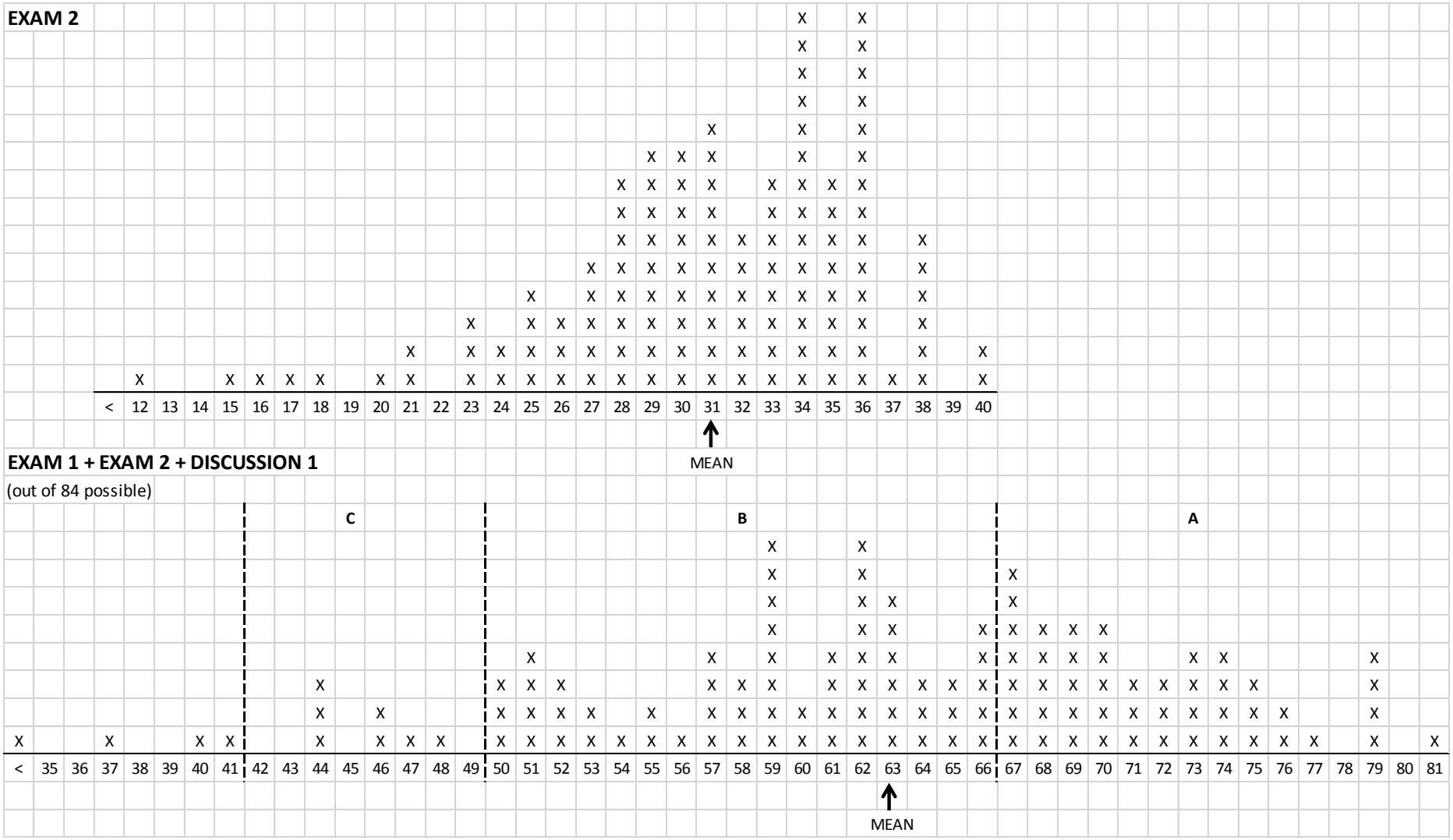
Coffee Hour

with Dr. Heilbronner (a new faculty member in neuroscience)

Tuesday (Nov 27) 10:00-11:00am
Surdyk's Café in Northrop Auditorium

Stop by for a minute or an hour!

Course News


EXAM 2
< 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40
MEAN
EXAM 1 + EXAM 2 + DISCUSSION 1
(out of 84 possible)
C
B
A
< 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81
MEAN

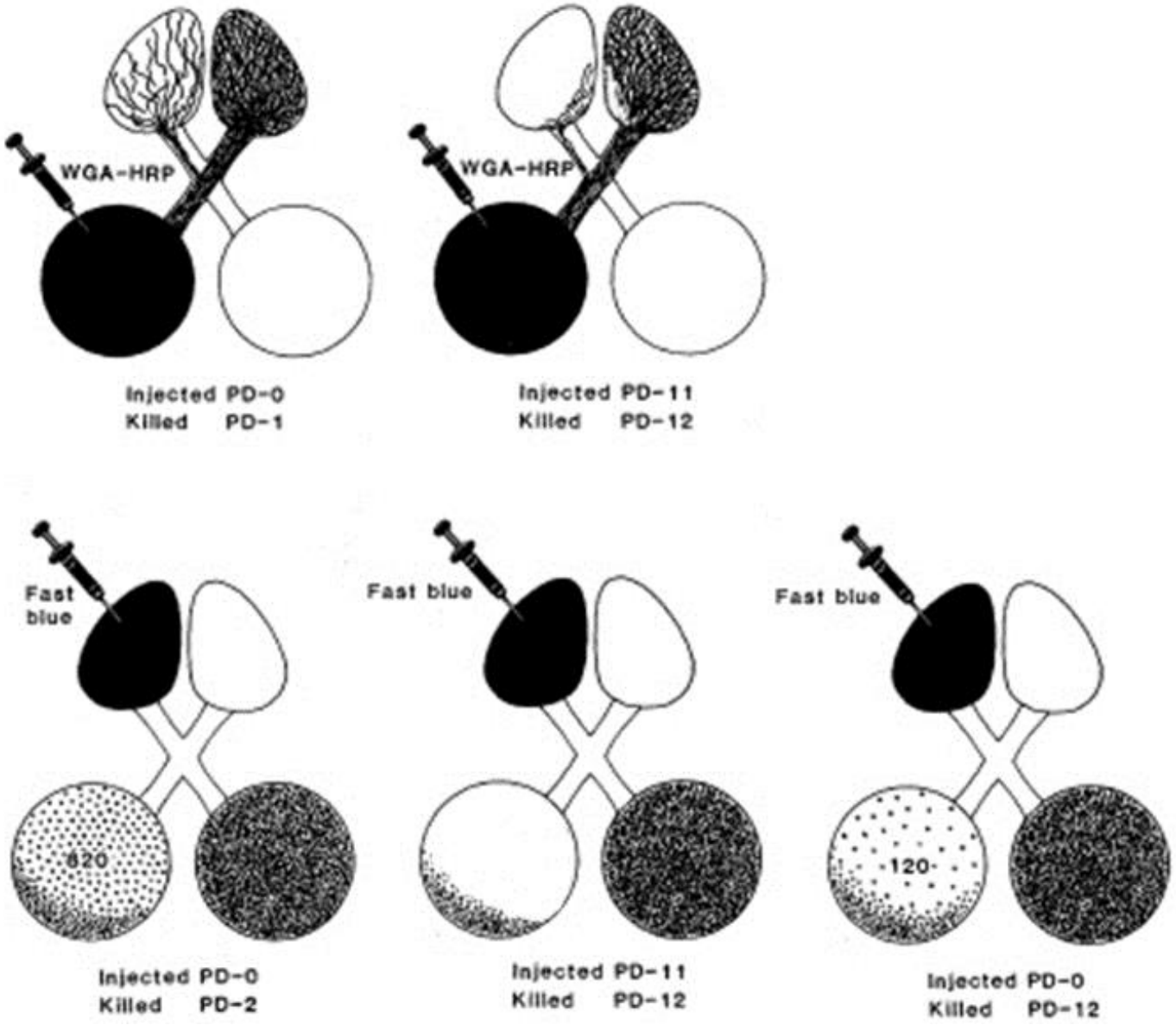
Development of Patterned Neuronal Connections

- Axon guidance and chemospecificity set up a rough pattern of connections between neurons and their target cells.
- Refinement improves the precision of the projection to that found in the adult via three simultaneous processes:
  - cell death
  - elimination of inappropriate connections
  - addition of appropriate connections (arborization of dendrites and axons)

Most neuronal systems exhibit transient projections.

