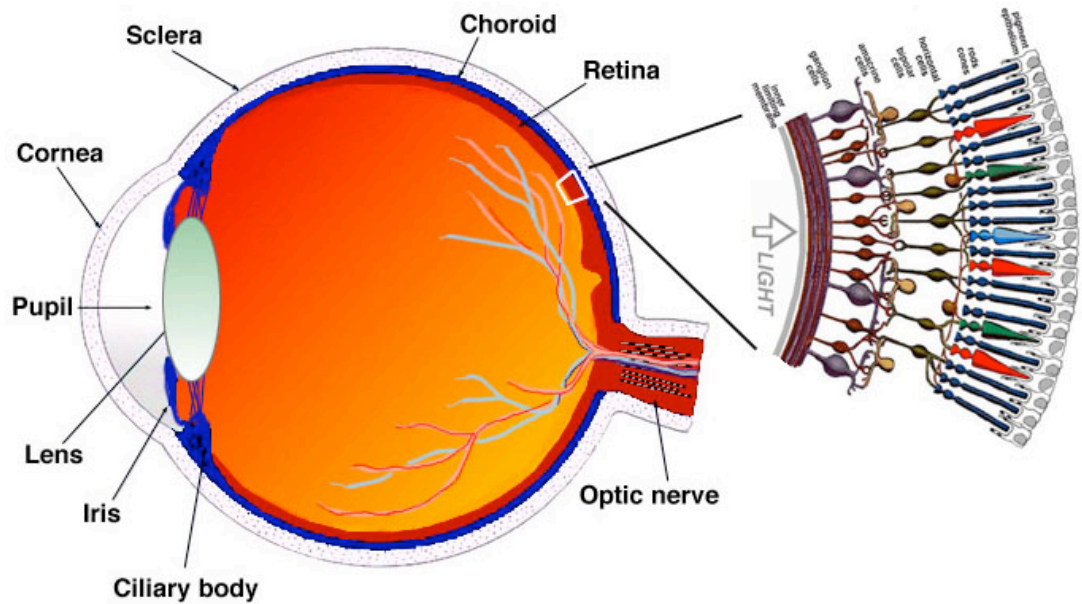


# The visual system

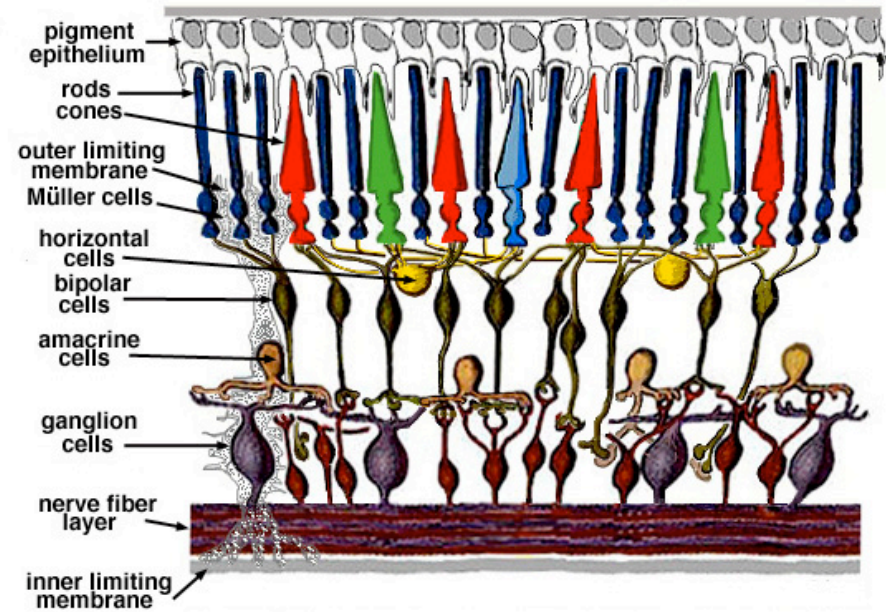
# The retina

- Light passes through the lens, through the inner layer of ganglion cells and bipolar cells to reach the rods and cones.



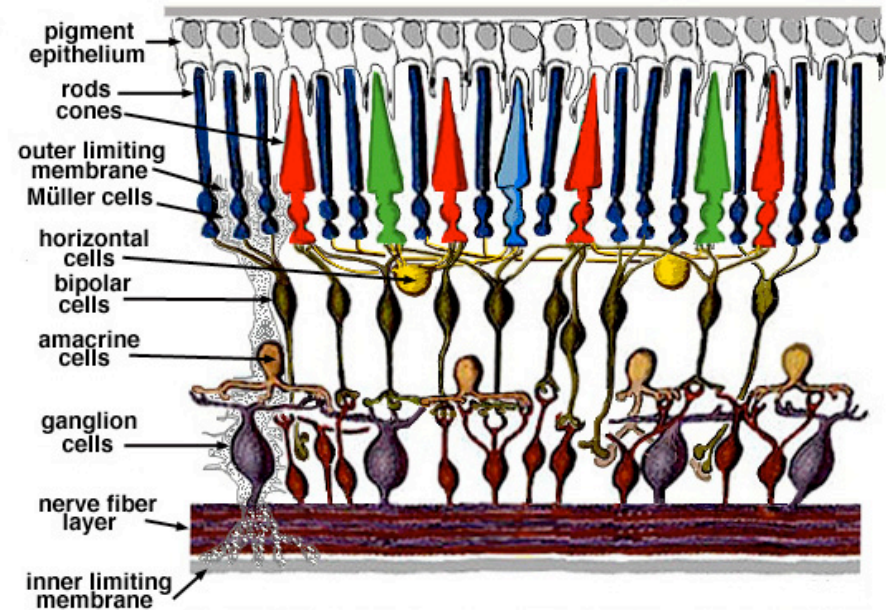
# The retina

- 0.5 mm thick



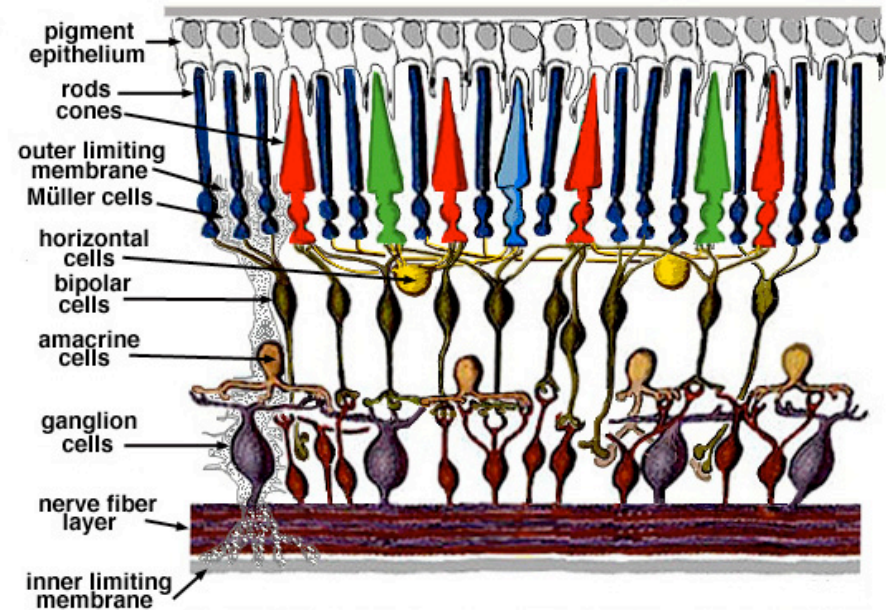
# The retina

- 0.5 mm thick
- The photosensors (the rods and cones) lie outermost in the retina.



