Specificity of Synaptic Connections I (i.e. Target Selection by Axons)

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Course News

Coffee Hour

Monday, Nov 5, 8:30-9:30am

Surdyk’s Café in Northrop Auditorium

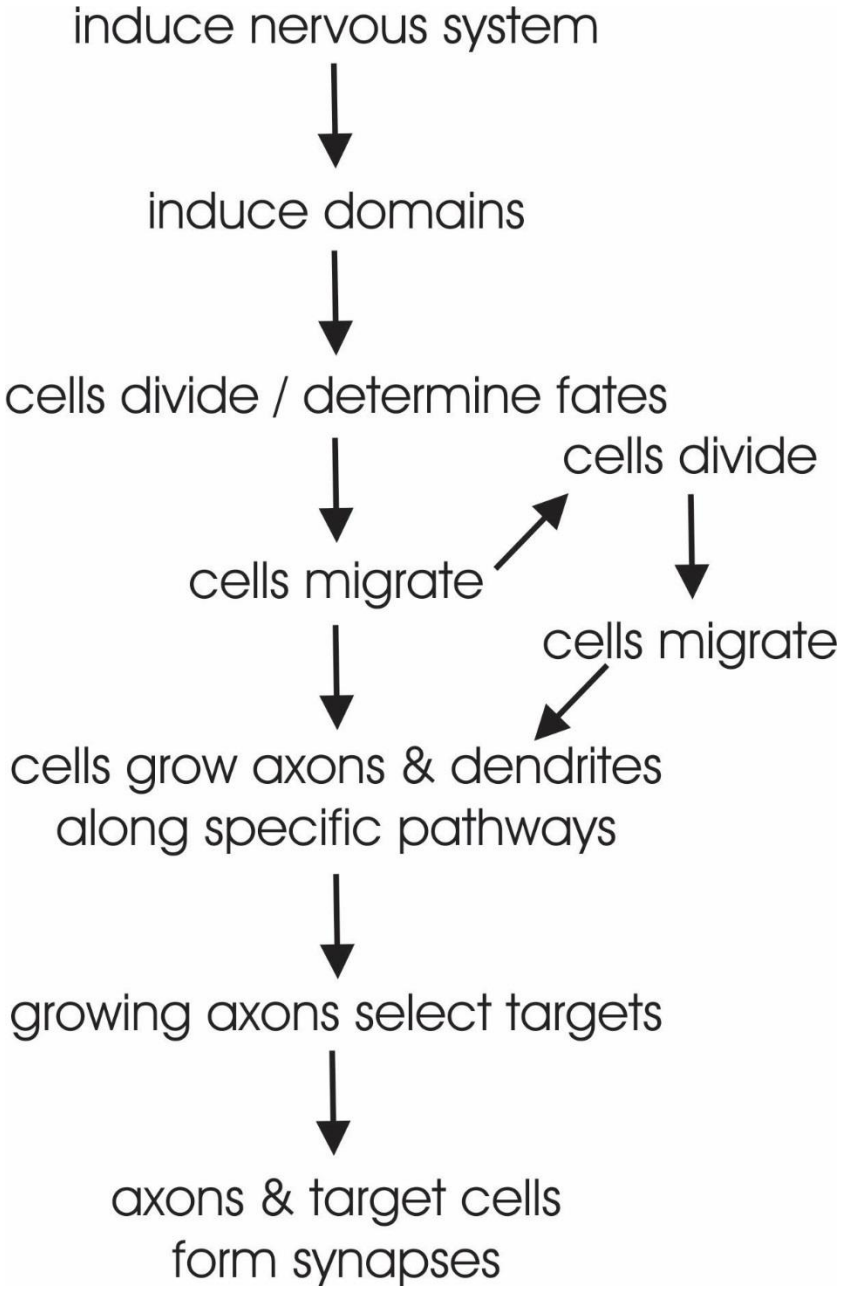
Stop by for a minute or an hour!

Course News

There will be no paper discussion next week.

The assigned paper will be covered on the next exam.

Everyone who participates in discussion #3
will get 3 points for discussion #2.


induce nervous system
induce domains
cells divide / determine fates
cells divide
cells migrate
cells migrate
cells grow axons & dendrites
along specific pathways
growing axons select targets
axons & target cells
form synapses

Specificity of Synaptic Connections

- An axon does not form connections with random cells but rather with a very specific cell or cells.
- The cell or cells with which an axon connects is dependent on the type and position of the cell giving rise to the axon.
- This phenomenon is referred to as the ‘specificity of connections’ or ‘neuronal specificity’.
- The cell(s) to which an axon connects/projects is called the ‘target’.

Levels of Target Specificity

Axons form synaptic connections with …

- a specific side of the body.
- specific cell populations.
- cells in a specific location within a population.
- specific cell types in a location.
- a specific part or region of a cell.

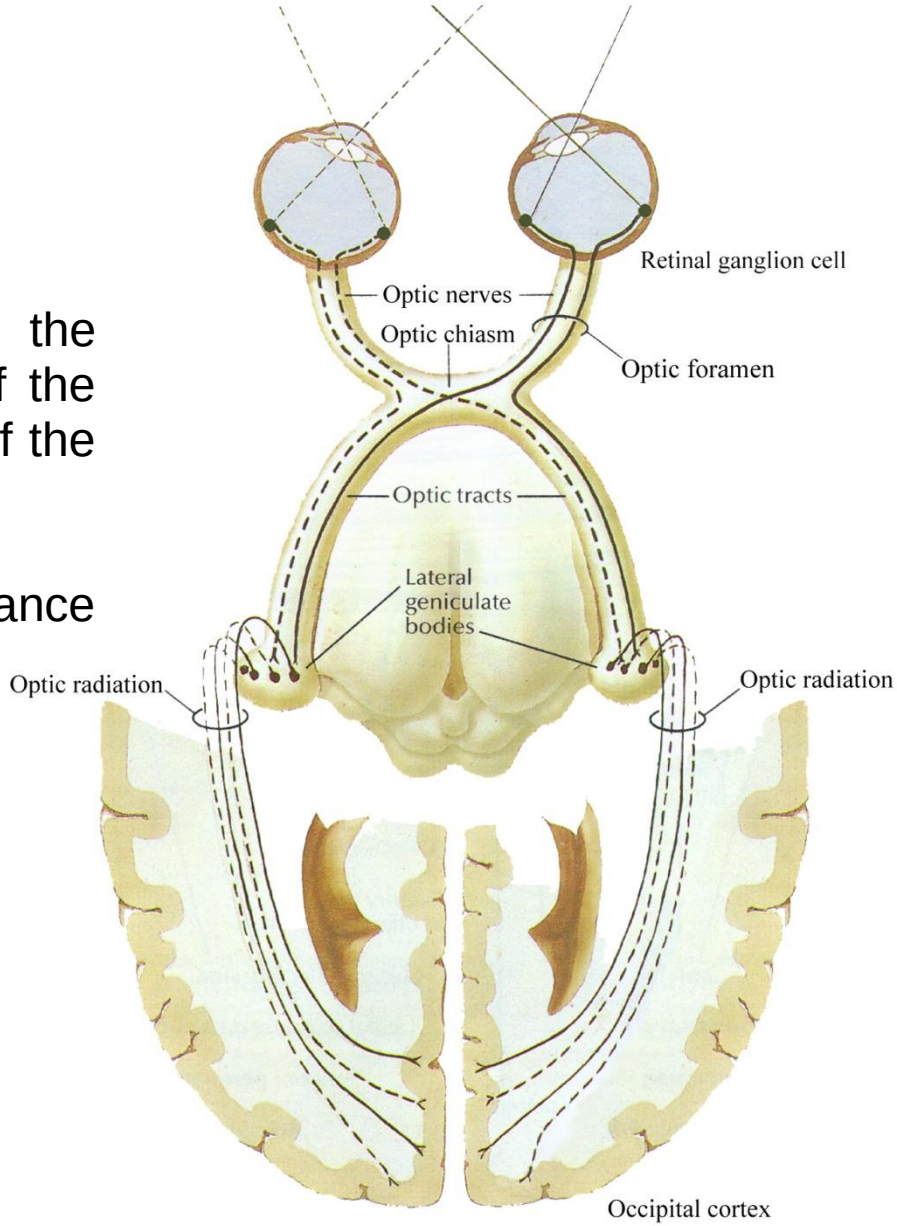
Levels of Target Specificity

Axons form connections with …

- a specific side of the body.