- Examples of transient axonal projections eliminated by refinement from the retina to:
  - the contralateral retina via the chiasm
  - the ‘wrong’ side of the brain
  - non-visual nuclei such as medial geniculate and VPL
  - the ‘wrong’ topographic positions within a visual nucleus

Loss of Ipsilateral Retinotectal Projections



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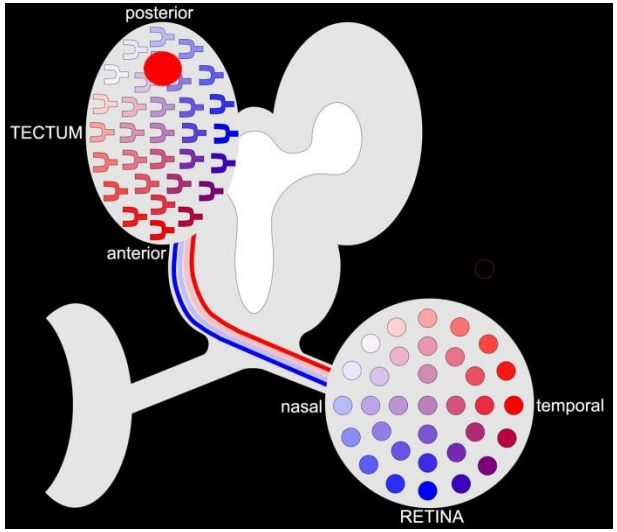


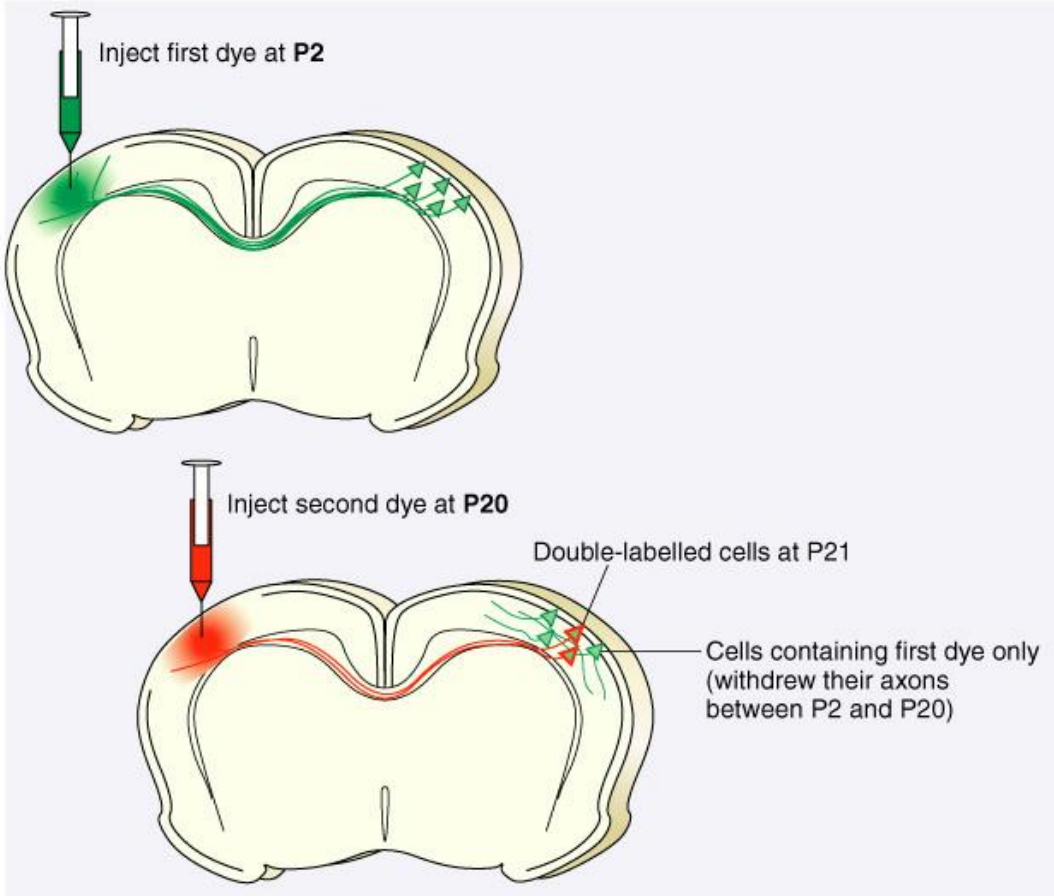
- Topographic precision in the retinotectal projection improves during development due to refinement processes.

Most neuronal systems exhibit transient projections.

- Examples of transient axonal projections from the retina:
  - LGN neurons initially are innervated by >20 retinal ganglion cells each, compared to ~3 in the adult.
  - These transient projections are eliminated during a discrete period of development.
  - The total number of retinal synapses per LGN neuron increases during this refinement period.

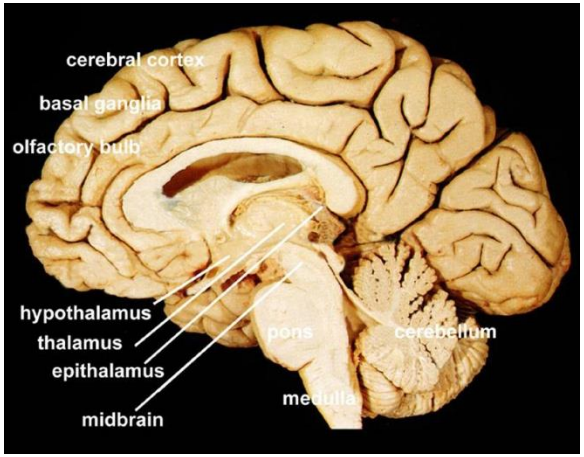
Most neuronal systems exhibit transient projections.

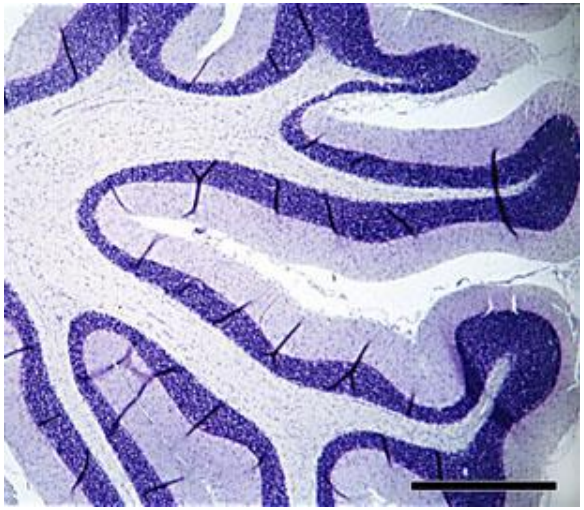
- Some cortical areas have a transient collasal projection.

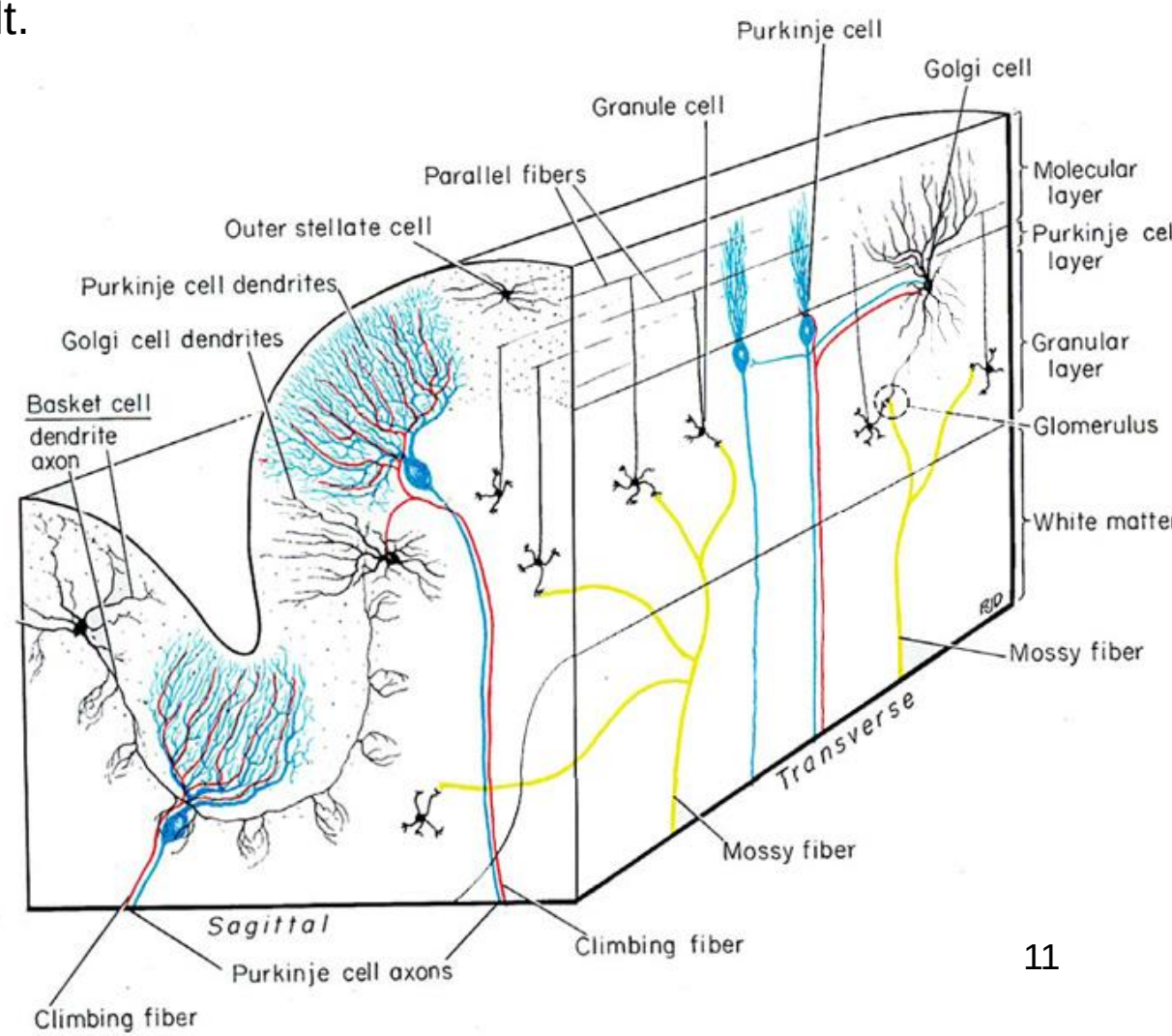


Most neuronal systems exhibit transient projections.