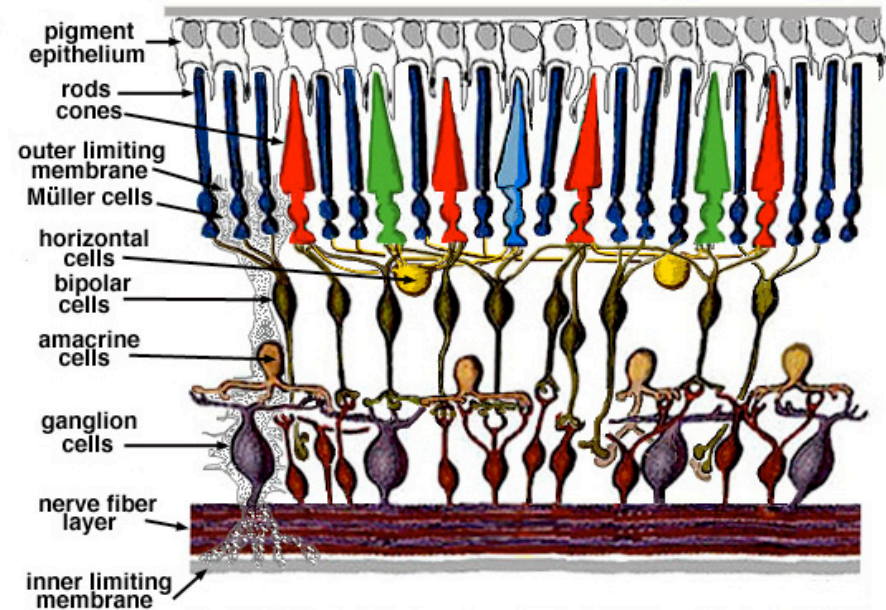
# The retina

- 0.5 mm thick
- The photosensors (the rods and cones) lie outermost in the retina.
- Interneurons



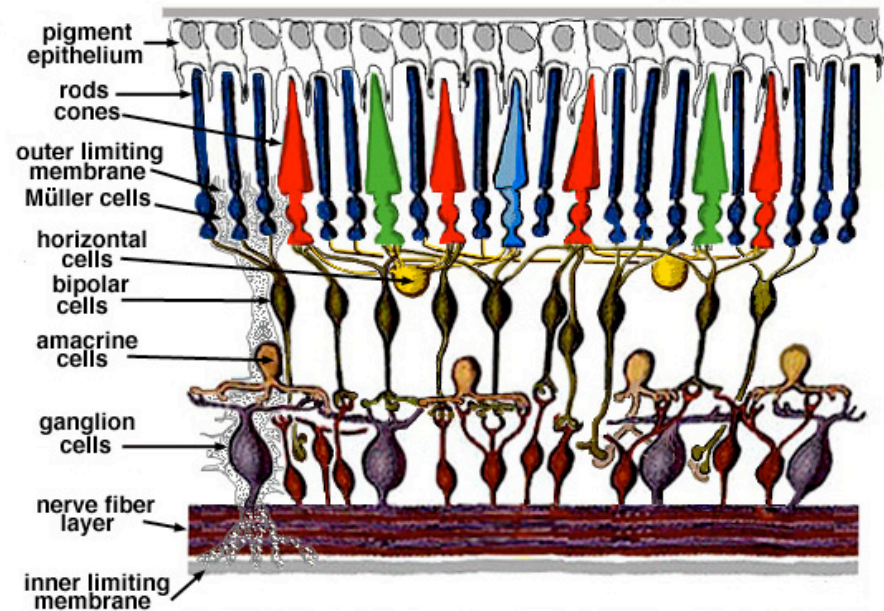
# The retina

- 0.5 mm thick
- The photosensors (the rods and cones) lie outermost in the retina.
- Interneurons
- Ganglion cells (the output neurons of the retina) lie innermost in the retina closest to the lens and front of the eye.



# The retina

- Receptive field:
  - The location where a visual stimulus causes a change in the activity of the visual neuron
  - For a rod or a cone, you could think of it as a pixel.
  - For the rest of the visual system, receptive fields are more complicated and more interesting!



# **Retinal interneurons**

- Photoreceptors synapse onto many interneurons.



# Retinal interneurons

- Photoreceptors synapse onto many interneurons.
- The interneurons synapse onto one another and onto ganglion cells.

# **Ganglion cells**

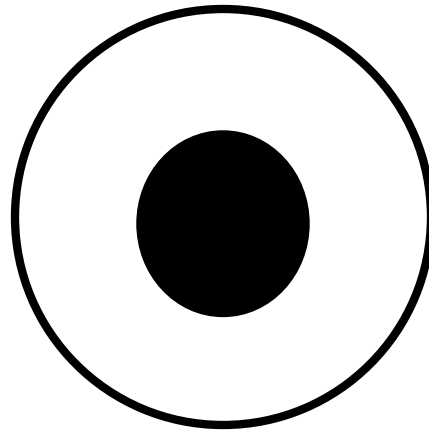
- There are at least 18 different morphological types of ganglion cell in the human retina.

# Ganglion cells

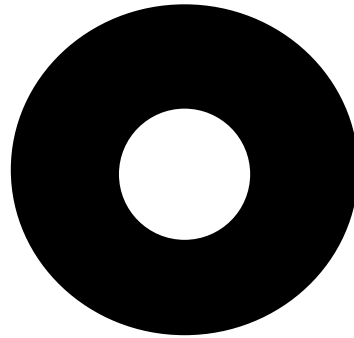
- There are at least 18 different morphological types of ganglion cell in the human retina.
- There are about a million ganglion cells.

# Ganglion cells

- Most ganglion cells have center-surround receptive fields.
- About 50% of those are OFF-center ON-surround.
- These are like the “bug detectors” in the Lettvin paper.



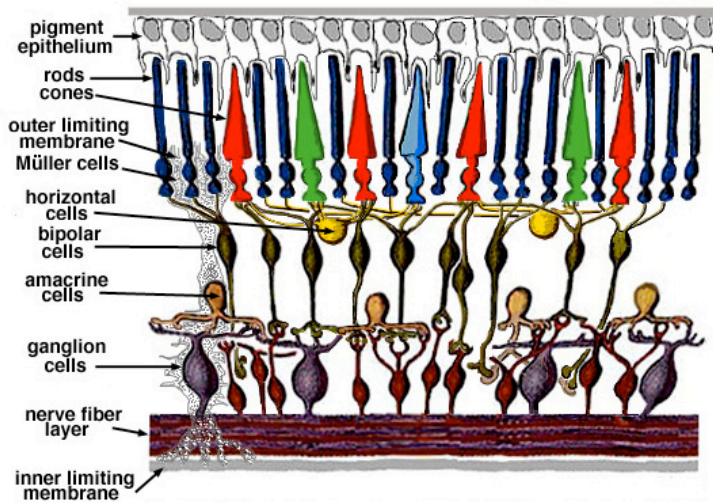
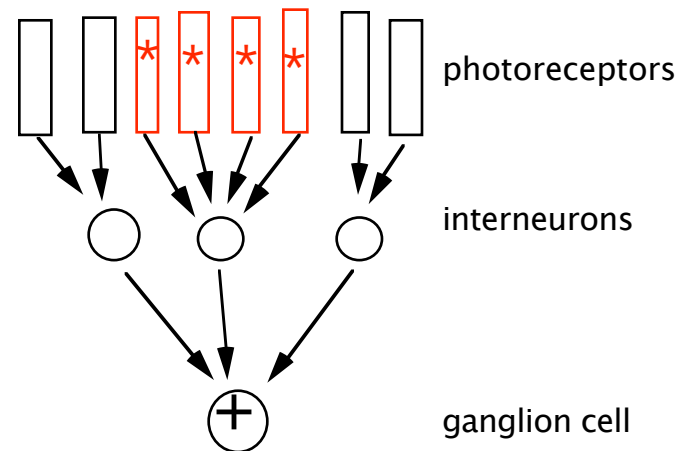
## **ON-center OFF-surround ganglion cells**



- In mammals, many cells respond best to a small spot of light on a dark background.