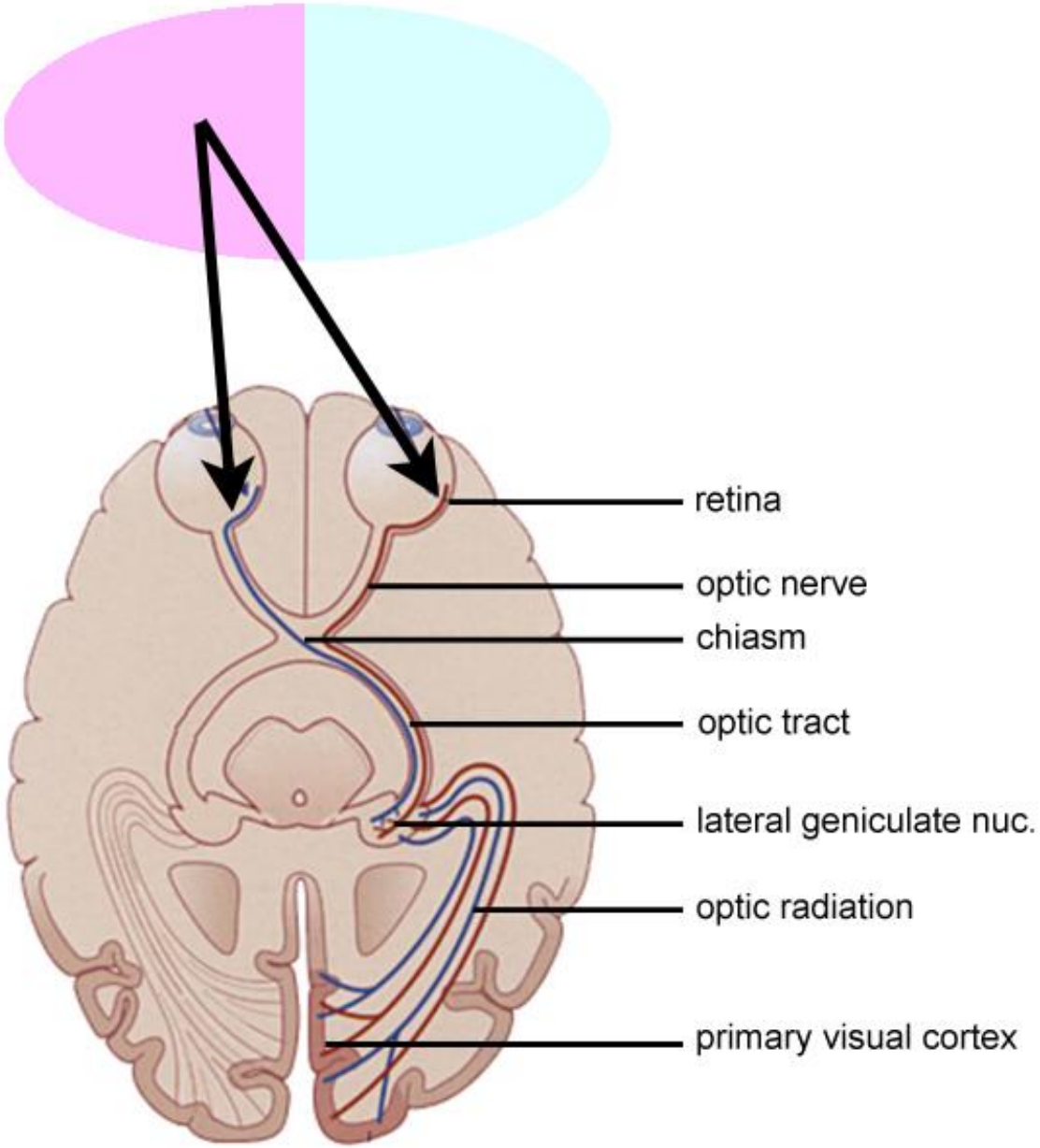
  e.g. Retinal axons connect to the ipsilateral or contralateral side of the brain depending on the position of the ganglion cells in the retina.

  This is determined by axon guidance mechanisms.



Central Visual Pathways

- The right visual hemifield from both eyes goes to the left side of the brain.
- The left visual hemifield from both eyes goes to the right side of the brain.

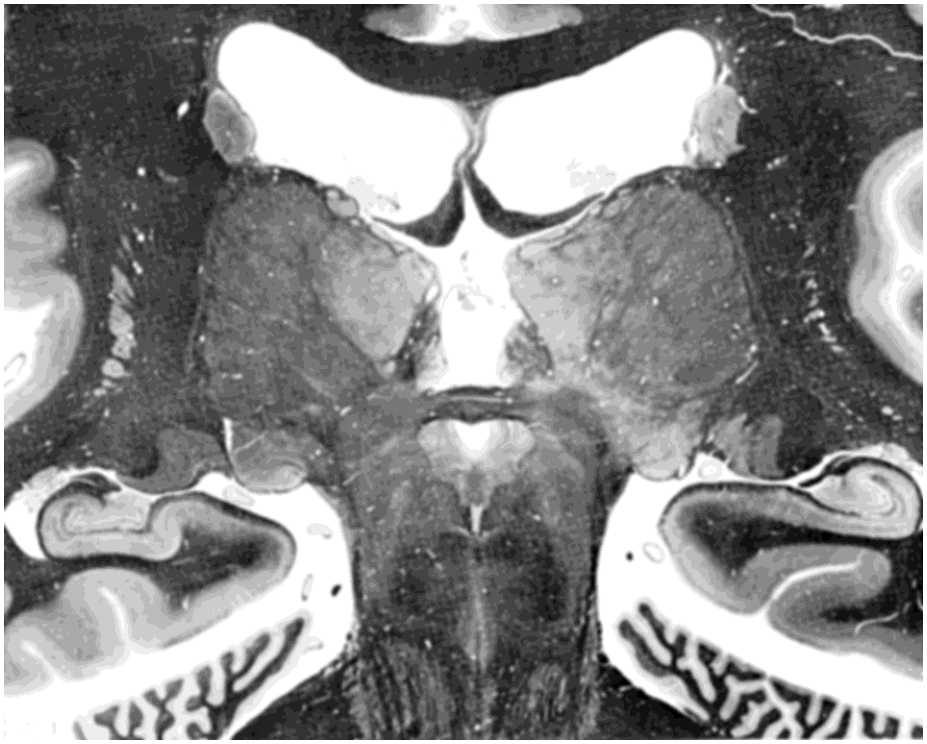


Levels of Target Specificity

Axons form connections with …

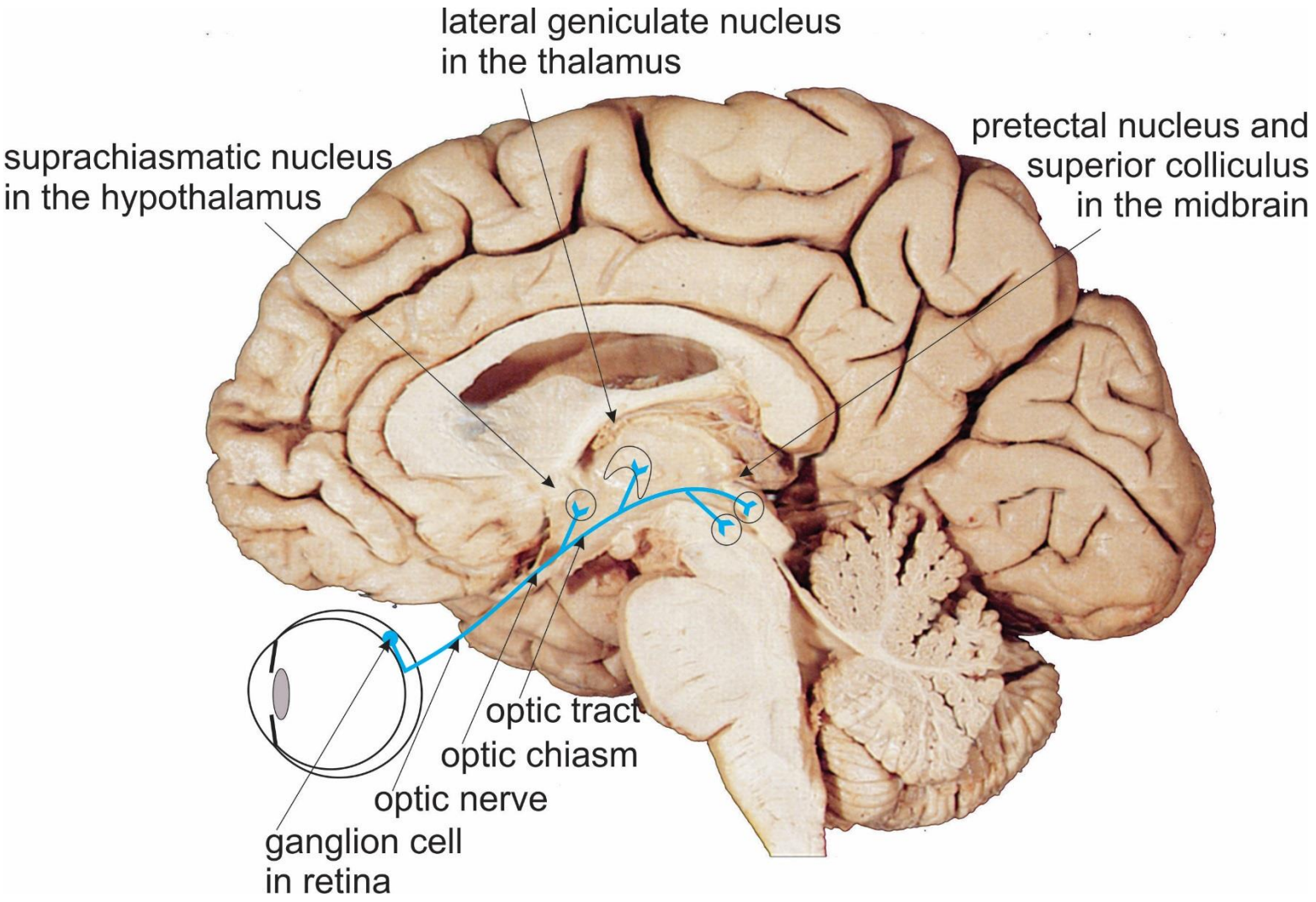
- specific cell populations.
  (e.g. particular nuclei in the brain)

  e.g. Retinal axons grow in the optic tract past numerous nuclei and select only certain ones in which to enter and form synaptic connections.



Central Visual Pathways

- Retinal axons synapse in several visual centers in the brain.

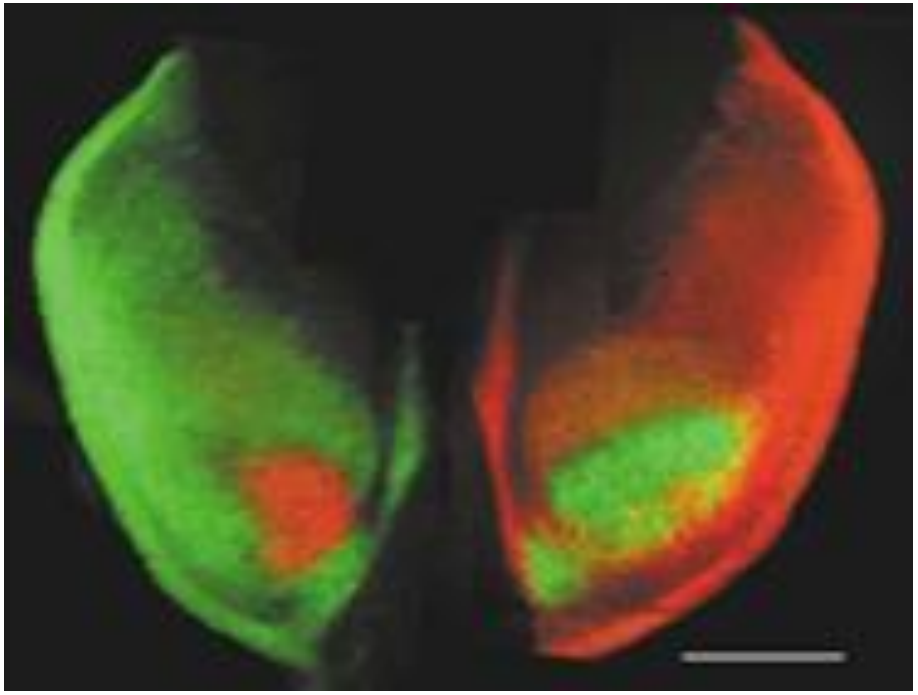


Levels of Target Specificity

Axons form connections with …

- cells in a specific location within a population.