- Initially during development Purkinje cells receive multiple climbing fibers compared to a single climbing fiber in the adult.







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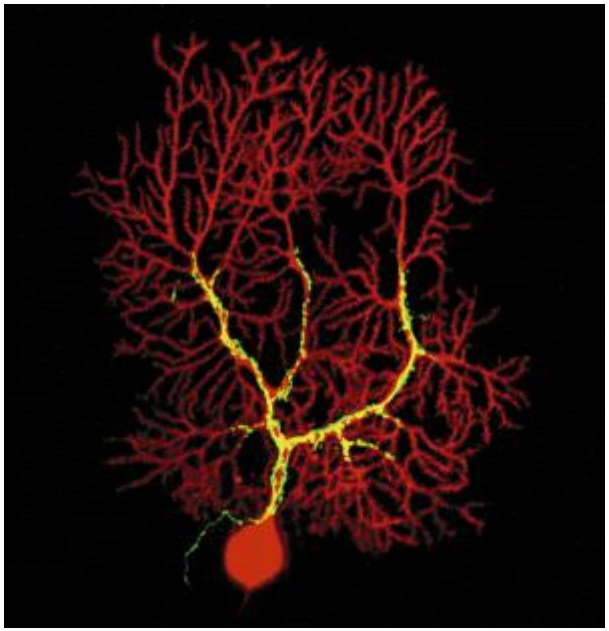


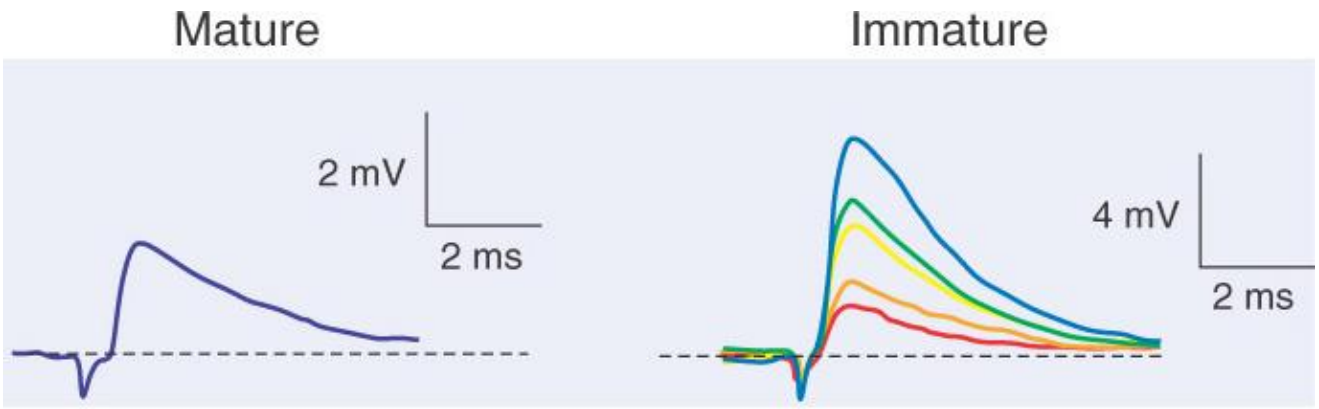
climbing fiber terminal
in green

Muscle

- Each muscle fiber (myofiber) has only a single neuromuscular junction in the adult.

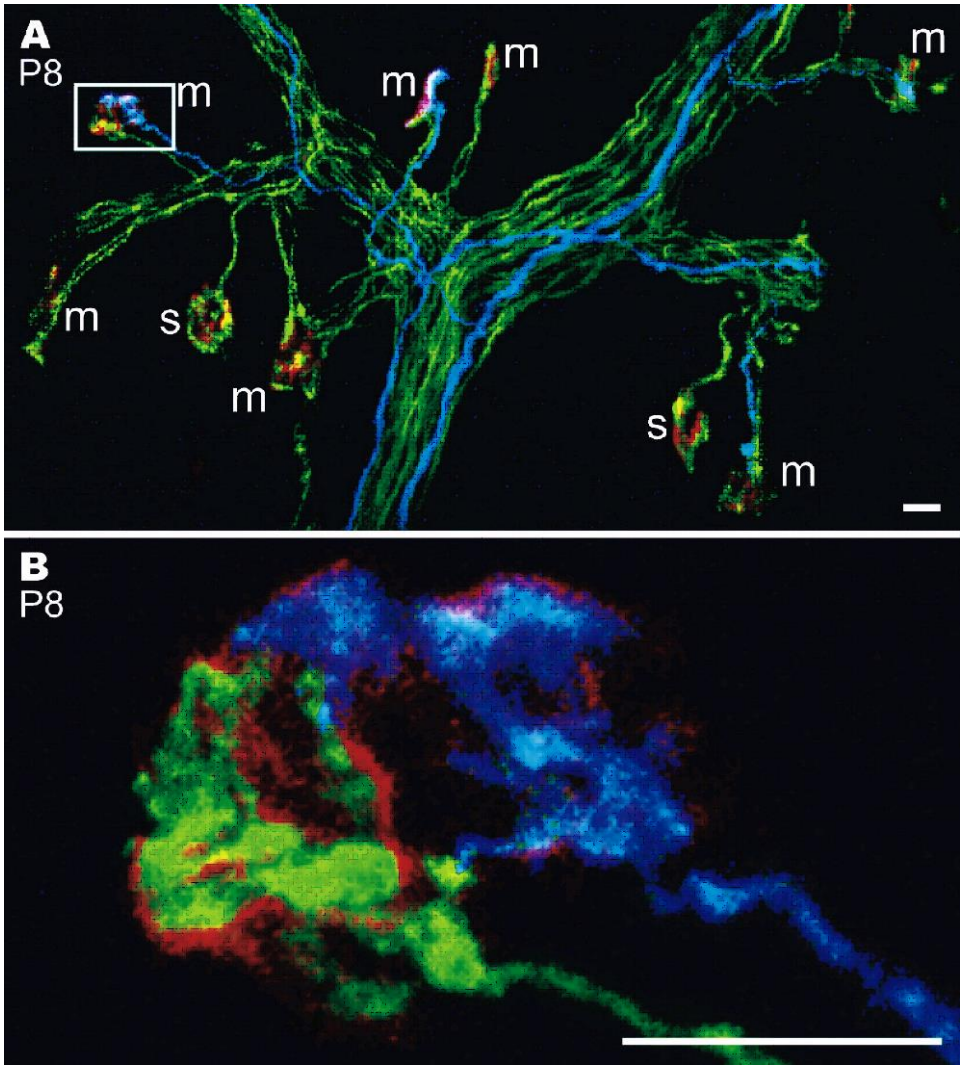
Transient projections can form functional synapses.

- Recording from a muscle fiber while stimulating its nerve showed transient polyneuronal innervation:
  - In adult animals, there was only one level of response in the muscle fiber regardless of the stimulus strength
  - In young animals, increased nerve stimulus strength (i.e. higher voltage) recruited more EPSP's in the muscle fiber.



Transient projections can form functional synapses.

- Loss of polyneuronal innervation in neuromuscular connections.