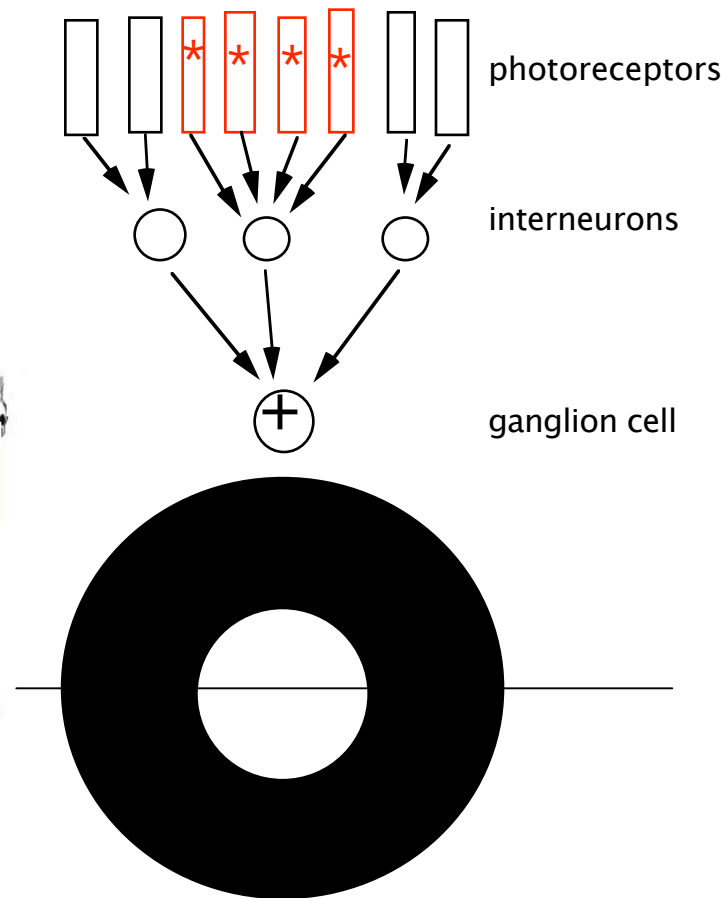
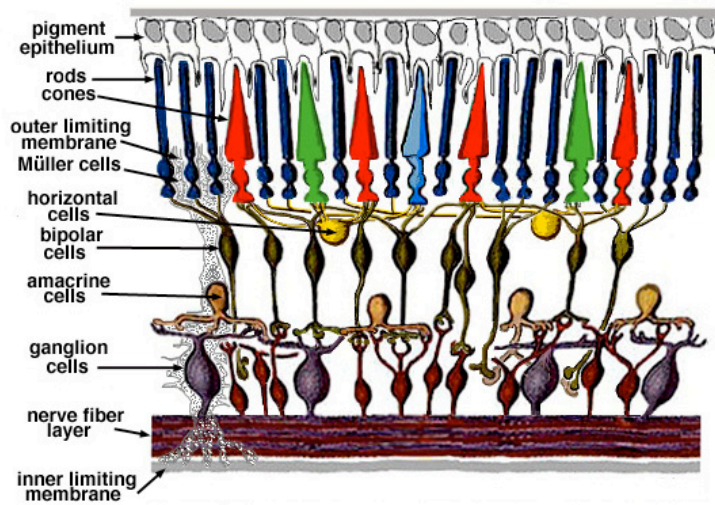
# ON-center OFF-surround ganglion cells

- Lighting up the center of the field excites the ganglion cell (turns it "ON").



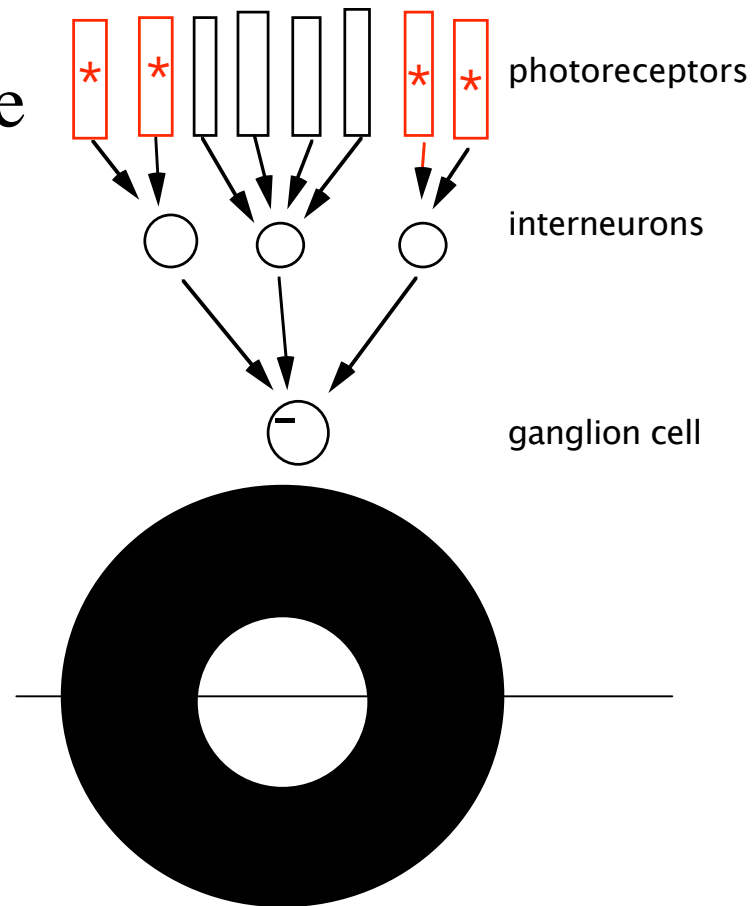
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# ON-center OFF-surround ganglion cells

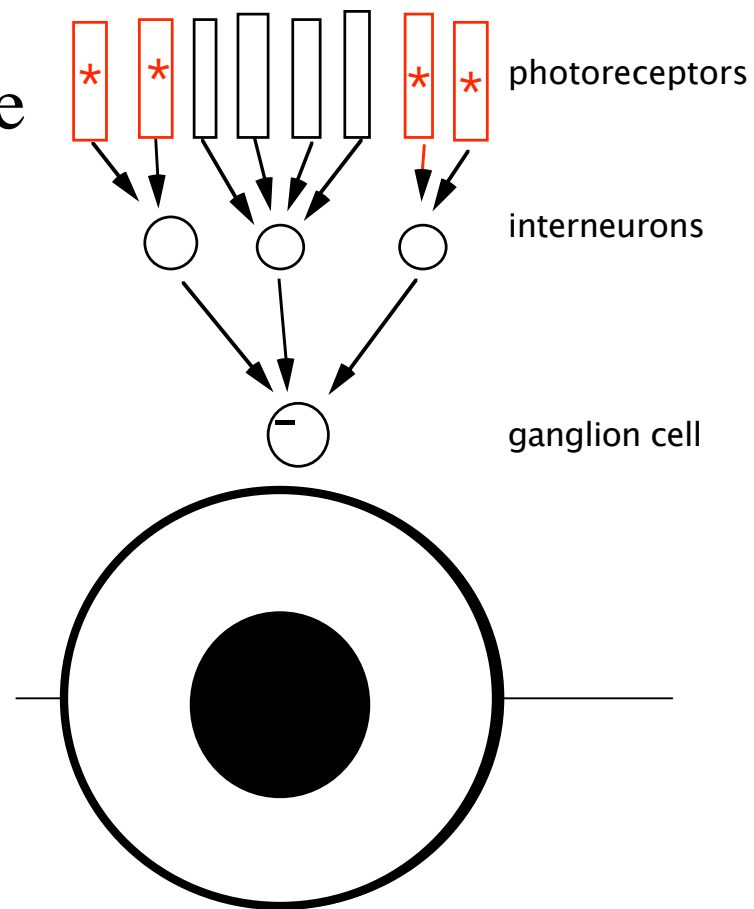
- Lighting up the surrounding part of the field inhibits the ganglion cell (turns it "OFF").