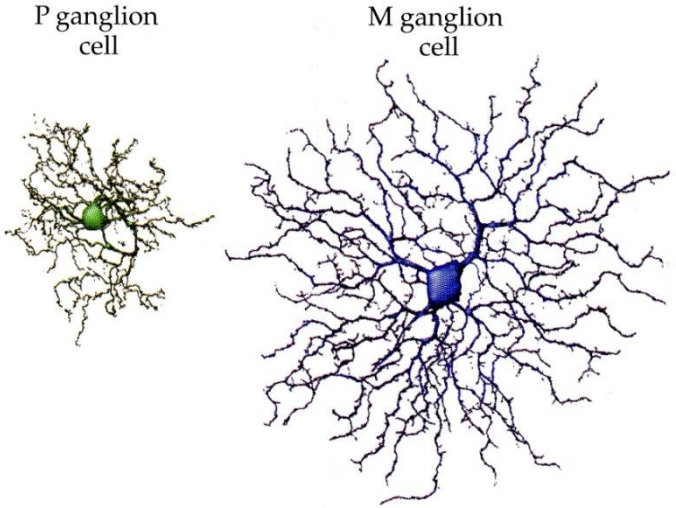
  e.g. Retinal axons from the ipsilateral and contralateral eyes connect to distinct regions of the central visual nuclei.

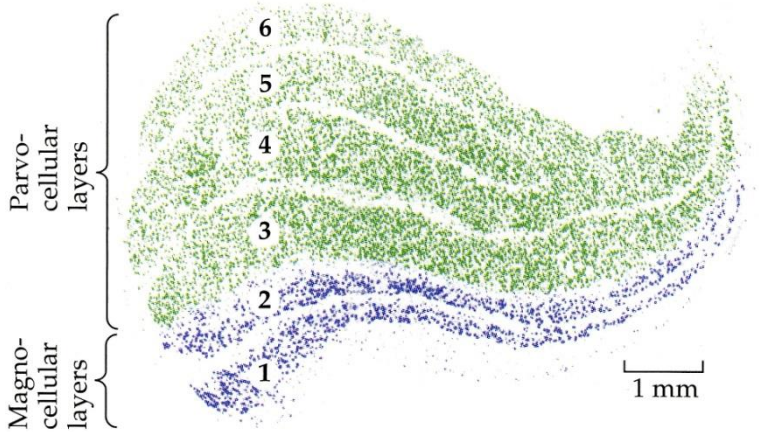


Projection from left (red) and right (green) eyes to the right and left lateral geniculate nuclei in mouse.

Central Visual Pathways

- The human lateral geniculate nucleus (LGN) has six cell layers.
- Axons from the two eyes synapse in different layers. (i.e. Cells in the LGN are monocular.)
- M and P ganglion cells also synapses in different layers of the LGN.





Levels of Target Specificity

Axons form connections with …

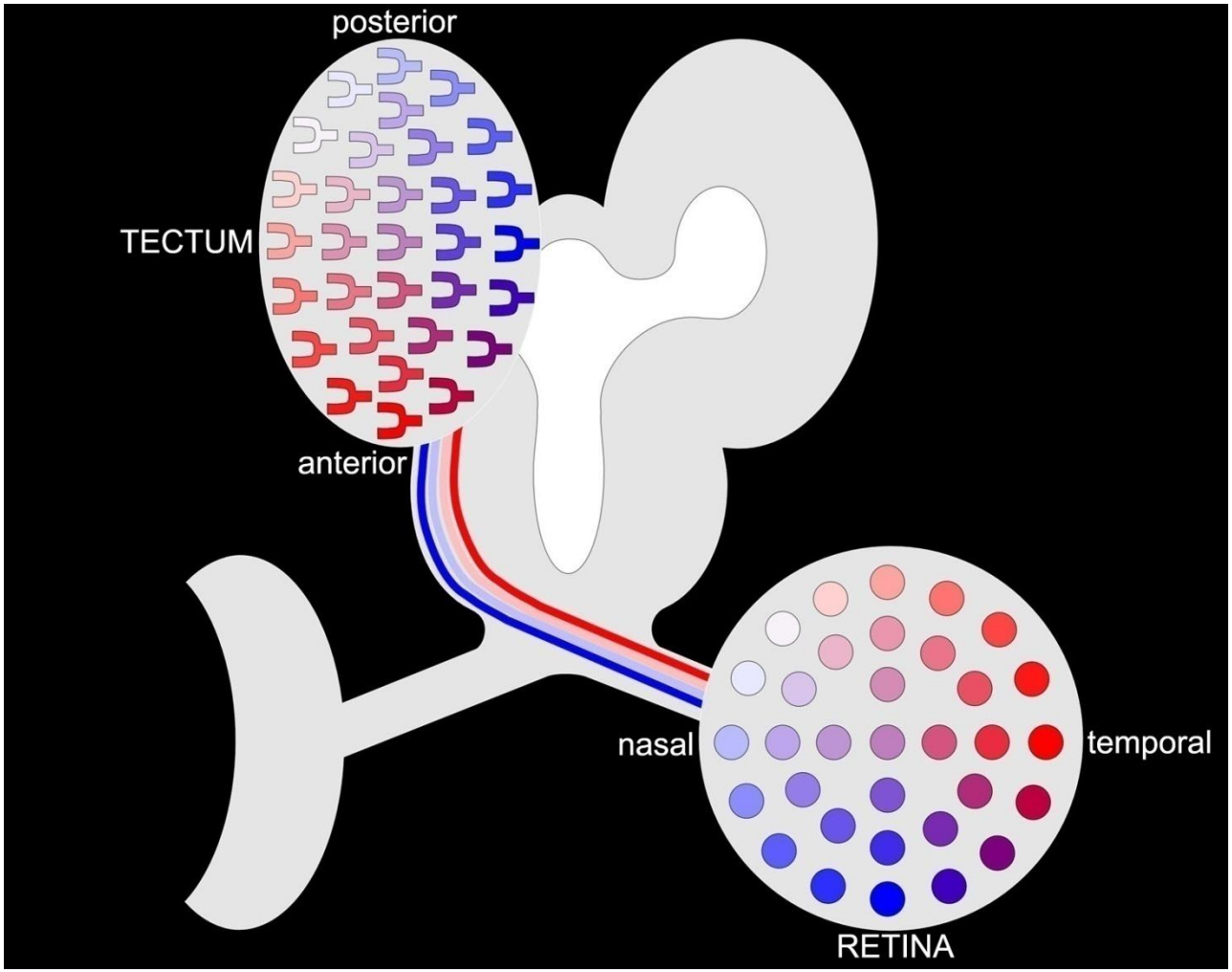
- cells in a specific location within a population.

  Typically, the spatial distribution of cells in a group is recreated in the pattern of their synapses.

  (topography of the projection; topographic projection)

Levels of Target Specificity

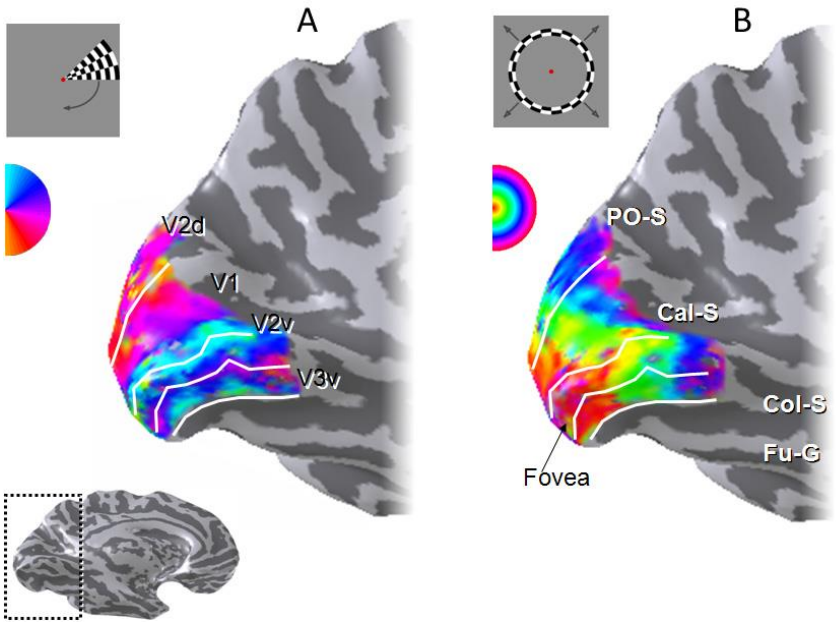
- e.g. Retinotopic projection

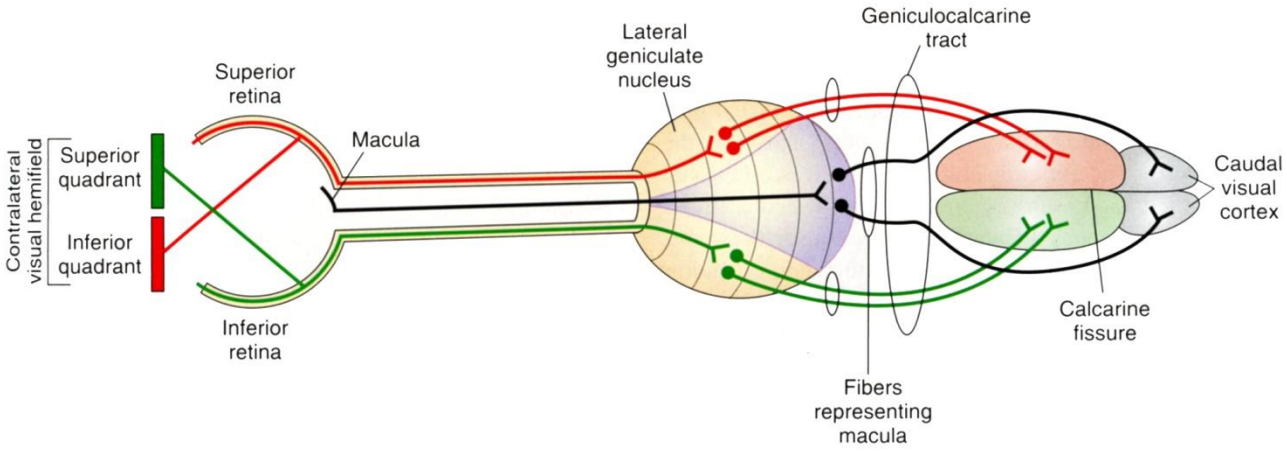


Central Visual Pathways

- The two dimensional distribution of the ganglion cells across the retina is maintained in the organization of the axons and connection through the entire pathway… retinotopic organization.