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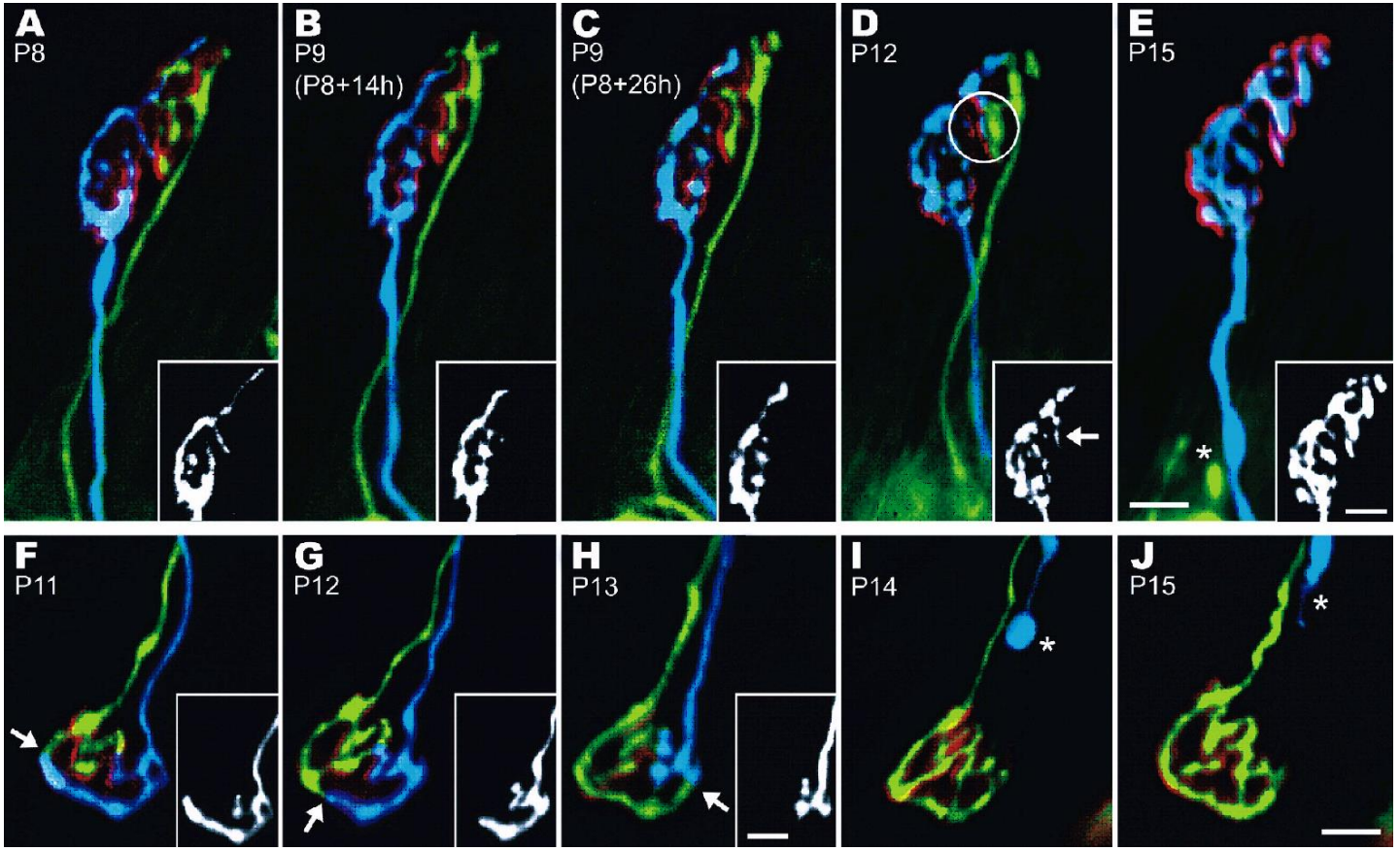


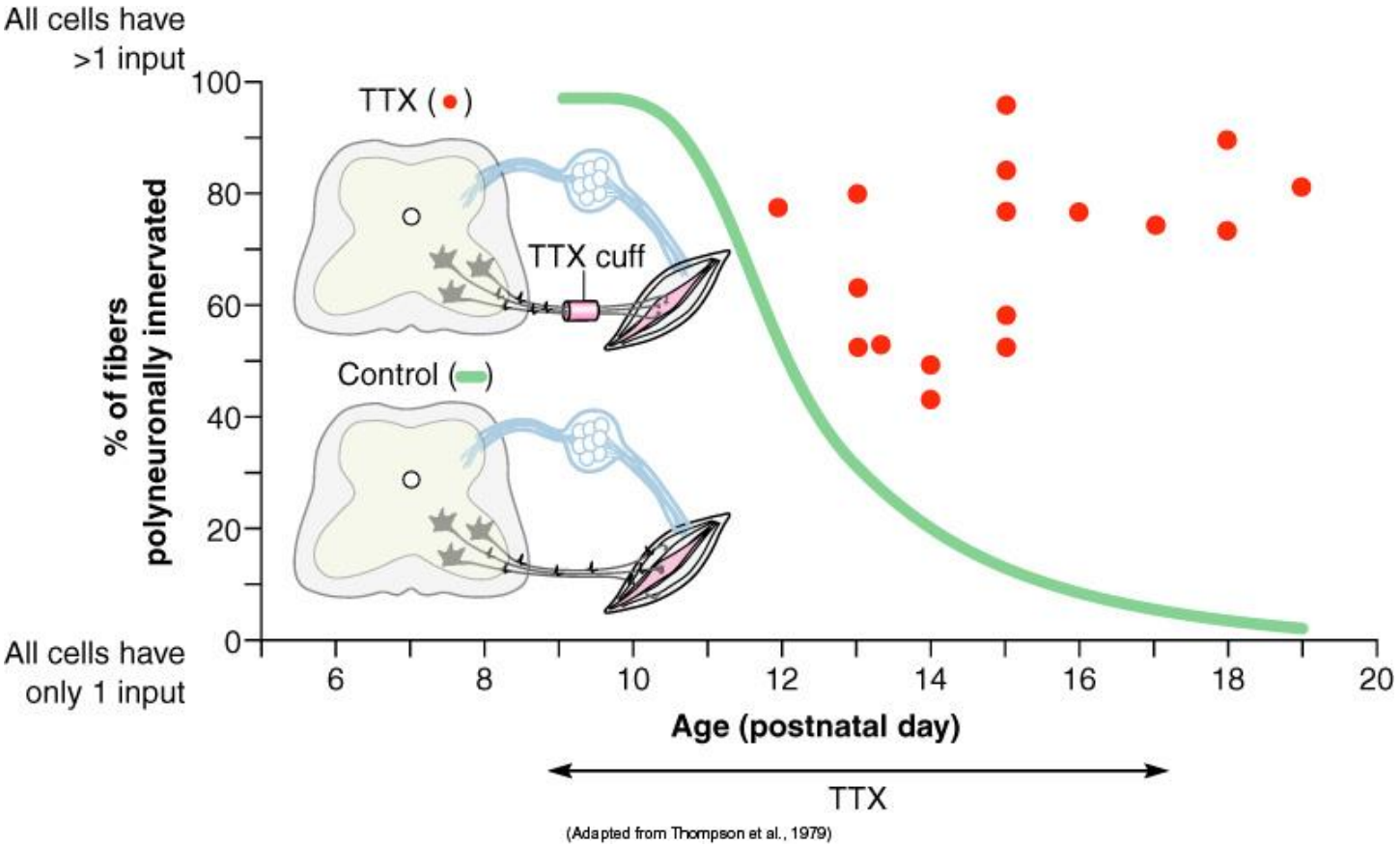
Transient projections can form functional synapses.

- In the neuromuscular system, there is a net loss in the number of synapses during refinement. However, the physical size of each synapse increases substantially.

- In many systems, some axonal branches and synapses are eliminated during refinement while others are added so that typically there is a net increase in the number of synapses.

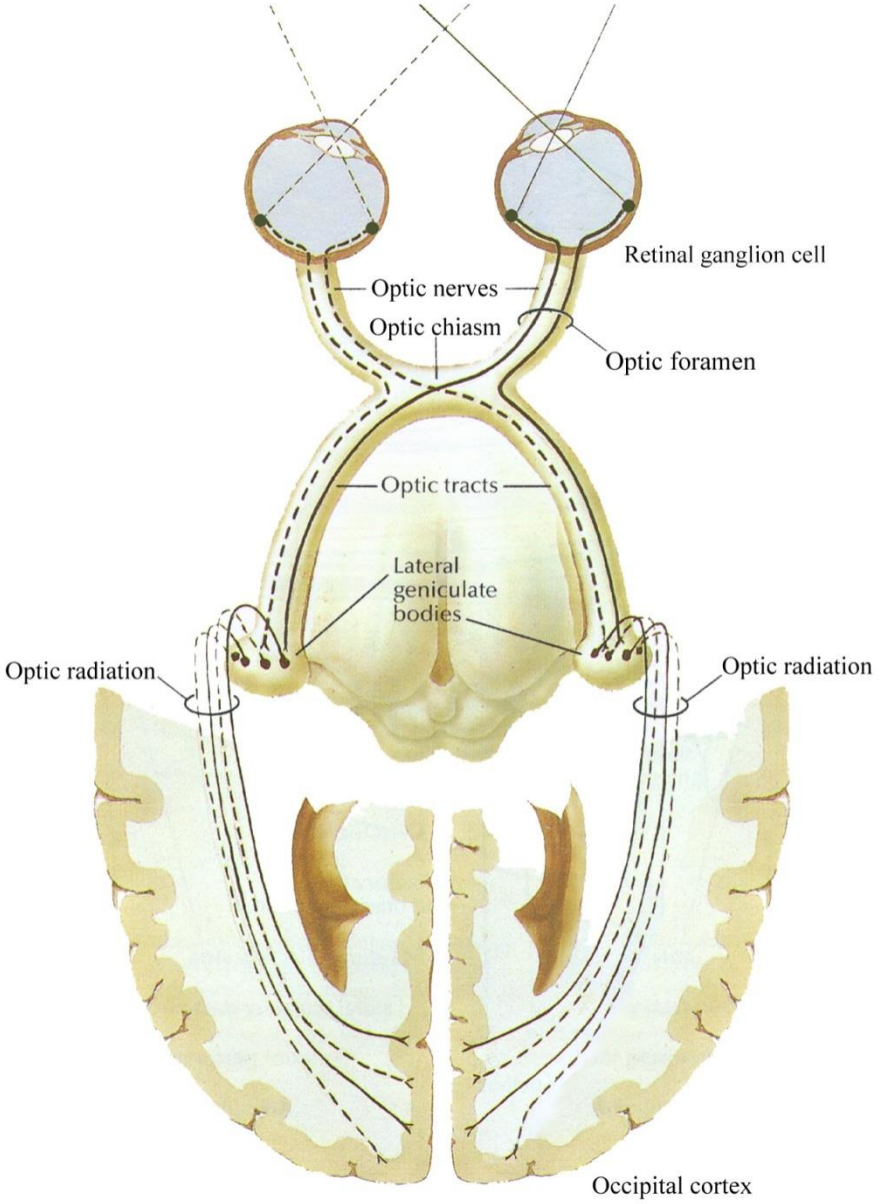
Refinement of connections is dependent on neuronal activity.