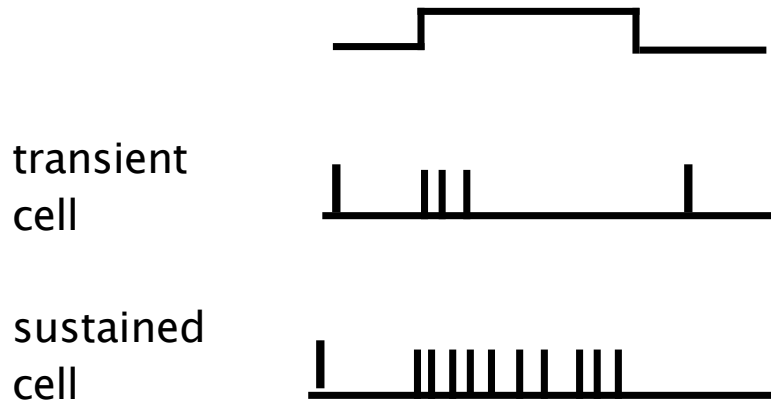
# ON-center OFF-surround ganglion cells

- Lighting up the surrounding part of the field inhibits the ganglion cell (turns it "OFF").



## Sustained vs. transient responses

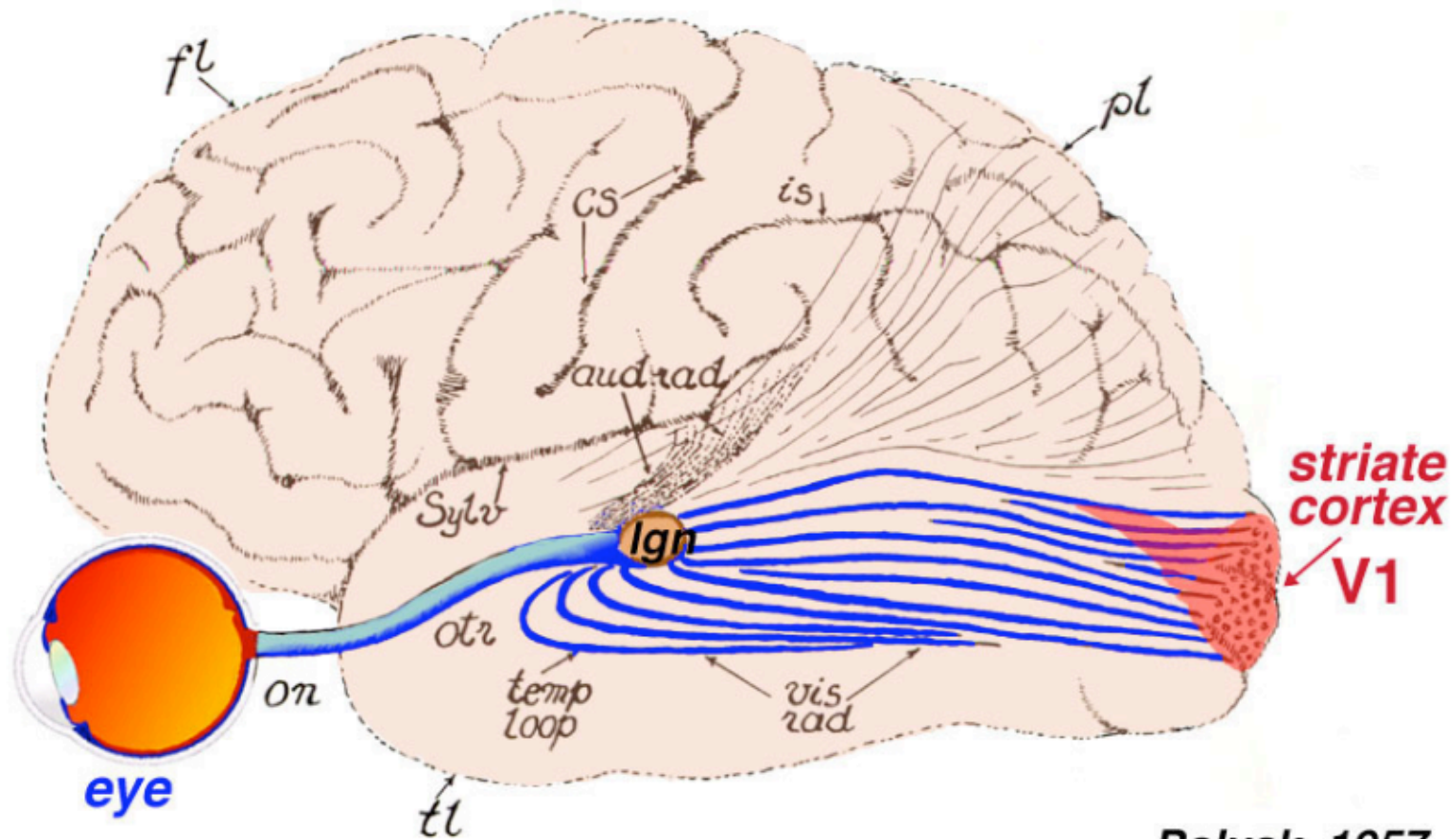
- Some respond transiently some give sustained responses.
- The frog “event detectors” have transient responses.
- The “dimming detectors” have sustained responses.



## Other types of ganglion cells

- Some ganglion cells don't have center-surround receptive fields. Some of these are like the “dimming detectors” that project to the tectum.
- Some respond best to particular color combinations (in animals with color vision).