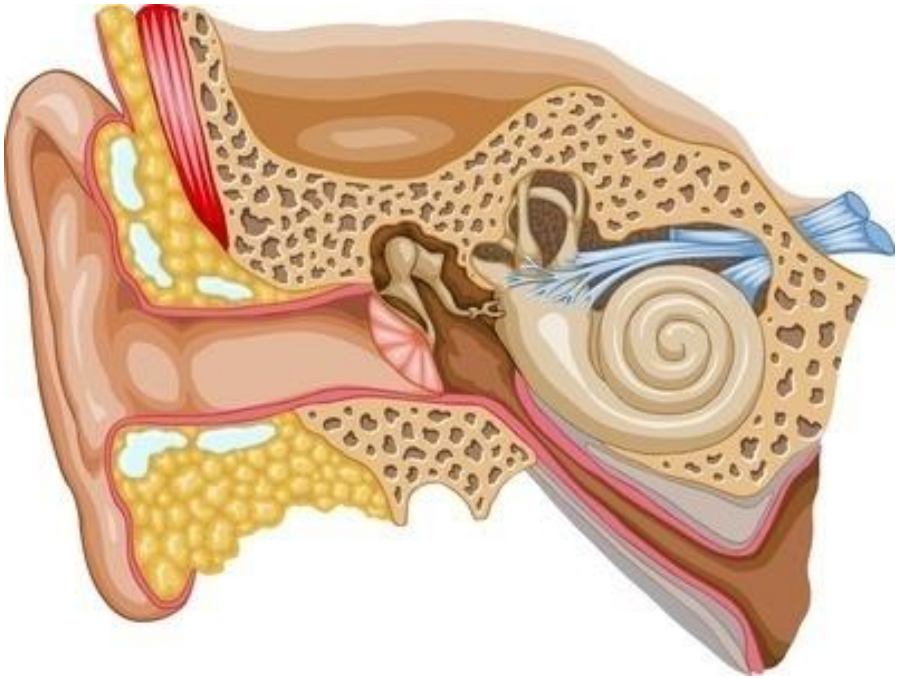
- The macula has the largest representation at all levels of the pathway.