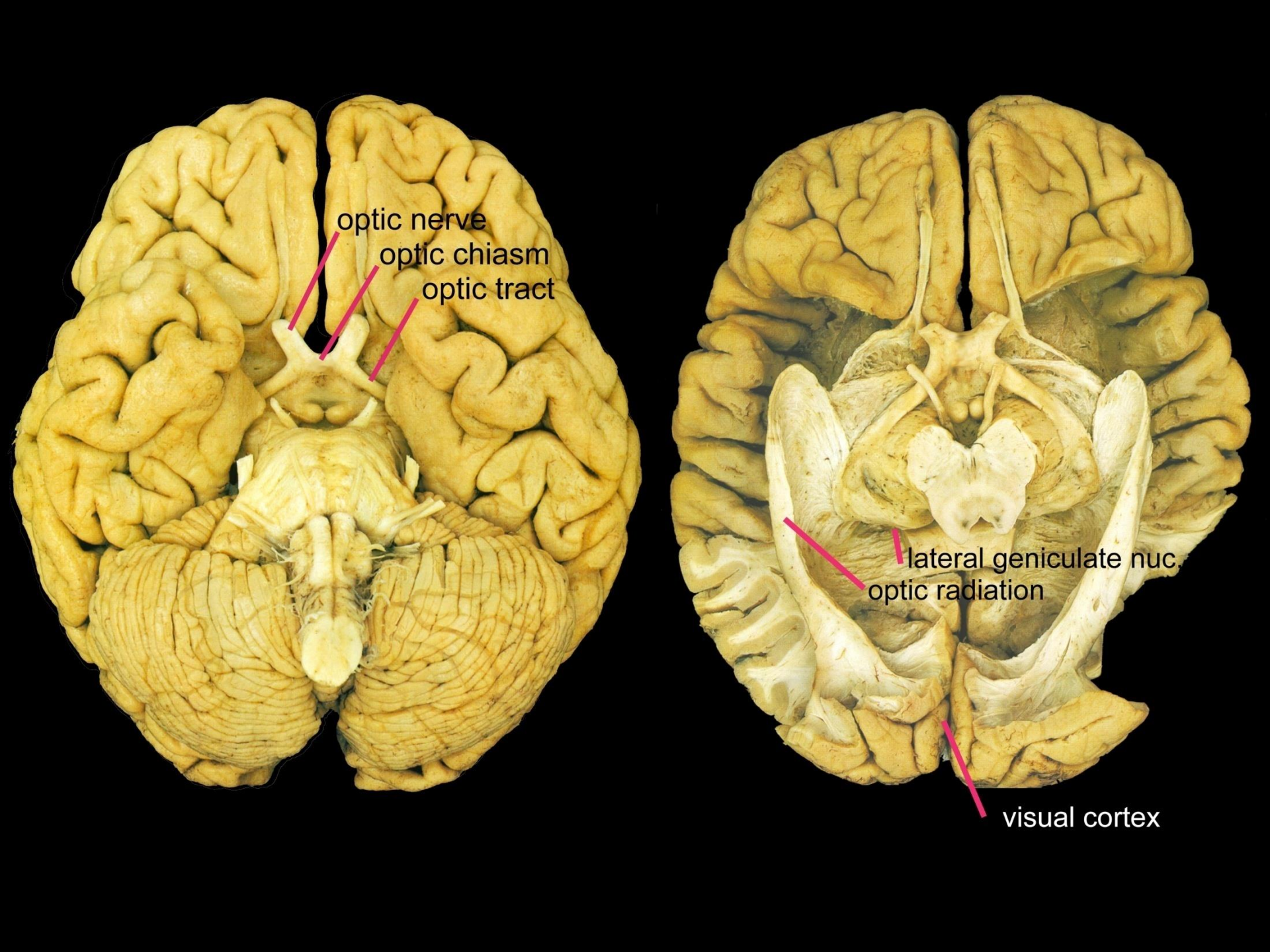
- Blocking motor neuron action potentials delays elimination of polyneuronal innervation of muscle.
- Increasing activity can accelerate loss of polyneuronal innervation.



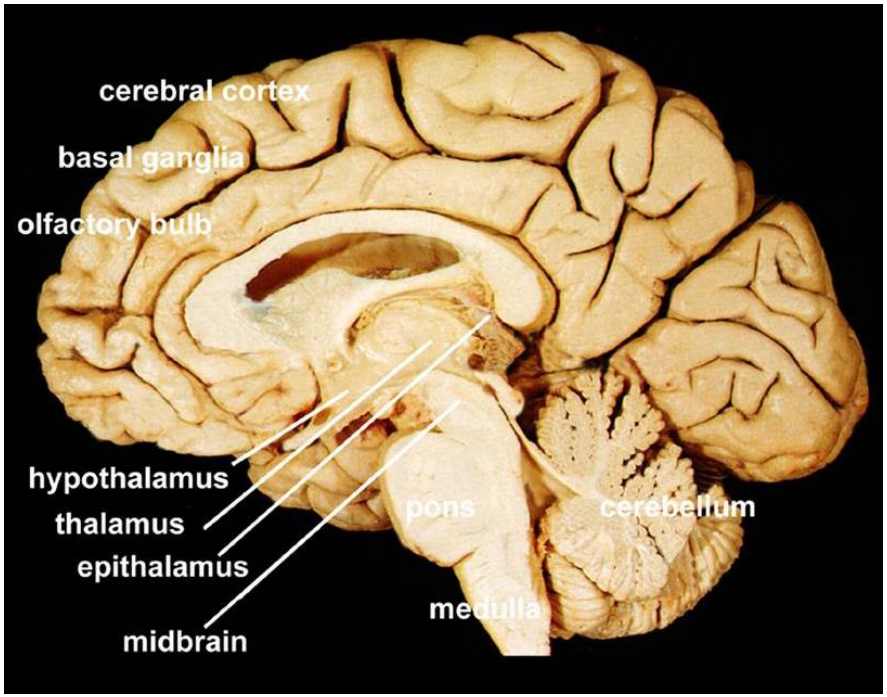
(Adapted from Thompson et al., 1979)

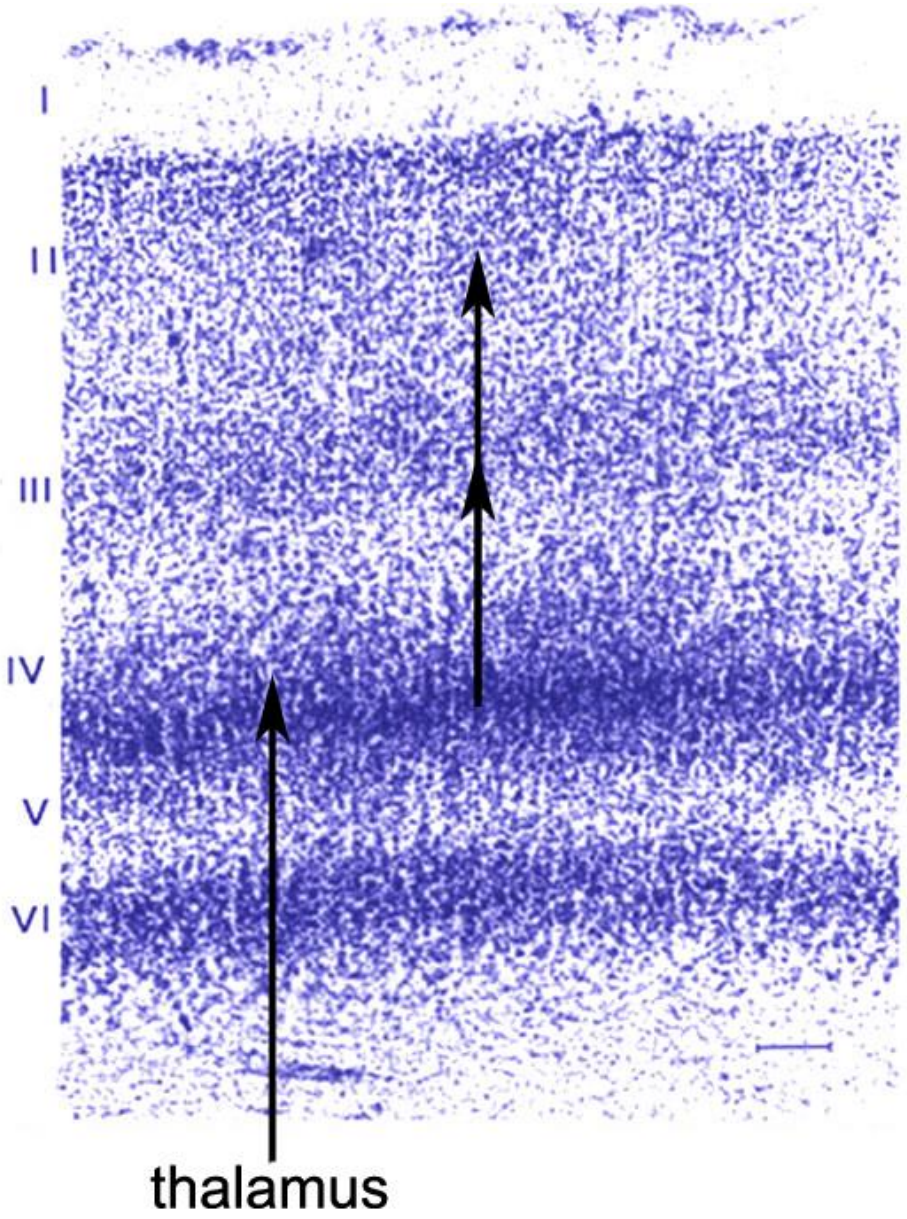
Visual experience drives development of visual cortex circuitry.