# Pathway from the eye to the cortex

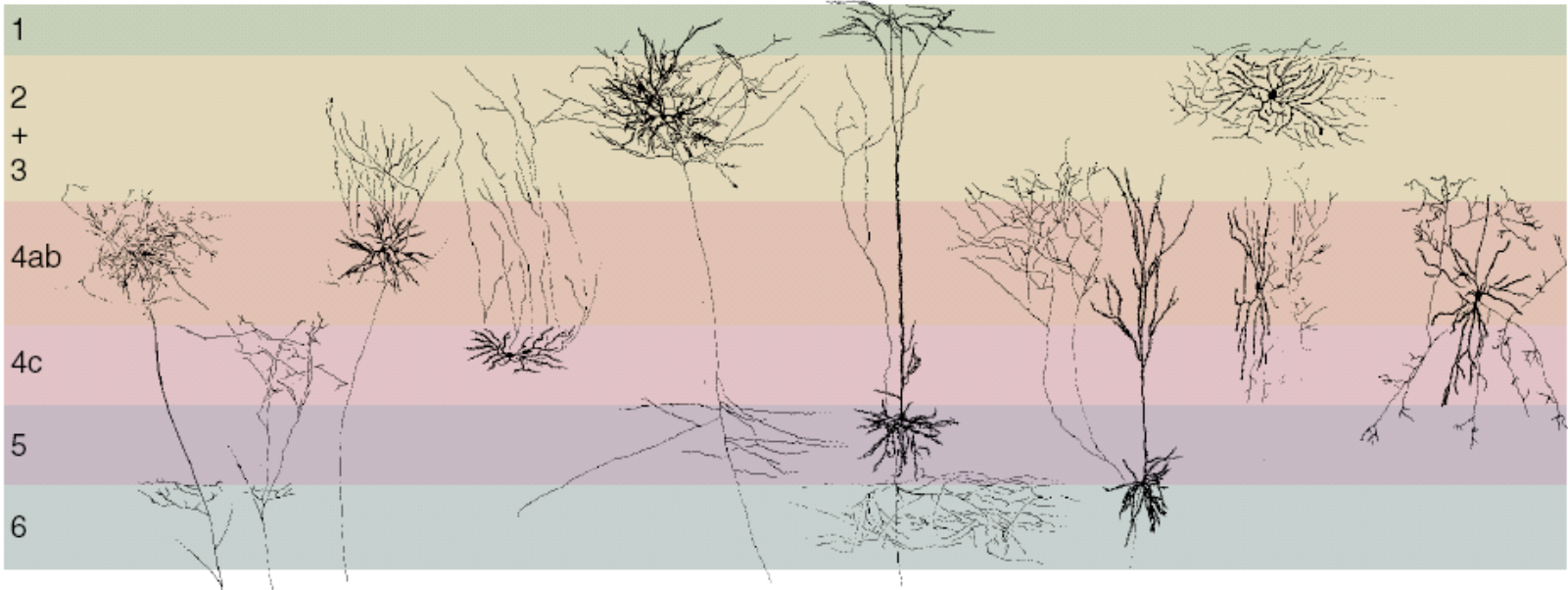


Polyak, 1957

# Striate cortex

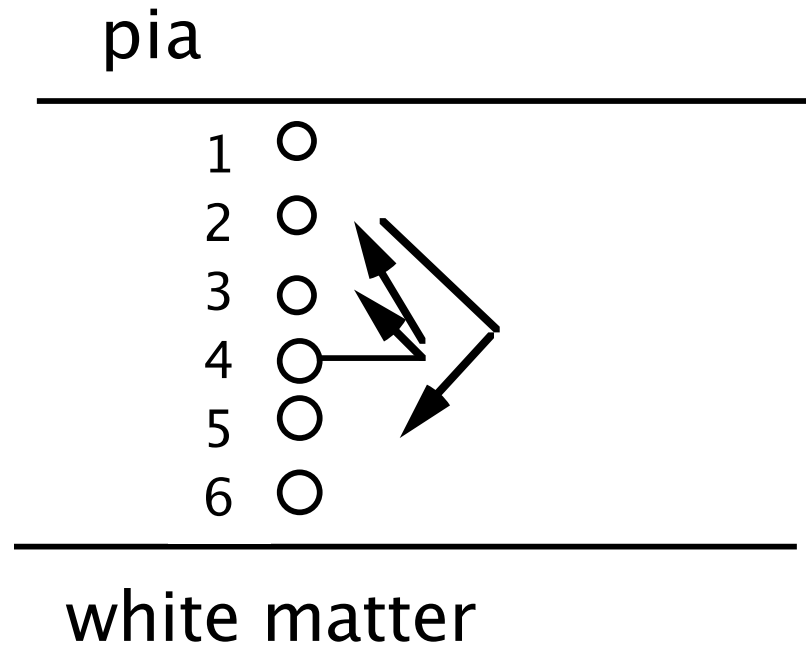
Also called V1, primary visual cortex, or area 17





# Cortical circuitry

- The basic arrangement of circuitry is perpendicular to the surface of the brain: columnar.
- Axons from lateral geniculate terminate in layer 4.

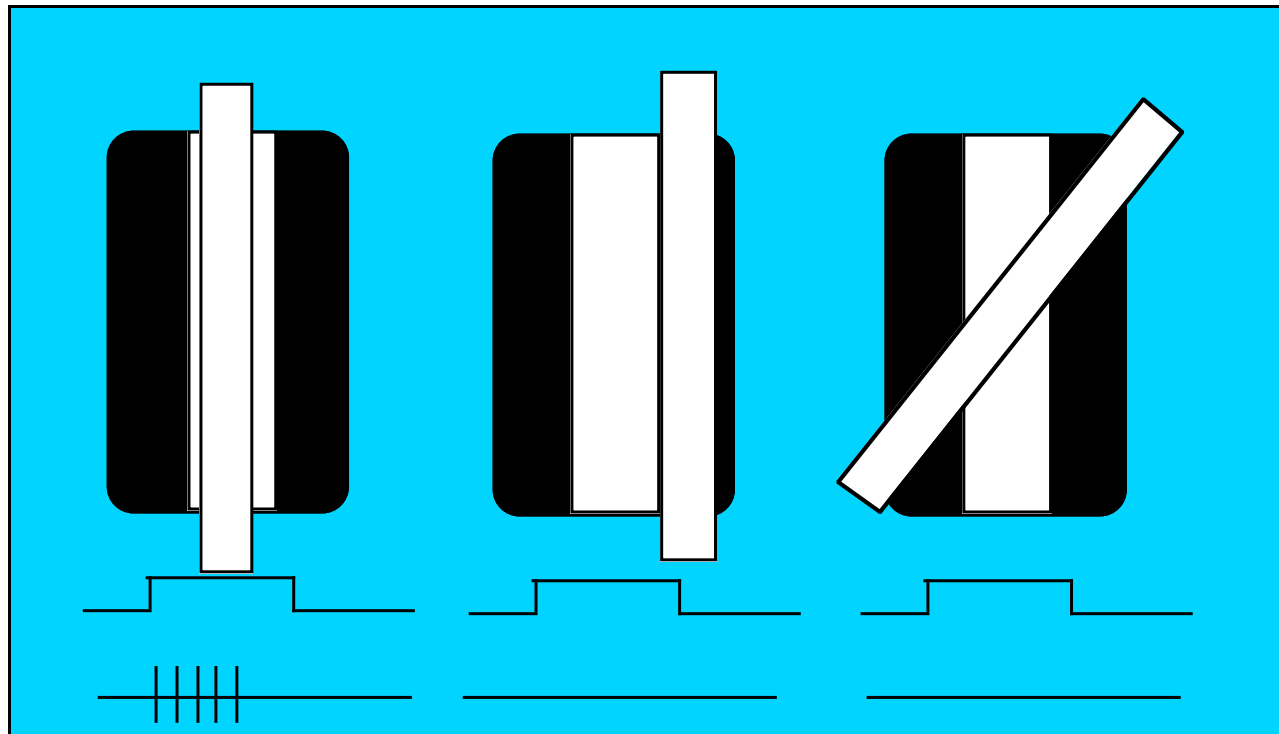


## **Receptive fields in striate cortex**

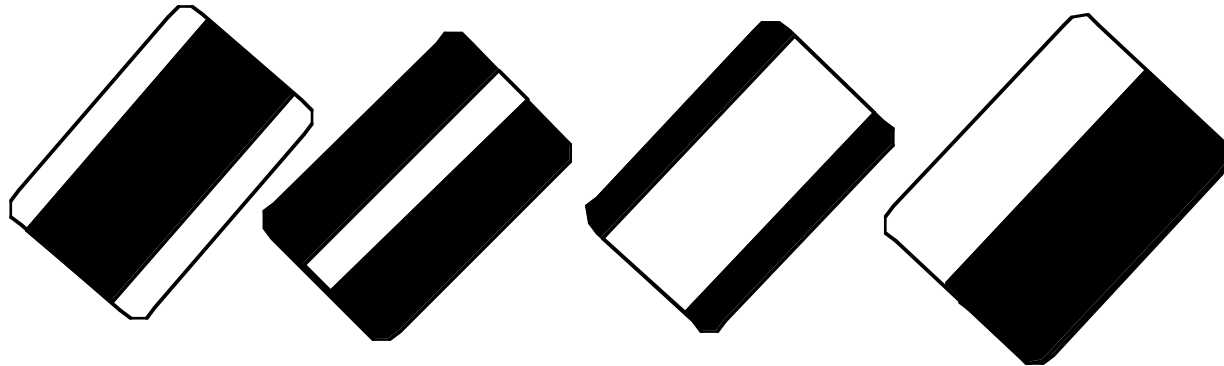
- Most cells in layer 4 have circular center-surround receptive fields.
- Most cells in the other layers respond only weakly to spots of light or dark. Instead, they respond best to lines or edges.