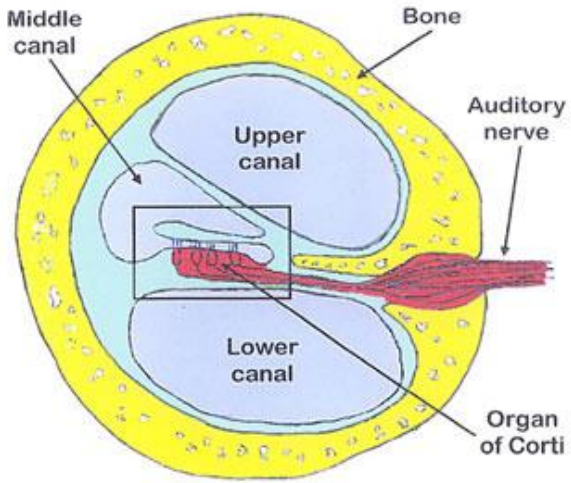


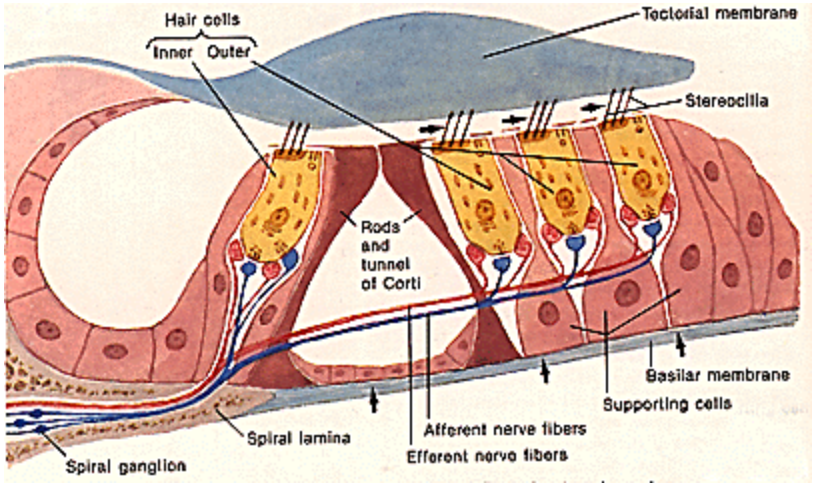


Levels of Target Specificity

- Tonotopic projection

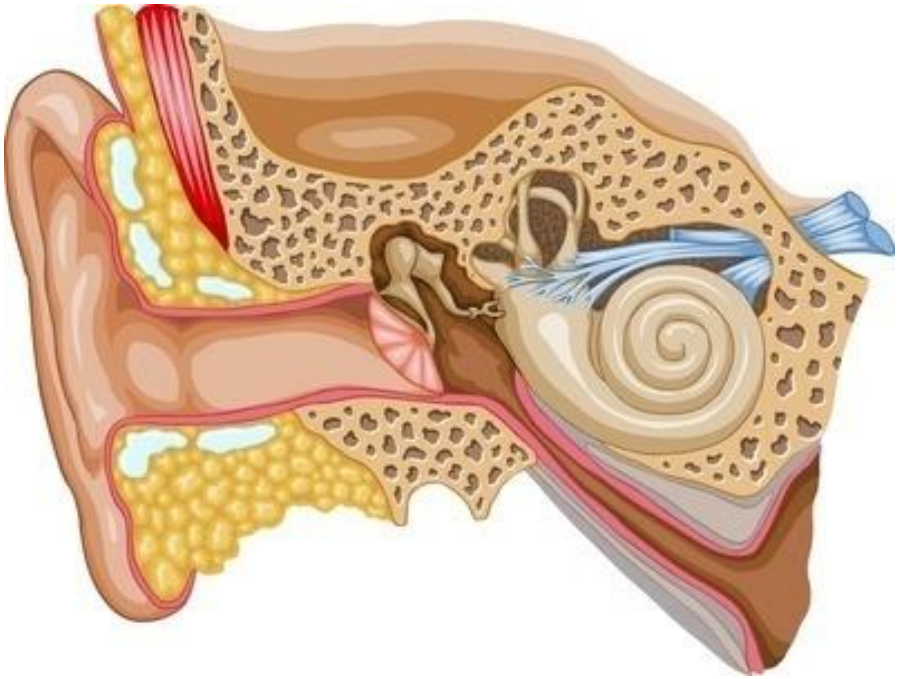


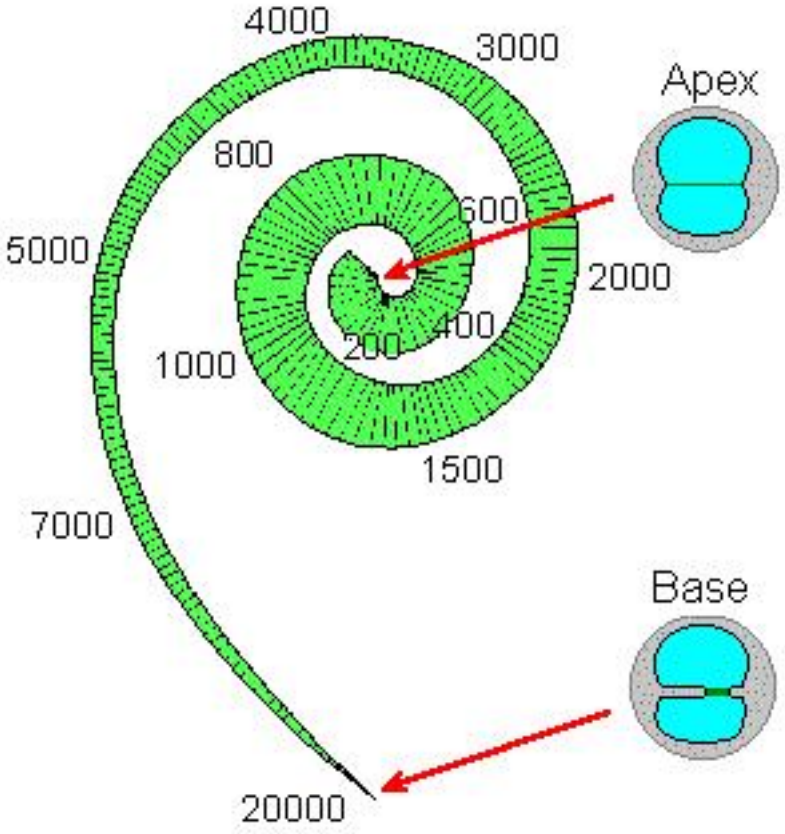




Levels of Target Specificity

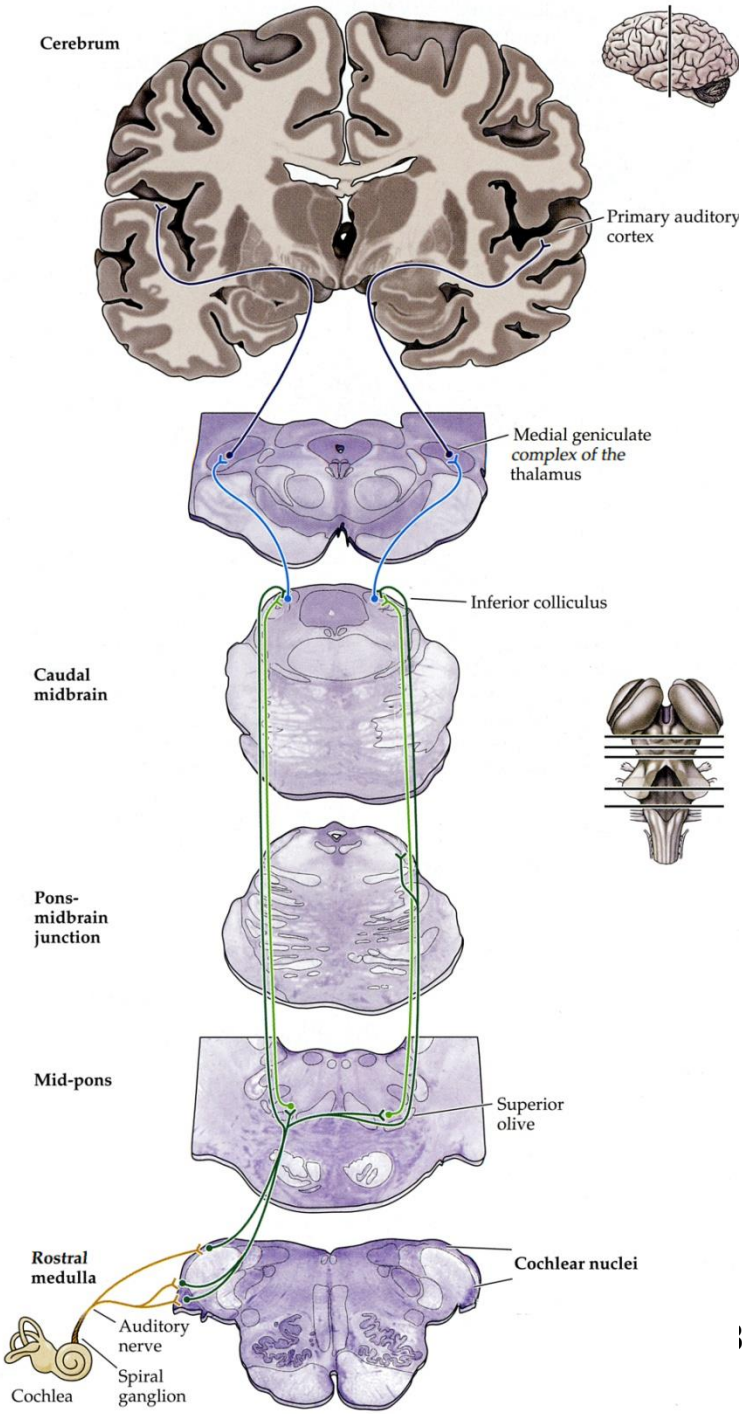
- Tonotopic projection





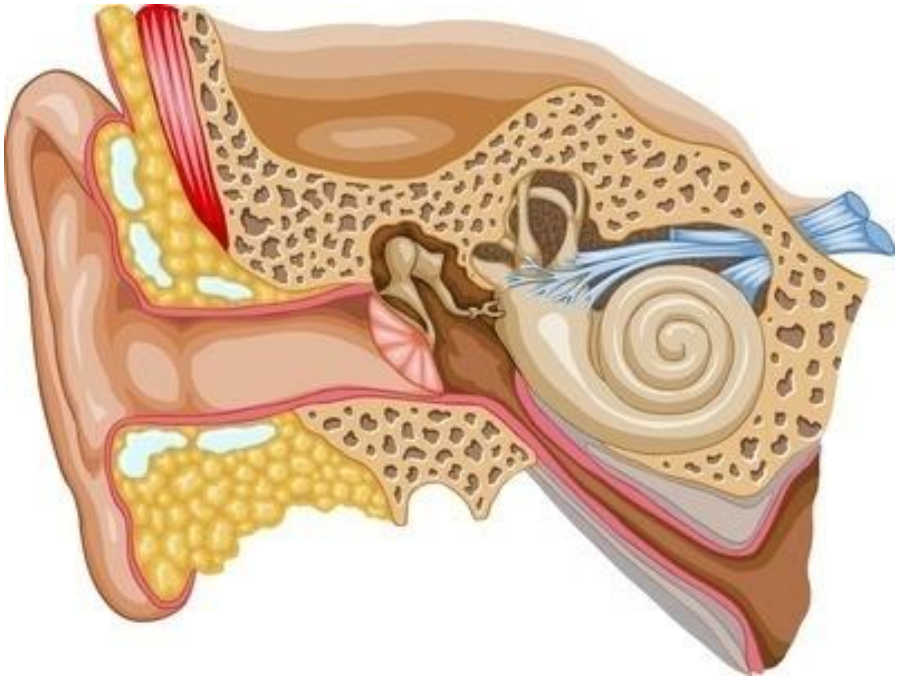
Auditory System

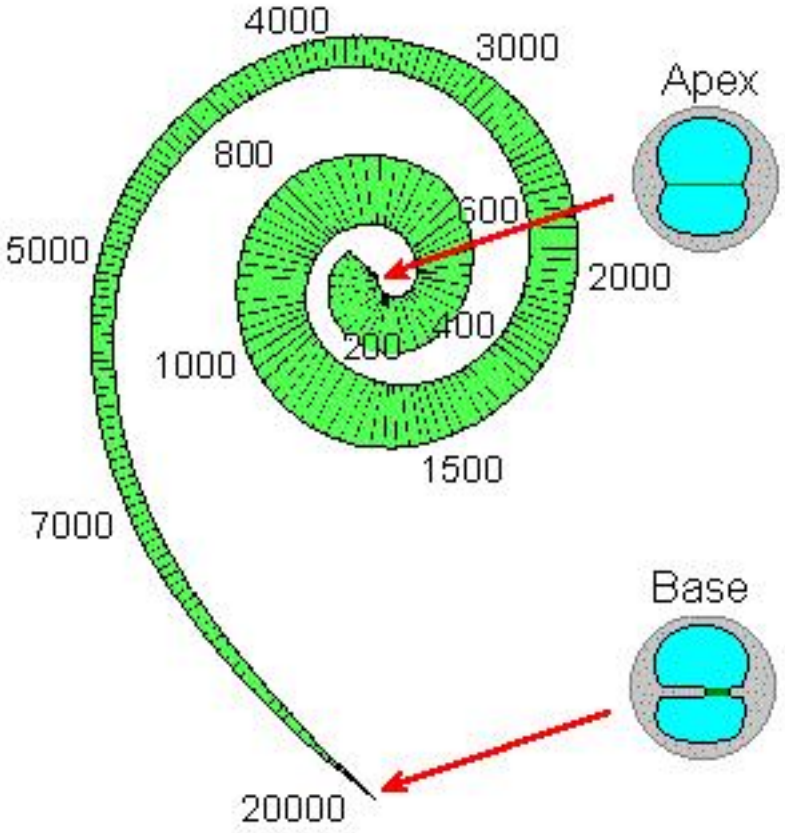
- Cochlear nerve axons synapse in the cochlear nuclei in the medulla.
- Neurons in the cochlear nuclei project bilaterally to the inferior colliculus (and other places).
- Neurons in the inferior colliculus project to the medial geniculate nucleus in the thalamus.
- Neurons in the medial geniculate project to primary auditory (A1) cortex in the temporal lobe.