optic nerve
optic chiasm
optic tract
lateral geniculate nuc.
optic radiation
visual cortex

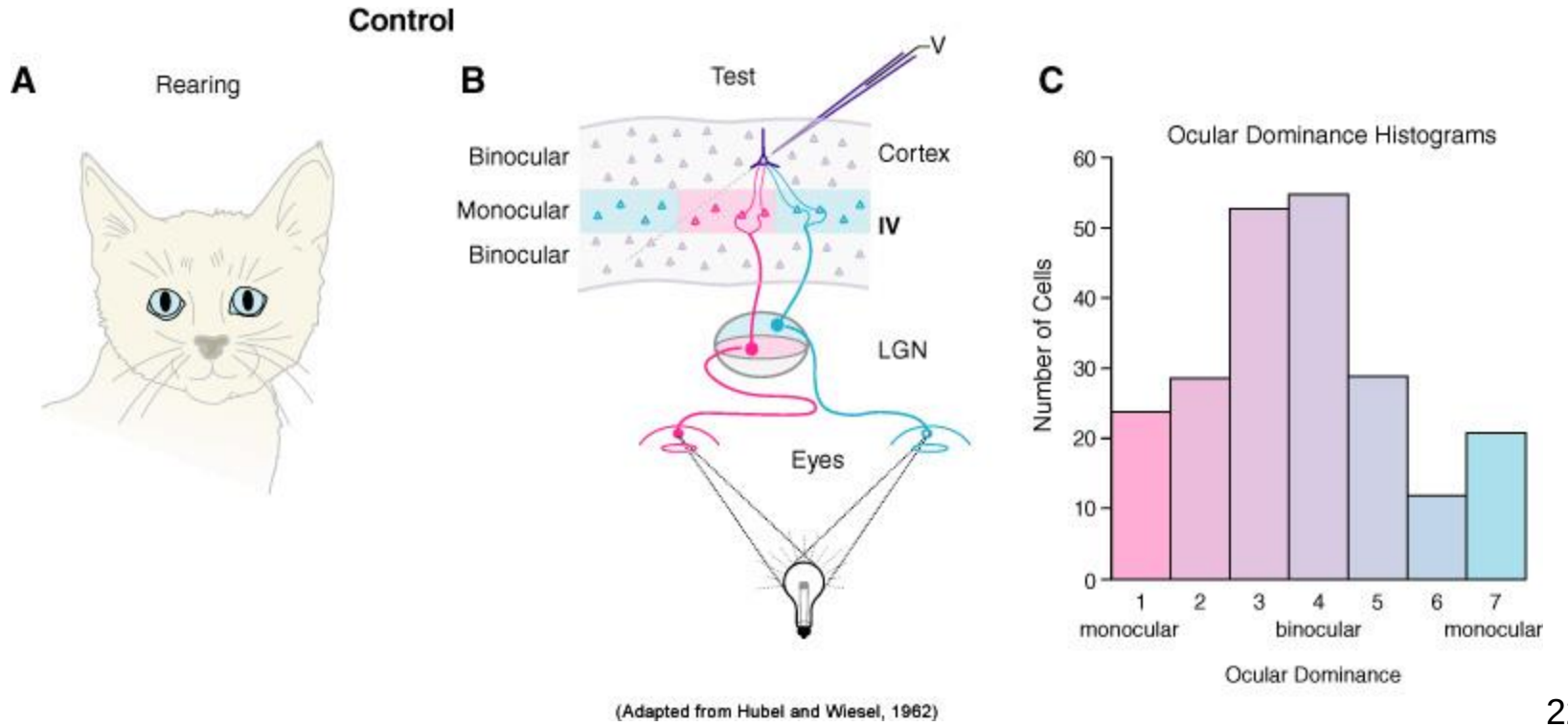
Visual experience drives development of visual cortex circuitry.





Visual experience drives development of visual cortex circuitry.

- In adult cat, the projection from the lateral geniculate nucleus to layer IV of visual cortex is segregated into alternating stripes subserving the output from each eye (ocular dominance columns / stripes).
- Cells in the other cortical layers are binocular.



(Adapted from Hubel and Wiesel, 1962)

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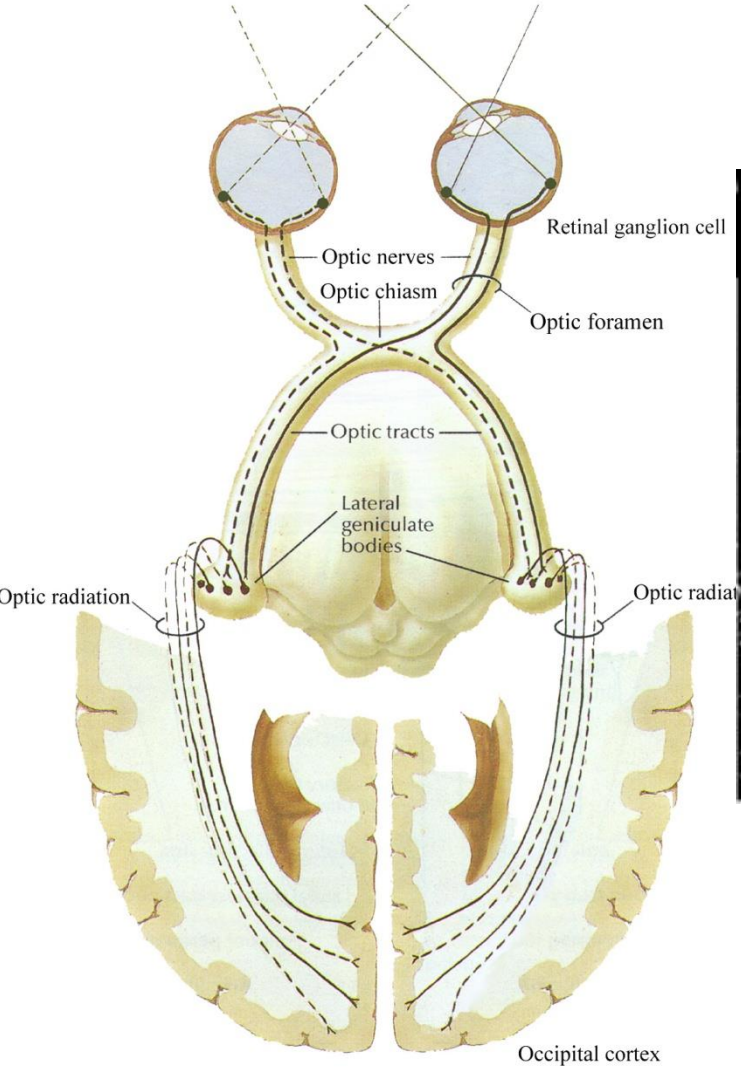
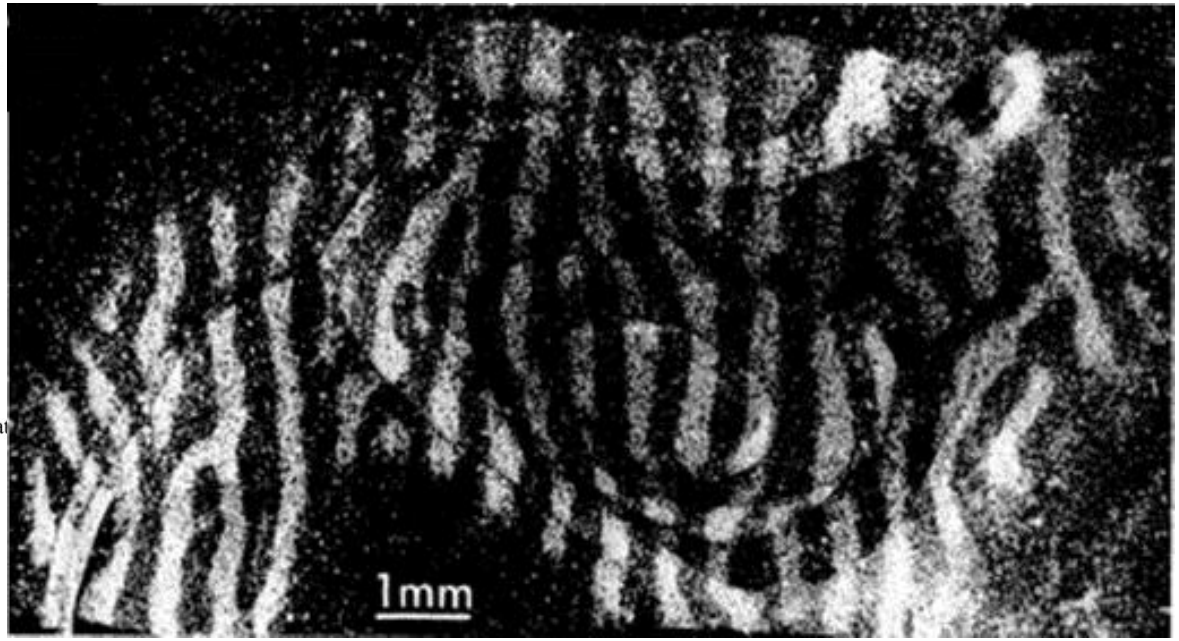
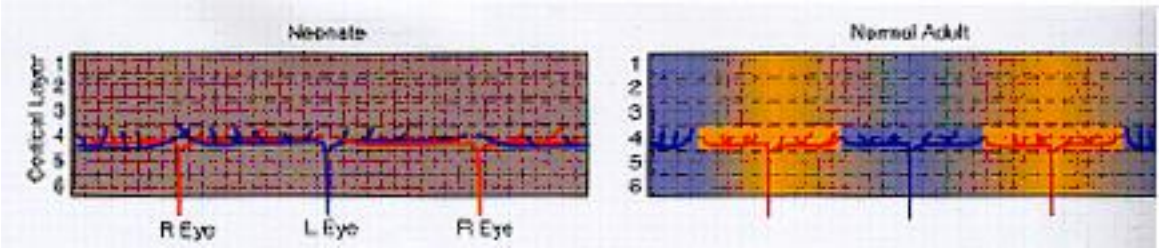