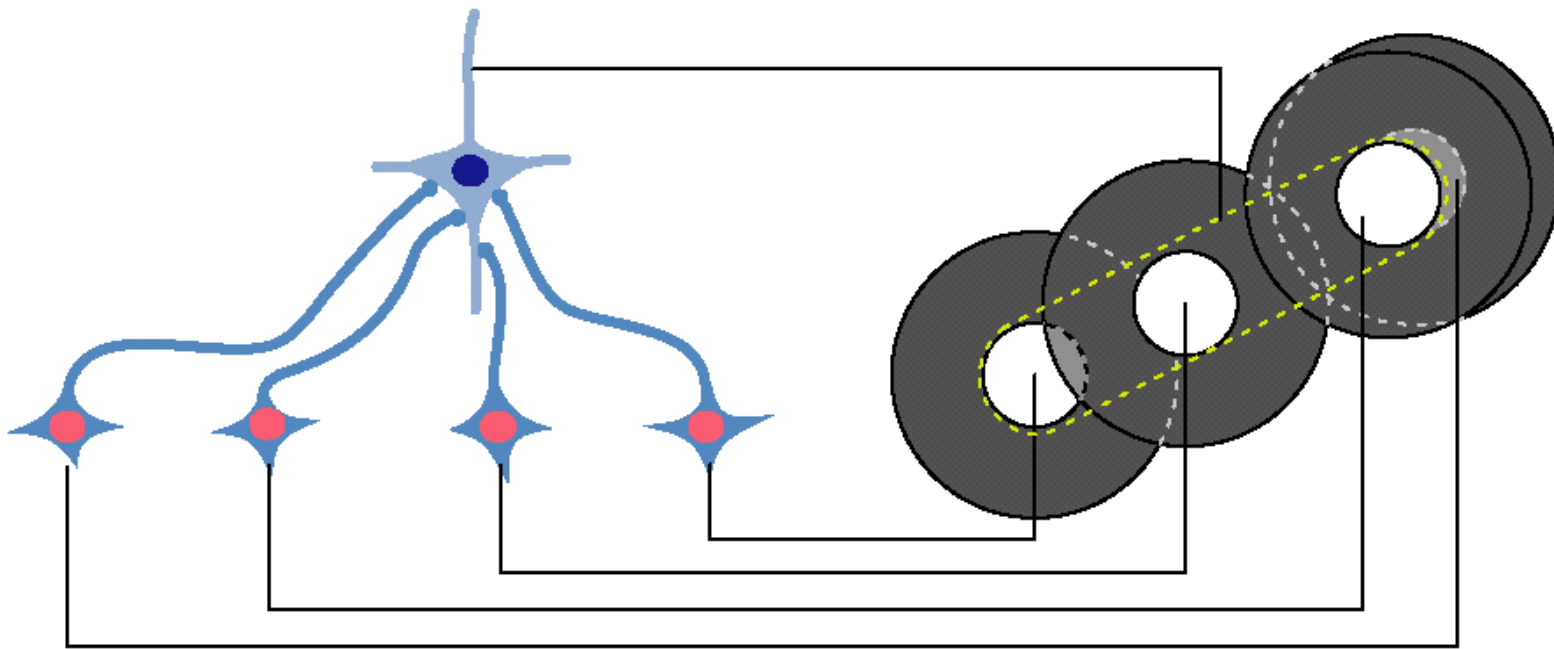
An elongated bar in the correct orientation and the correct position is the best stimulus for a simple cell.



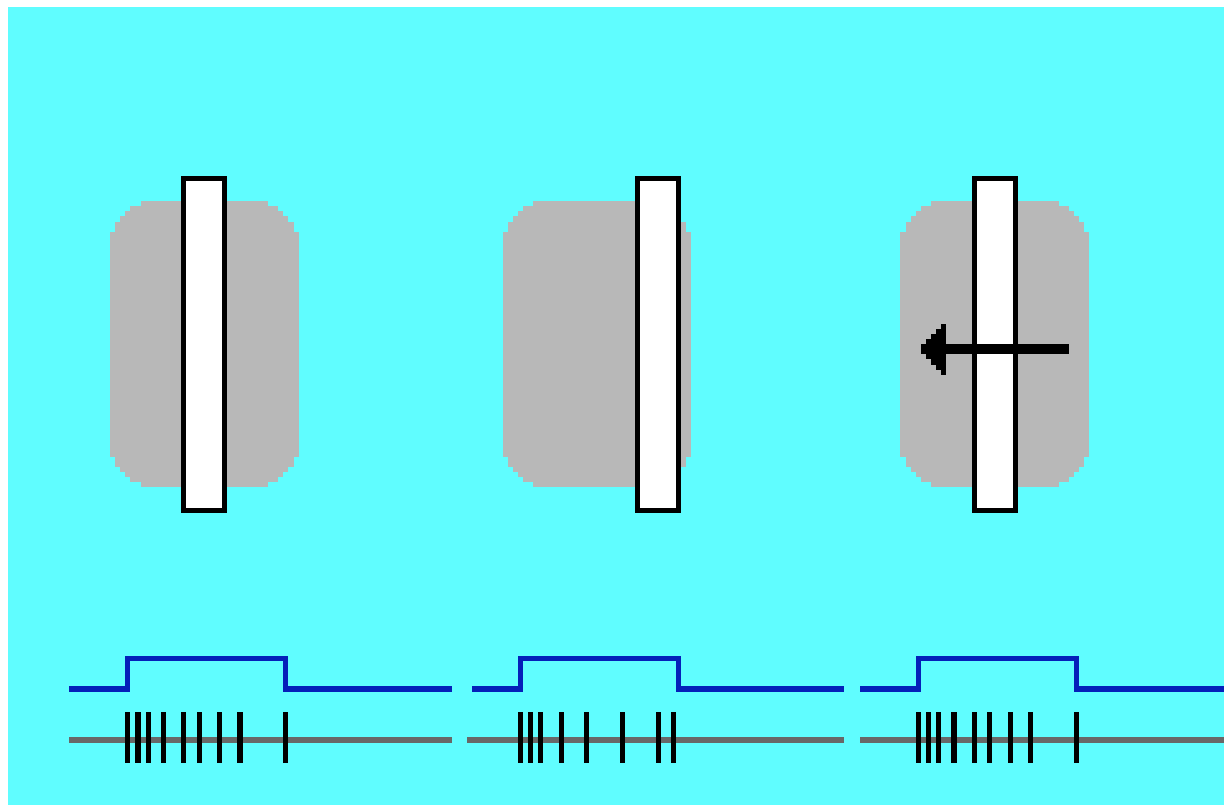
## Examples of other types of orientation-selective receptive field preferences



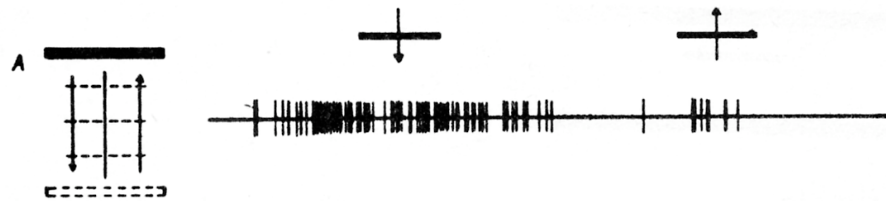
Model of how center-surround cells can be building blocks for simple cells.