Levels of Target Specificity

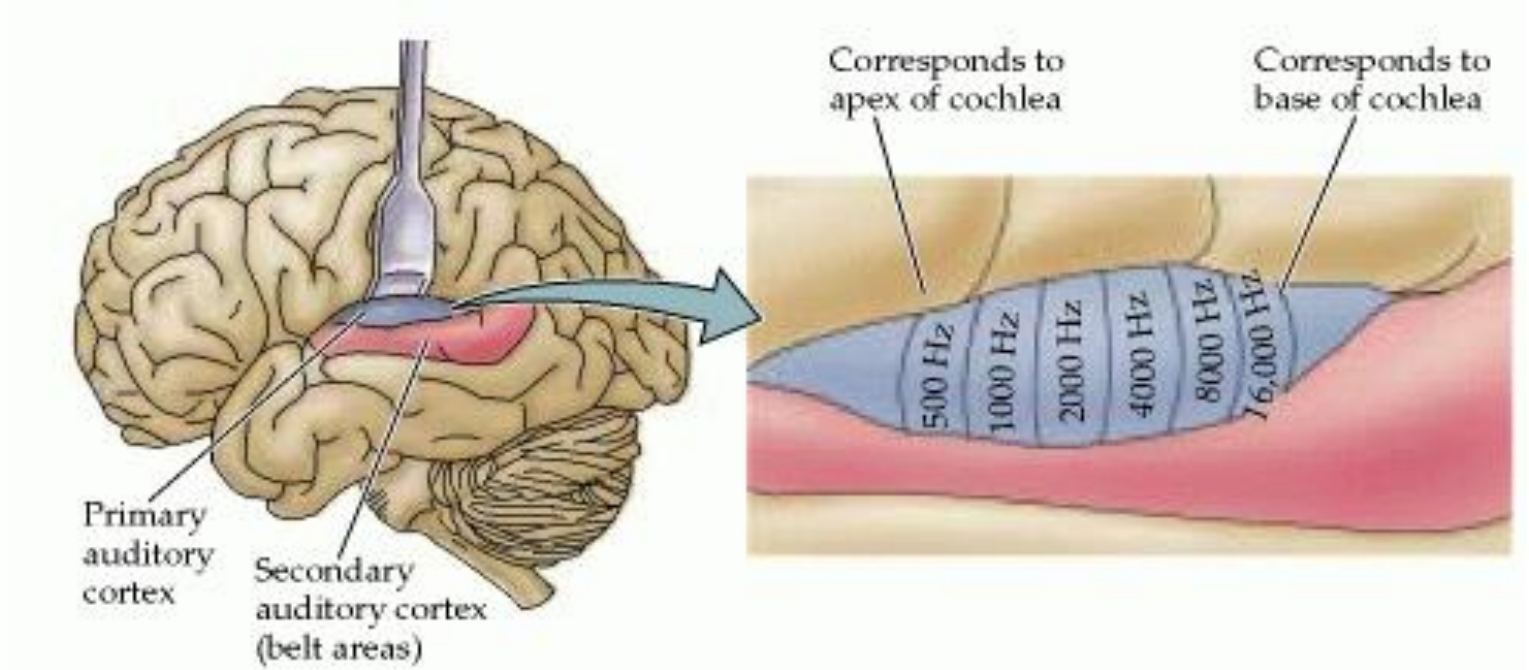
- Tonotopic projection





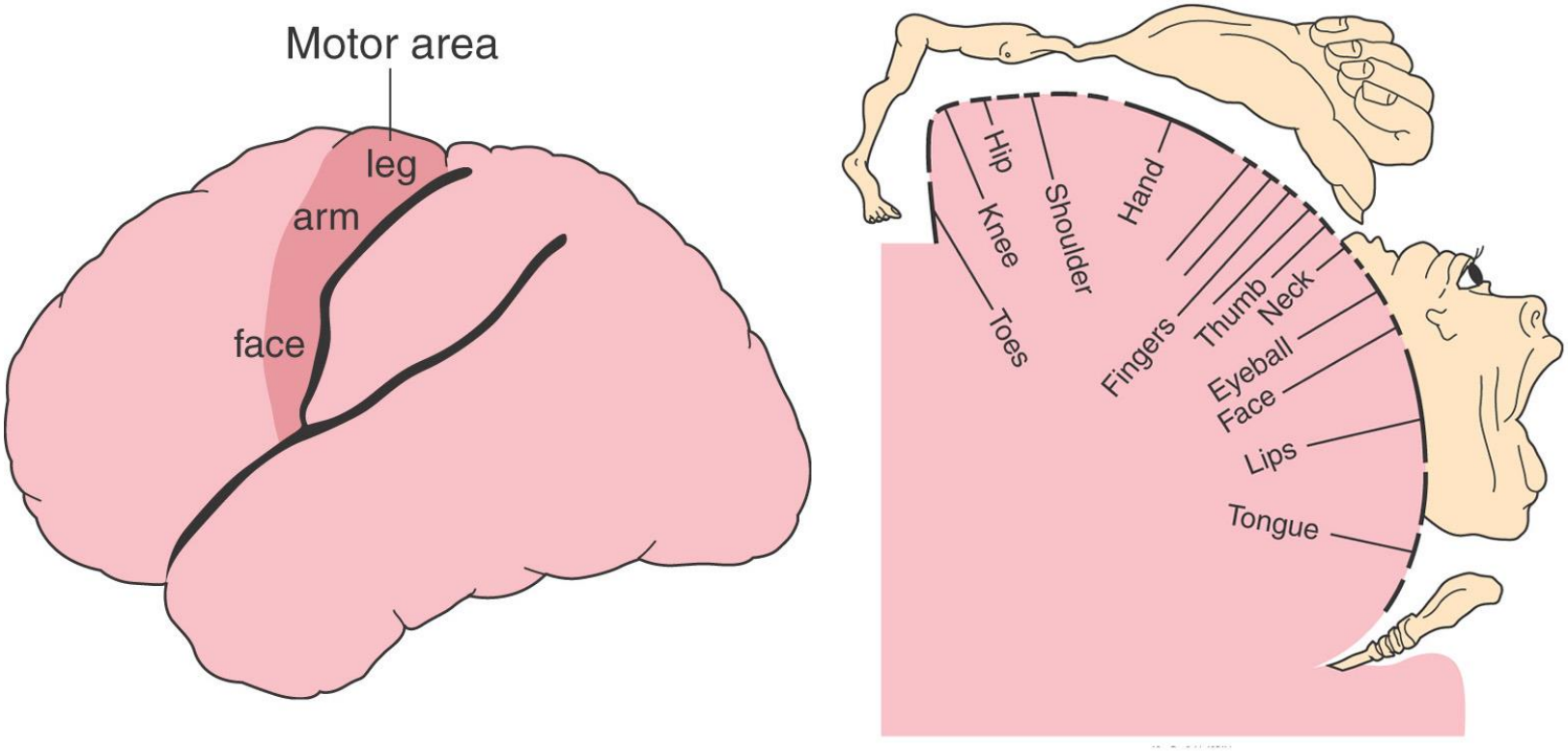
Levels of Target Specificity

- Tonotopic projection

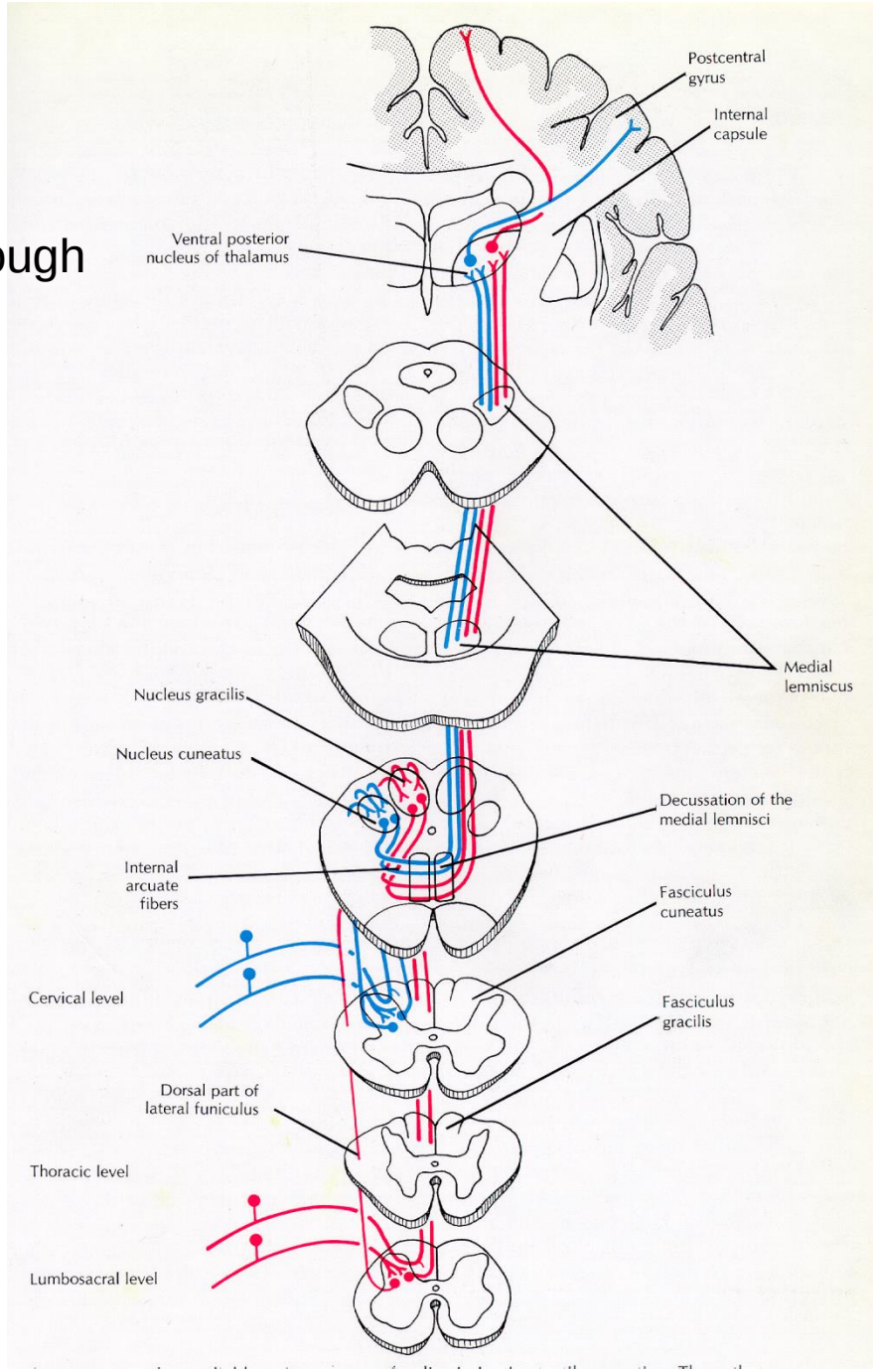


Levels of Target Specificity

- Somatotopic projection
  (motor and somatosensory homunculus)