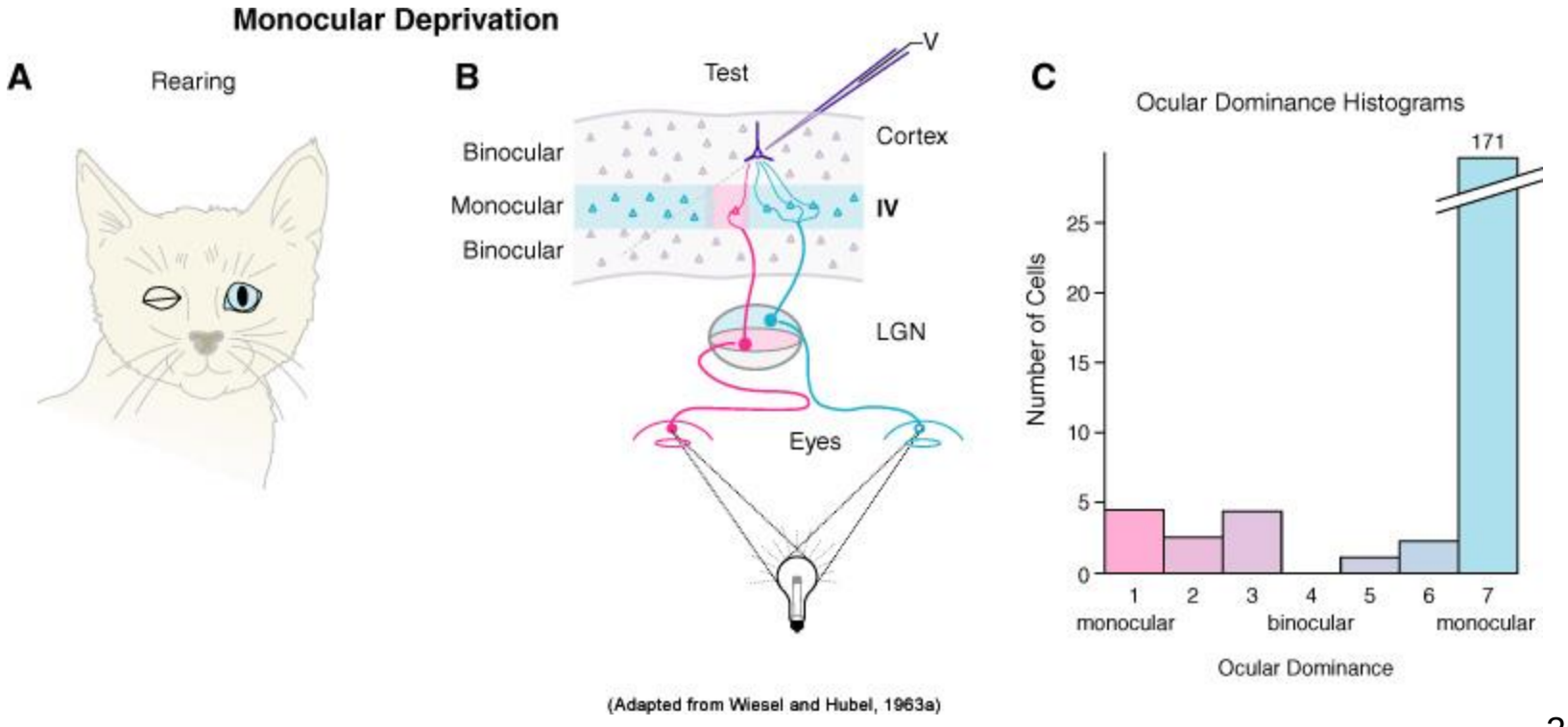
Visual experience drives development of visual cortex circuitry.

- Initially during development, the input from the two eyes overlaps in layer IV.
- Blocking activity prevented segregation of the ocular dominance columns.



Visual experience drives development of visual cortex circuitry.

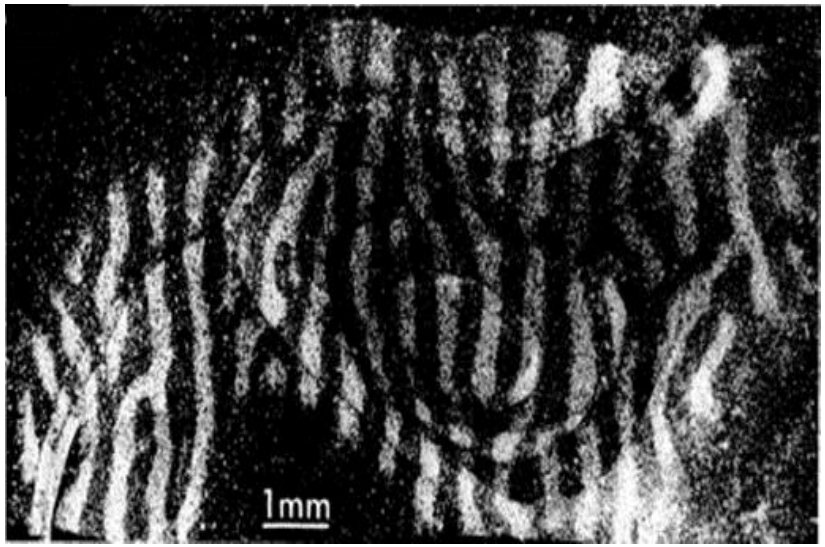
- Changing the nature of the visual activity during the "critical period" of development changes the refinement:
  - Monocular lid suture resulted in the open eye having larger columns and the closed eye having smaller columns in layer IV of visual cortex.



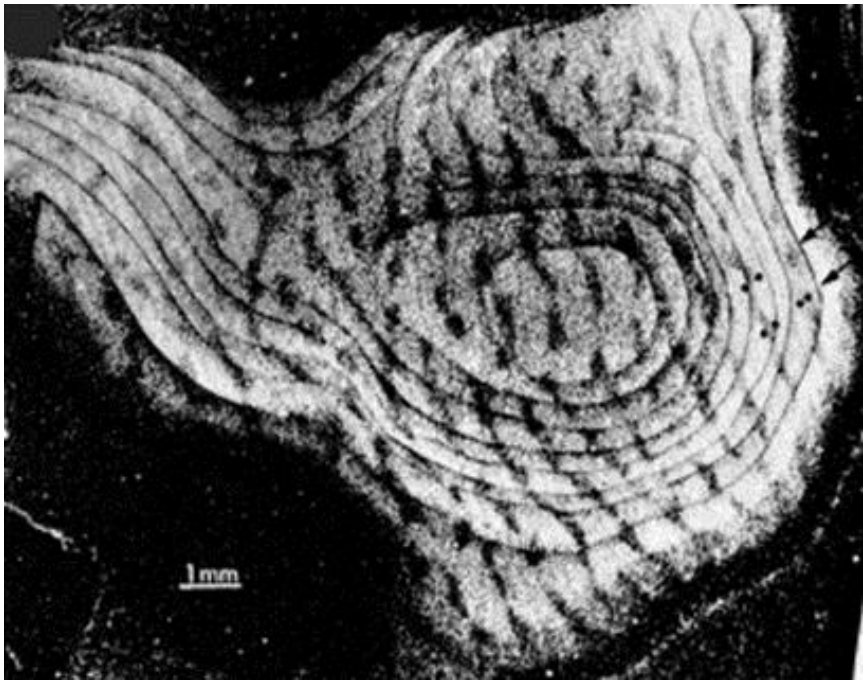
(Adapted from Wiesel and Hubel, 1963a)