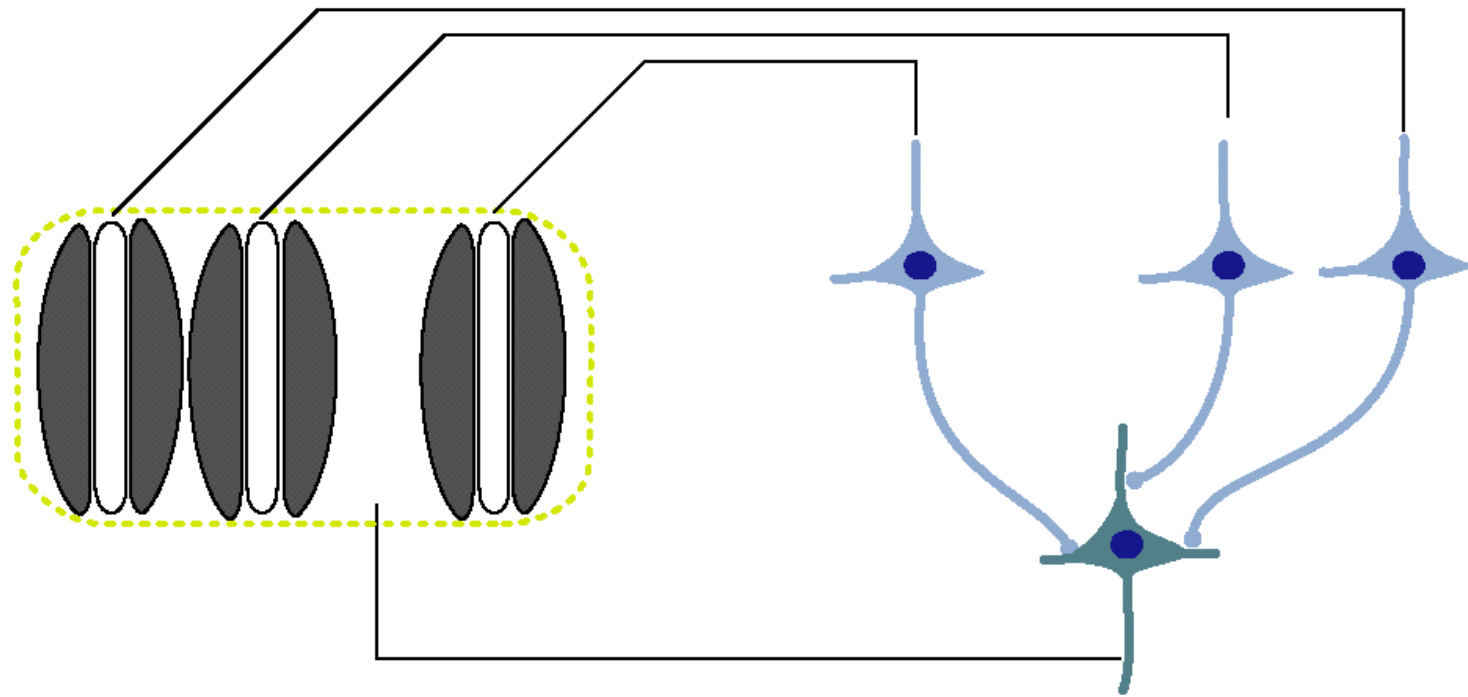
Complex cells also prefer oriented lines but they don't require a particular location.



Many complex cells are directionally-selective.

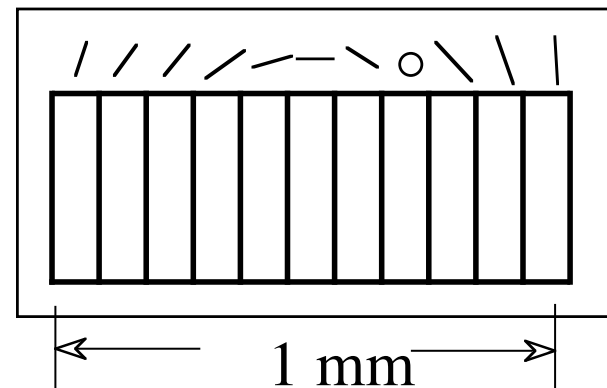


# Model of how simple cells could be building-blocks for complex cells

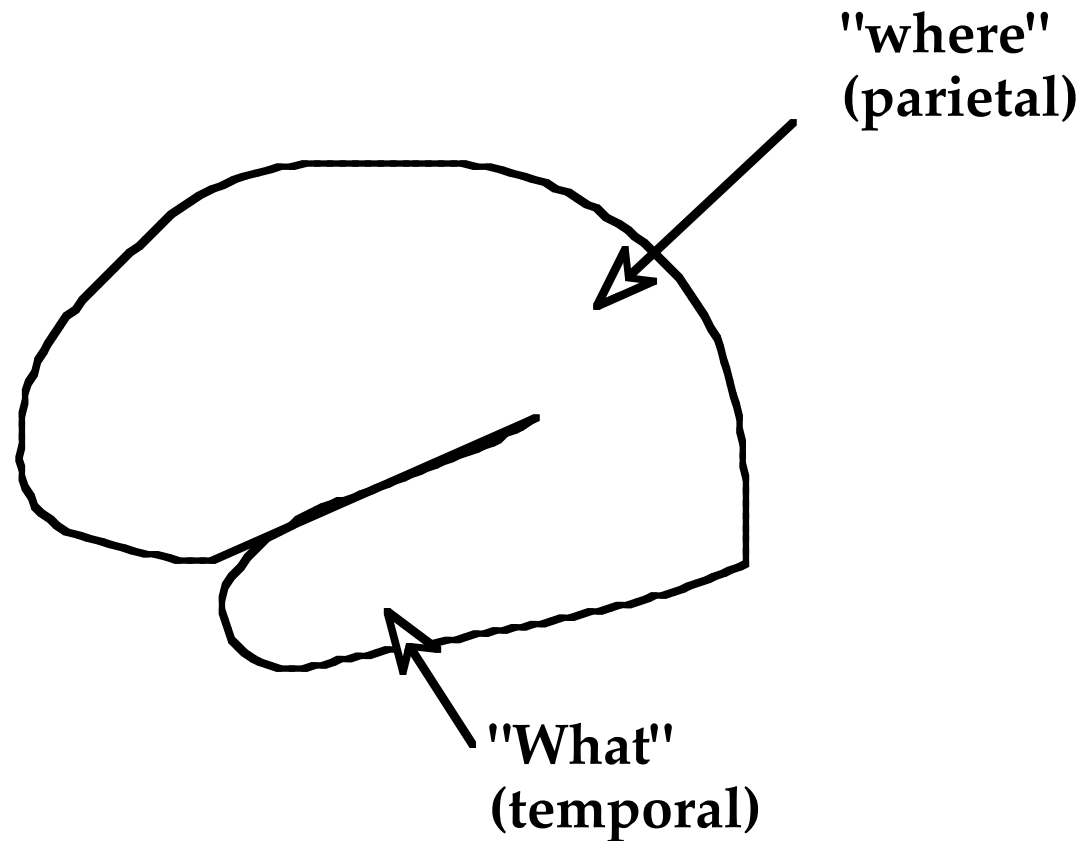


# Orientation columns

- Cortex -- as a whole -- is organized into columns.
- In striate cortex, the orientation column is the basic unit.
  - All of the cells outside of layer 4 will respond best to stimuli of the same orientation.
  - Some cells will be direction selective, others not.