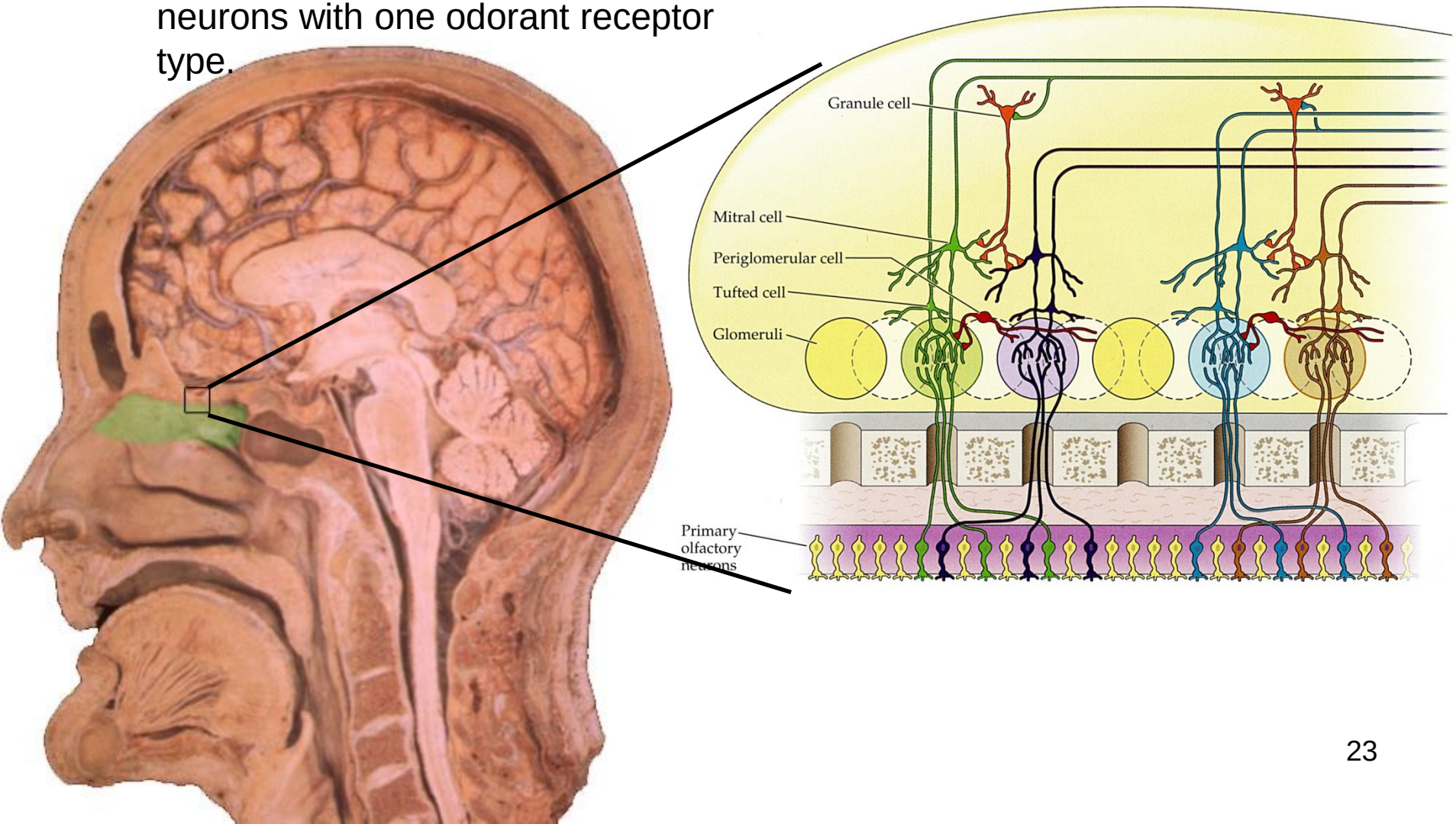


- Topography is maintained through multiple levels in a system.



The olfactory map is functional, not spatial.

- Axons synapse in glomeruli. Each glomerulus receives input from neurons with one odorant receptor type.



The olfactory map is functional, not spatial.

- Olfactory receptor neurons express only one of approximately 1000 olfactory receptor proteins in rodents (339 in humans)

- Olfactory receptor neurons expressing the different receptor proteins are intermixed across the nasal epithelium.

- Receptor neurons expressing a single receptor protein typically project to two of ~2500 glomeruli in the olfactory bulb.

- Individual glomeruli only receive receptor axons expressing the same receptor protein.

Levels of Target Specificity

Axons form connections with …

- specific cell types in a location.

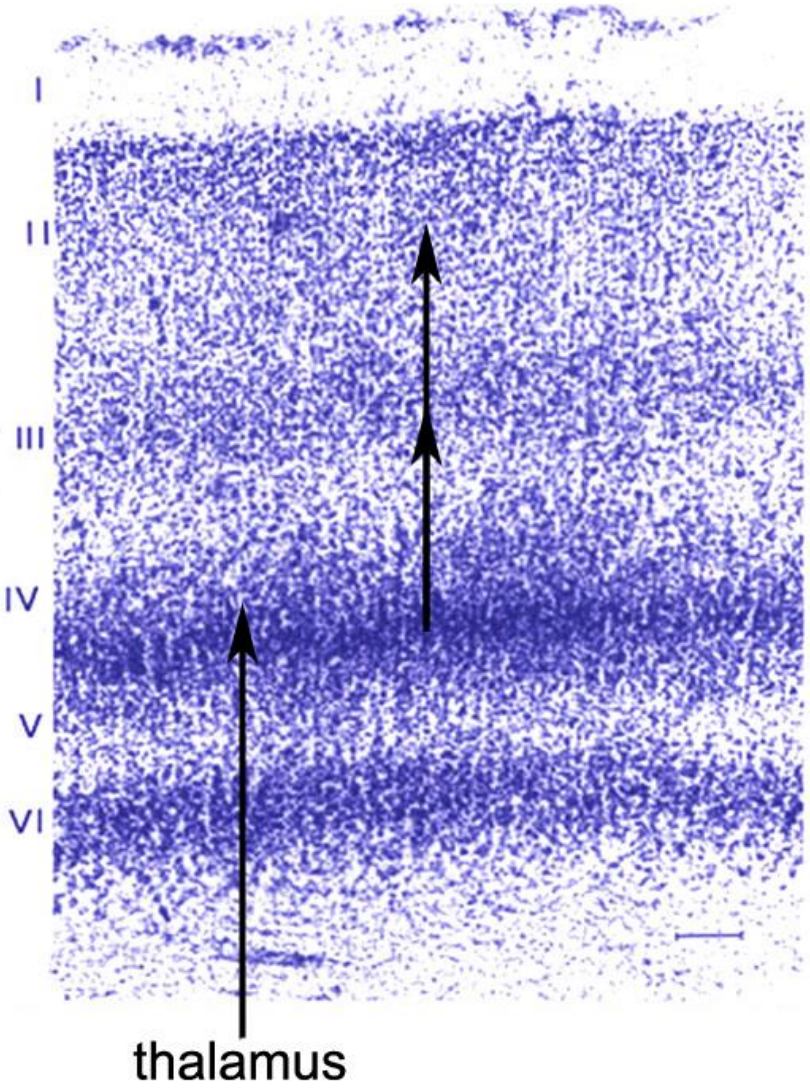
  Although there are typically multiple cell types in a target region, axons usually synapse with only one cell type.

Levels of Target Specificity

Axons form connections with … specific cell types in a location.

Axons connect with neurons, not with glia.

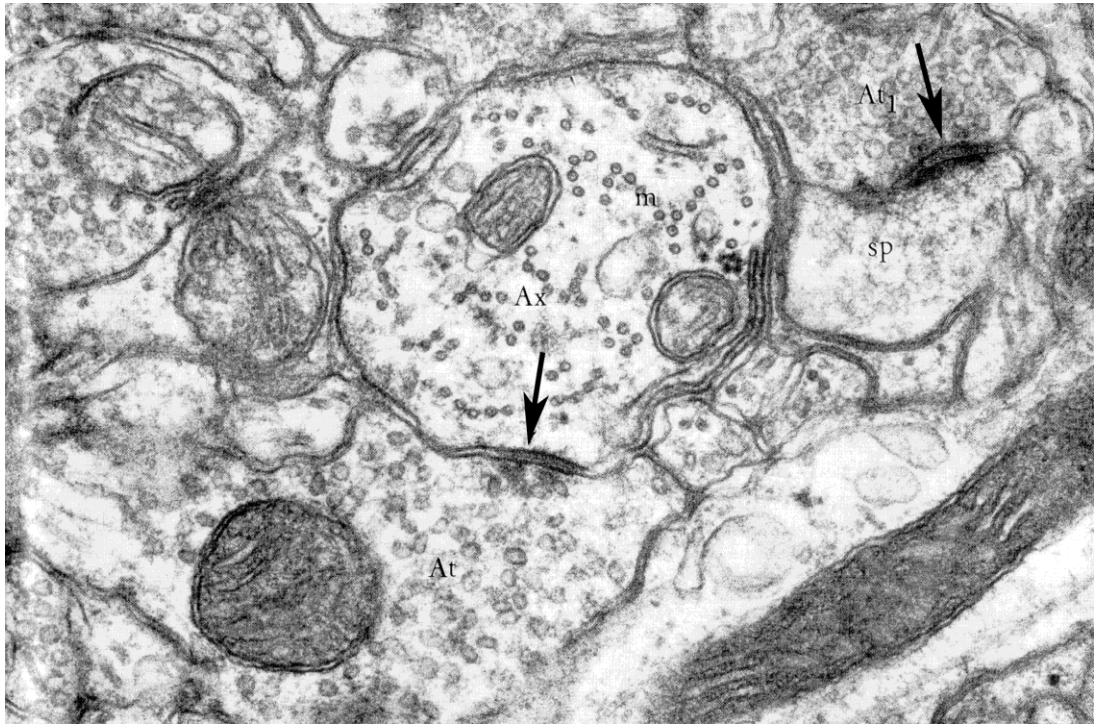
Some populations of axons project only to cells in specific layers of a tissue.
e.g. Thalamic neurons project to spiny stellate neurons in layer IV of neocortex.



Levels of Target Specificity

Axons form connections with …

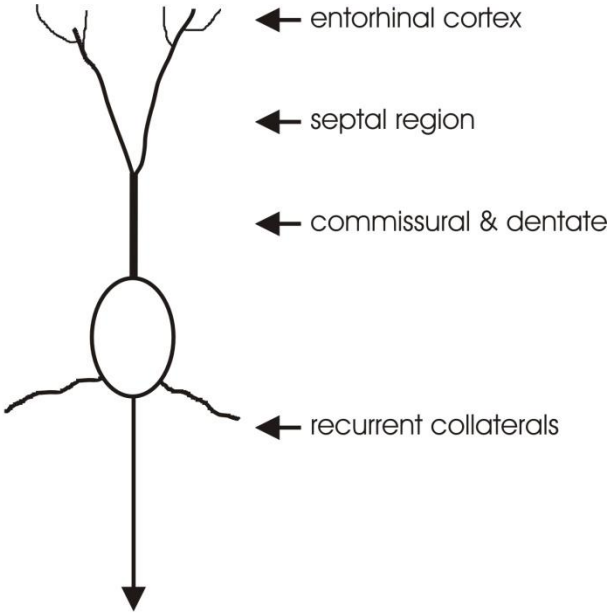
- specific part or region of a cell.
  - Axodendritic synapse (arrow on the right)
  - Axosomatic synapse
  - Axoaxonic synapse (arrow in the center)