Visual experience drives development of visual cortex circuitry.

normal

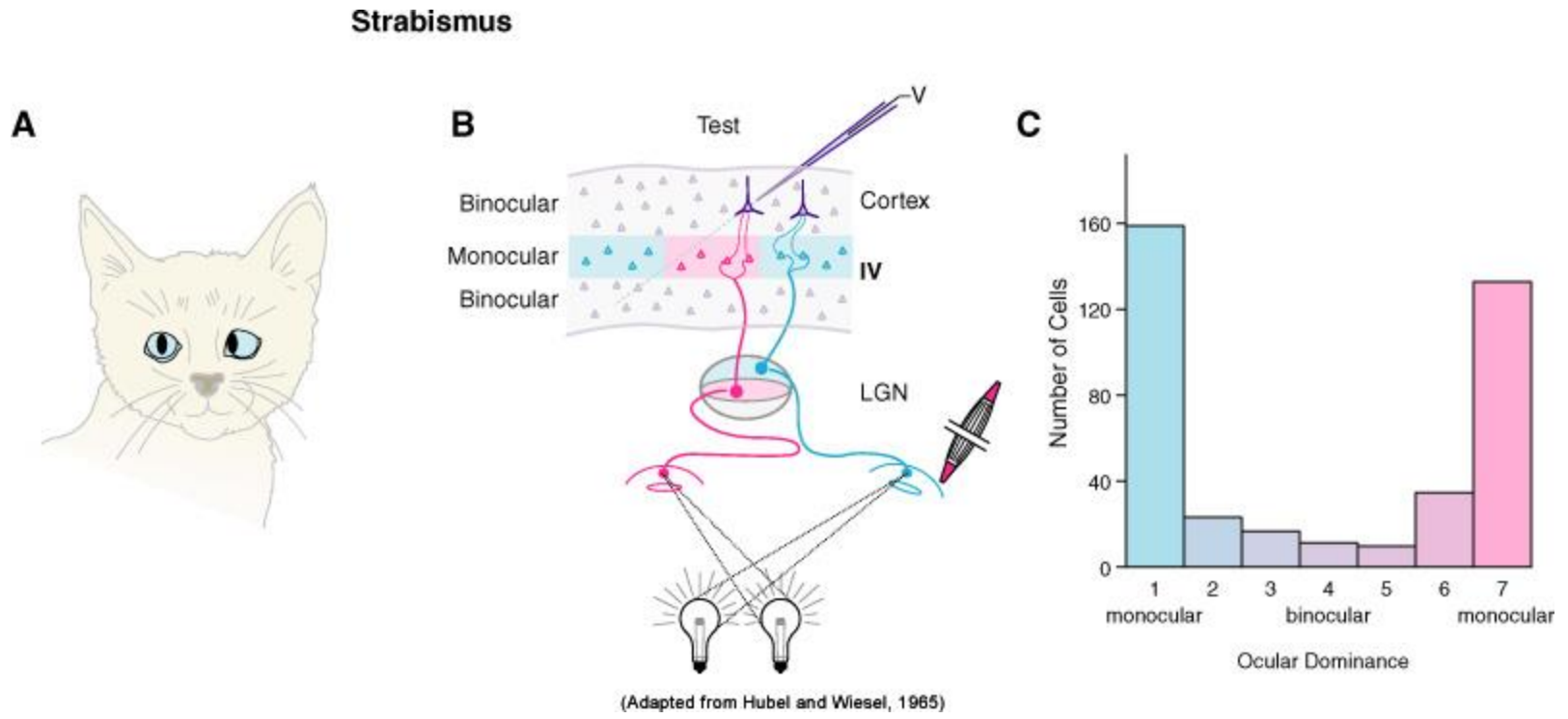


monocular deprivation



Visual experience drives development of visual cortex circuitry.

- Changing the nature of the visual activity during the "critical period" of development changes the refinement:
  - Induced strabismus (amblyopia) resulted in all layers being monocular.



(Adapted from Hubel and Wiesel, 1965)

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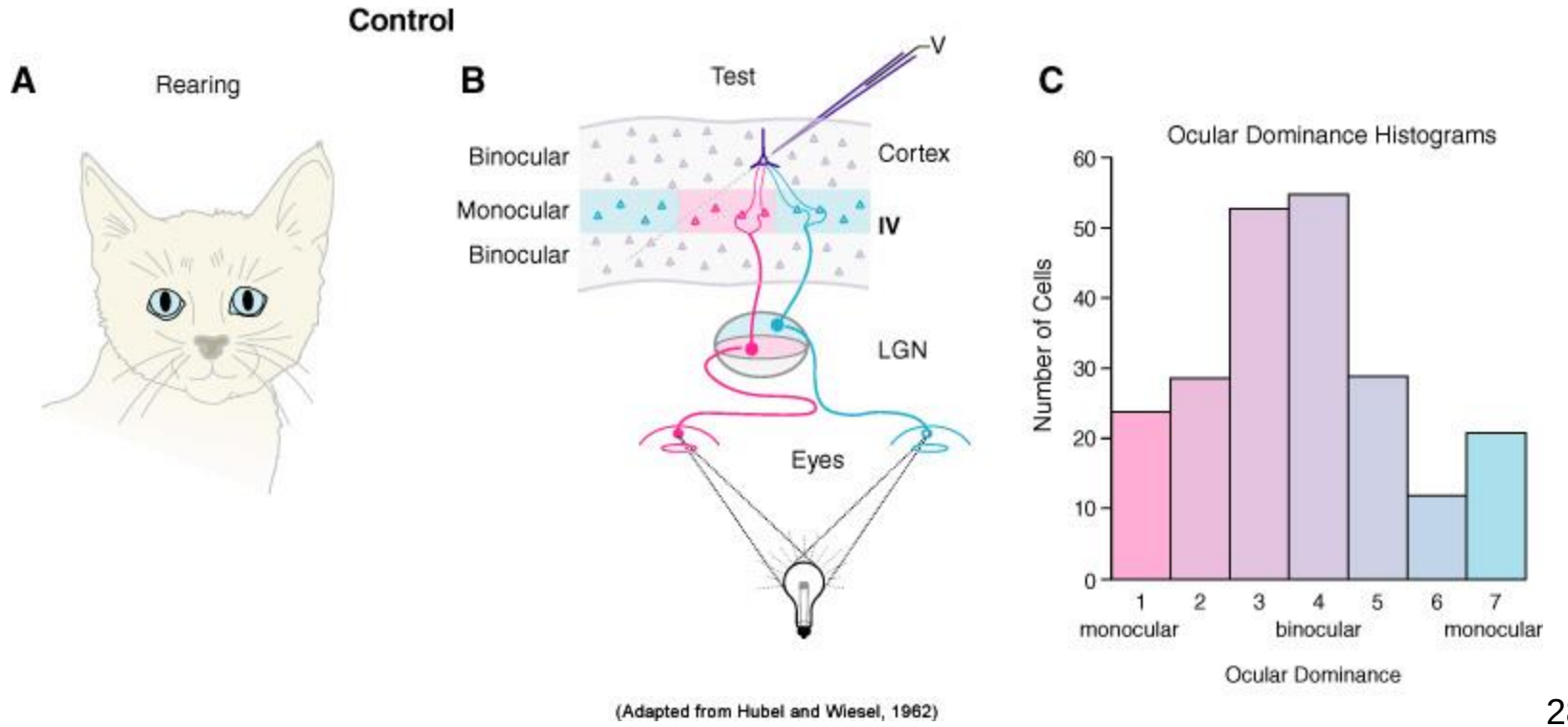


(Adapted from Hubel and Wiesel, 1962)

Visual experience drives development of visual cortex circuitry.

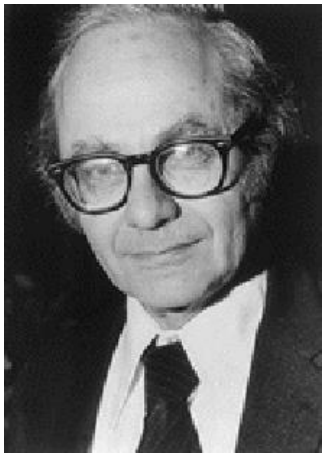
- Ocular dominance column experiments:
  - TTX into one eye during the critical period resulted in the projection for other eye becoming dominant.
  - TTX into one eye during critical period and suturing the other eye resulted in the sutured eye becoming dominant.
  - TTX into both eyes during critical period froze development.
  - TTX into both eyes and stimulating both optic nerves simultaneously resulted in no ocular dominance columns developing.
  - TTX into both eyes and stimulating both optic nerves in an alternating sequence resulted in ocular dominance columns developing.

Rules of Refinement

- Presynaptic activity drives refinement.
- In competition between two axon populations for synaptic sites, the more active population keeps synapses, and the less active population loses synapses.
- Axons that fire together wire together.
- Before refinement, the predominant inputs to a target cell arise from neighboring cells. Neighboring cells will have the same activity. After refinement, all inputs to a target cell arise from neighboring cells.

Visual experience drives development of visual cortex circuitry.

- David Hubel & Torsten Wiesel received the Nobel Prize in Physiology & Medicine in 1981.



Have a fun, relaxing and safe Thanksgiving holiday!

Friends do not let friends (or anyone else) drink and drive!