Levels of Target Specificity

Axons form connections with …

- specific part or region of a cell.
  (e.g. certain distance on dendrite from cell body)



pyramidal neuron
in CA1 region of hippocampus

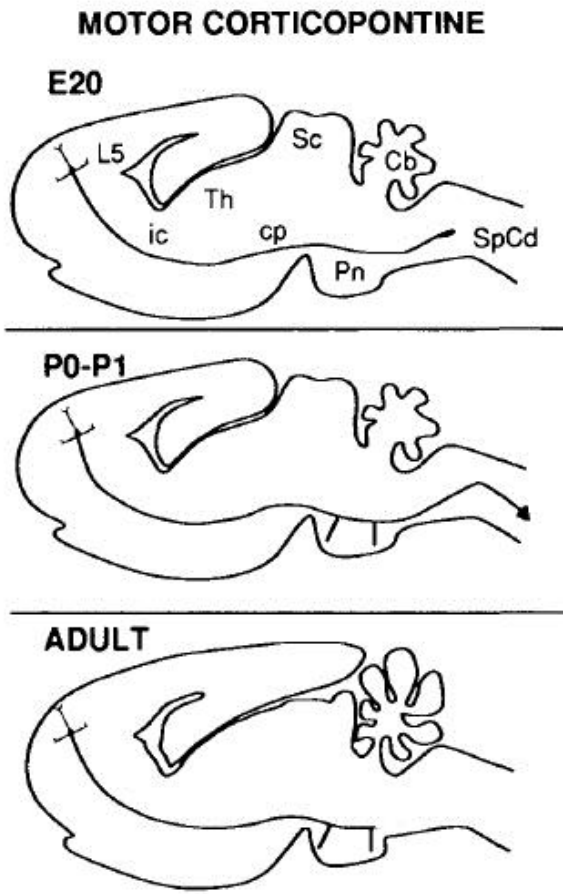
Possible Mechanisms Involved in Cell Population Specificity

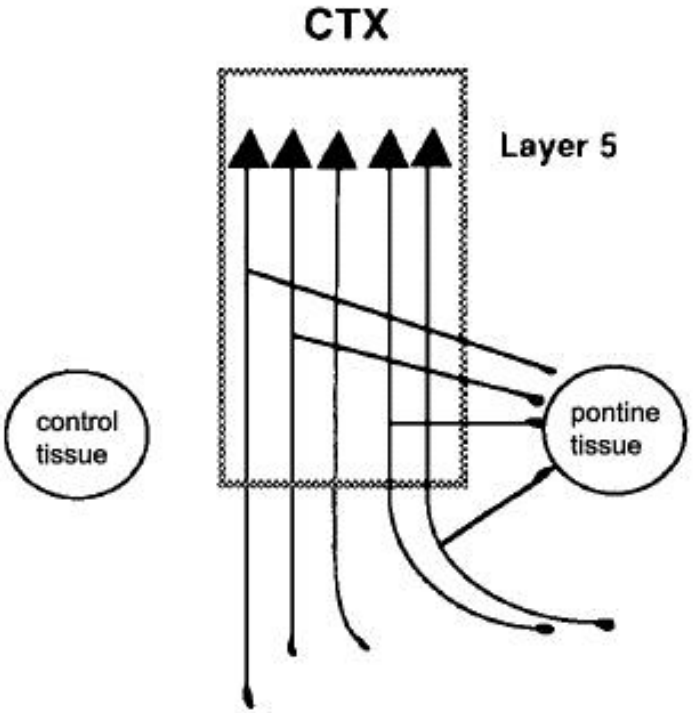
- Guidance of growing axons into proper pathway is essential.

Possible Mechanisms Involved in Cell Population Specificity

- Target cells can have a tropic effect on axons growing in nearby tract.

  e.g. Pontine cells attract branches of corticopontine axons.





Possible Mechanisms Involved in Cell Population Specificity

- Neurotrophins can act as a tropic factor.

  e.g. Glial Derived Neurotrophic Factor (GDNF) released from the epidermis attracts a certain population of sympathetic axons. These axons express GFRα1, the GDNF receptor.

Possible Mechanisms Involved in Cell Population Specificity

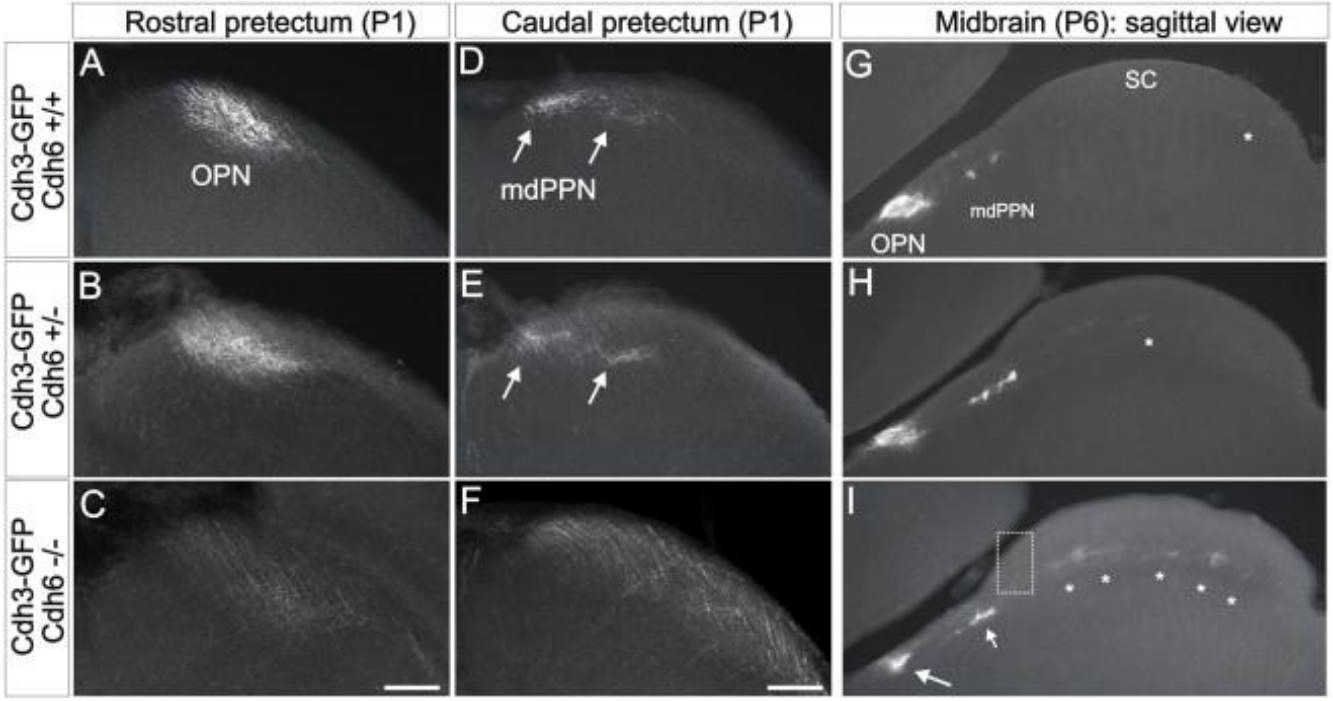
- ‘Error’ correction is also essential.

  Transient projections, that is projections present during development but not in the adult, are eliminated during development.

  retina → other eye
  wrong side of brain
  wrong nuclei: vpl, mgn, inf. coll.

Mechanisms Involved in Cell Population Specificity

- Cadherins have been implicated in nuclear specificity:
  - Connections of retinal ganglion cells to non-image forming nuclei were altered in cadherin-6 knockout mice.



(Osterhout et al., 2011)

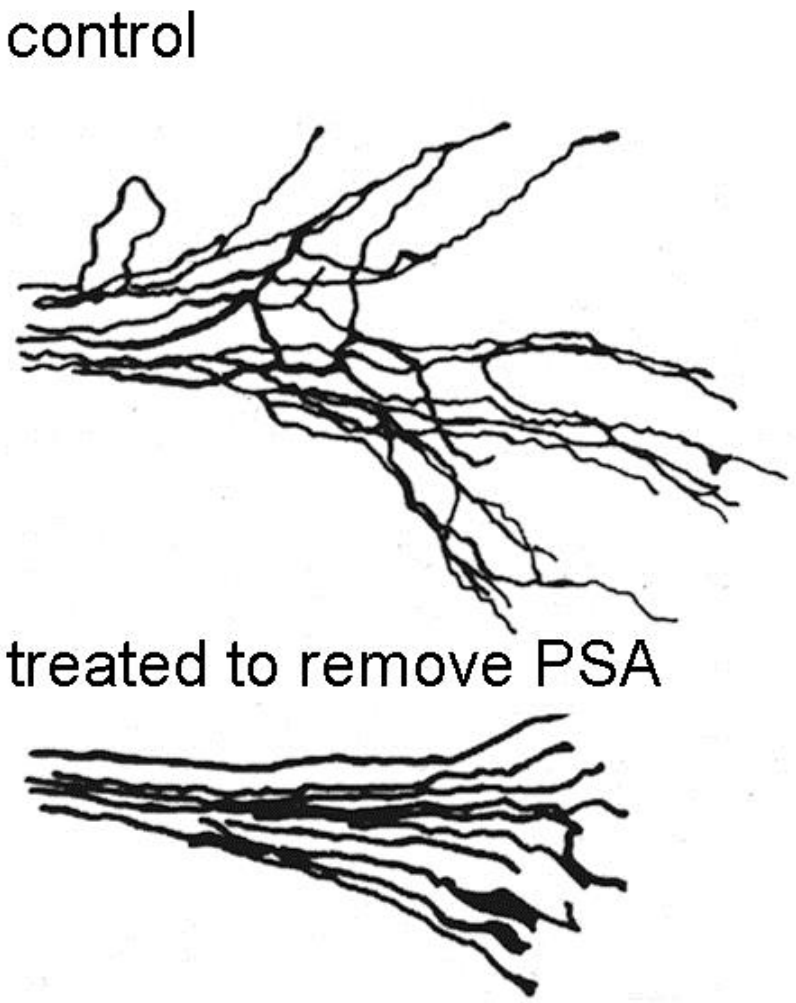
Axon growth changes within the target cell population.

- Axons grow in tracts mainly using adhesion to other axons (fasciculate).
- As axons enter their target cell population, they defasciulate and slow their growth.
- The target cell population initiates defasciculation – Eliminate the target cells, then axons do not defasiculate.
- Defasciculation is due to reduce adhesivity among axons.

Axon growth changes within the target cell population.

e.g. axons from motor neurons entering muscle:

- Motor axons defasciculate as they enter their target muscle.
- The amount of polysialic acid (PSA) bound to N-CAM & L1 on motor axons increases as they defasciculate.
- PSA reduces the adhesivity of N-CAM & L1.
- Removal of PSA from the axons increased fasciculation and reduced muscle innervation.



Axon growth changes within the target cell population.

e.g. retinal axons in developing frog:

- In the optic tract, retinal axons grow at 60 μm/hr.
- In the tectum, retinal axons grow at 16 μm/hr.

Axon growth changes within the target cell population.

- Retinal axon growth cones change as they slow in the target.