# Output of striate cortex: more than 40 other regions!

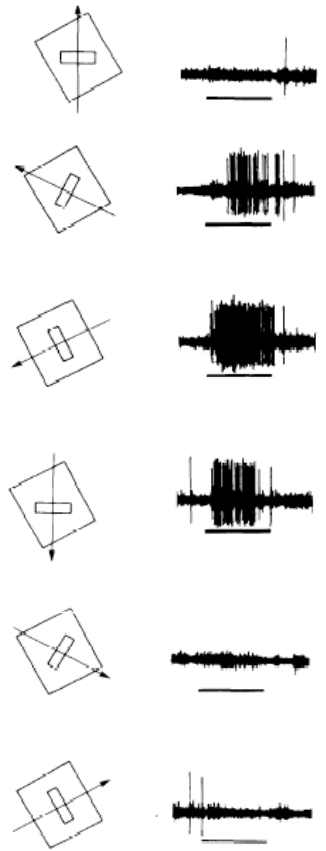




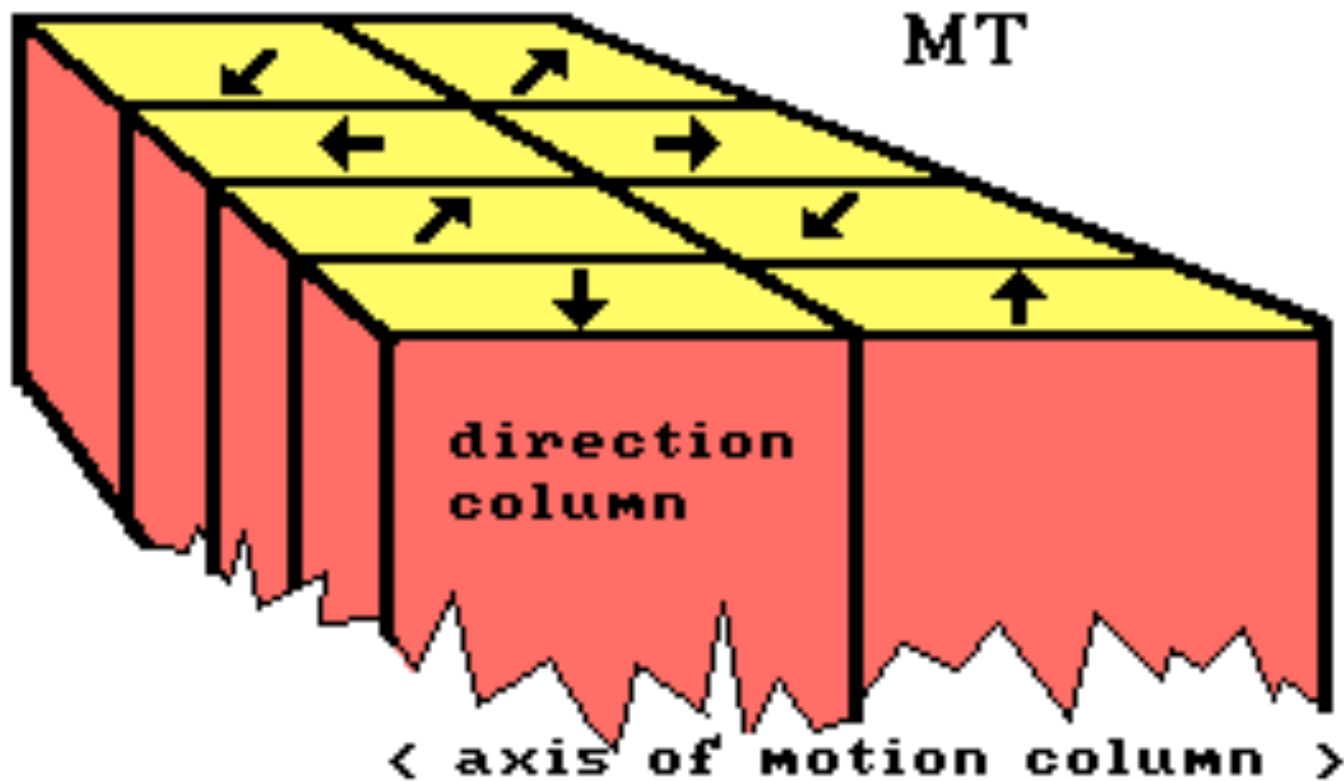
## The “where” stream

- Cells in some of these regions respond almost exclusively to moving objects.
  - Some respond to circular or spiraling movement.
  - Some respond to “visual flow.”
  - Some respond best to approaching or receding objects.
  - ....

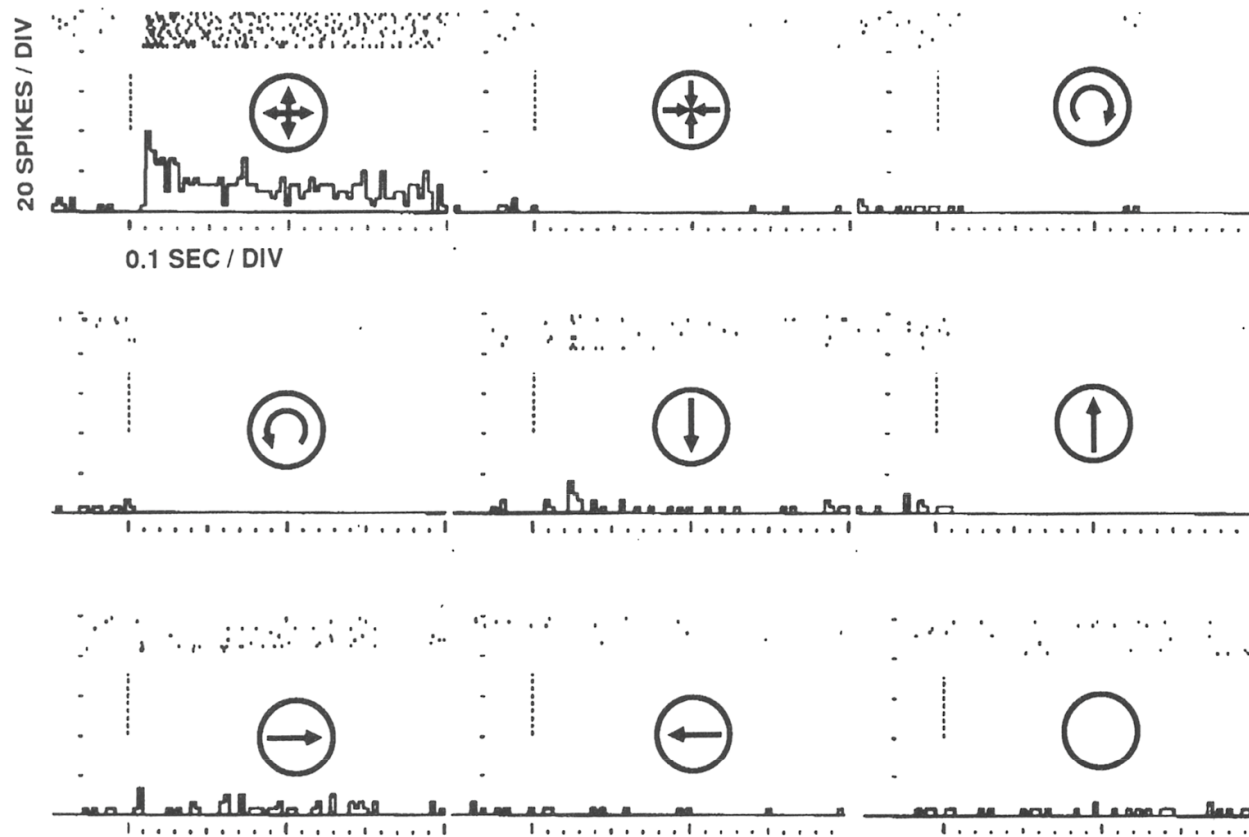
Area MT is a well-studied “motion area.” Most of the cells in MT respond best to moving stimuli, and most of those cells have well-defined direction preferences.



Area MT, like many other cortical areas, shows columnar organization.

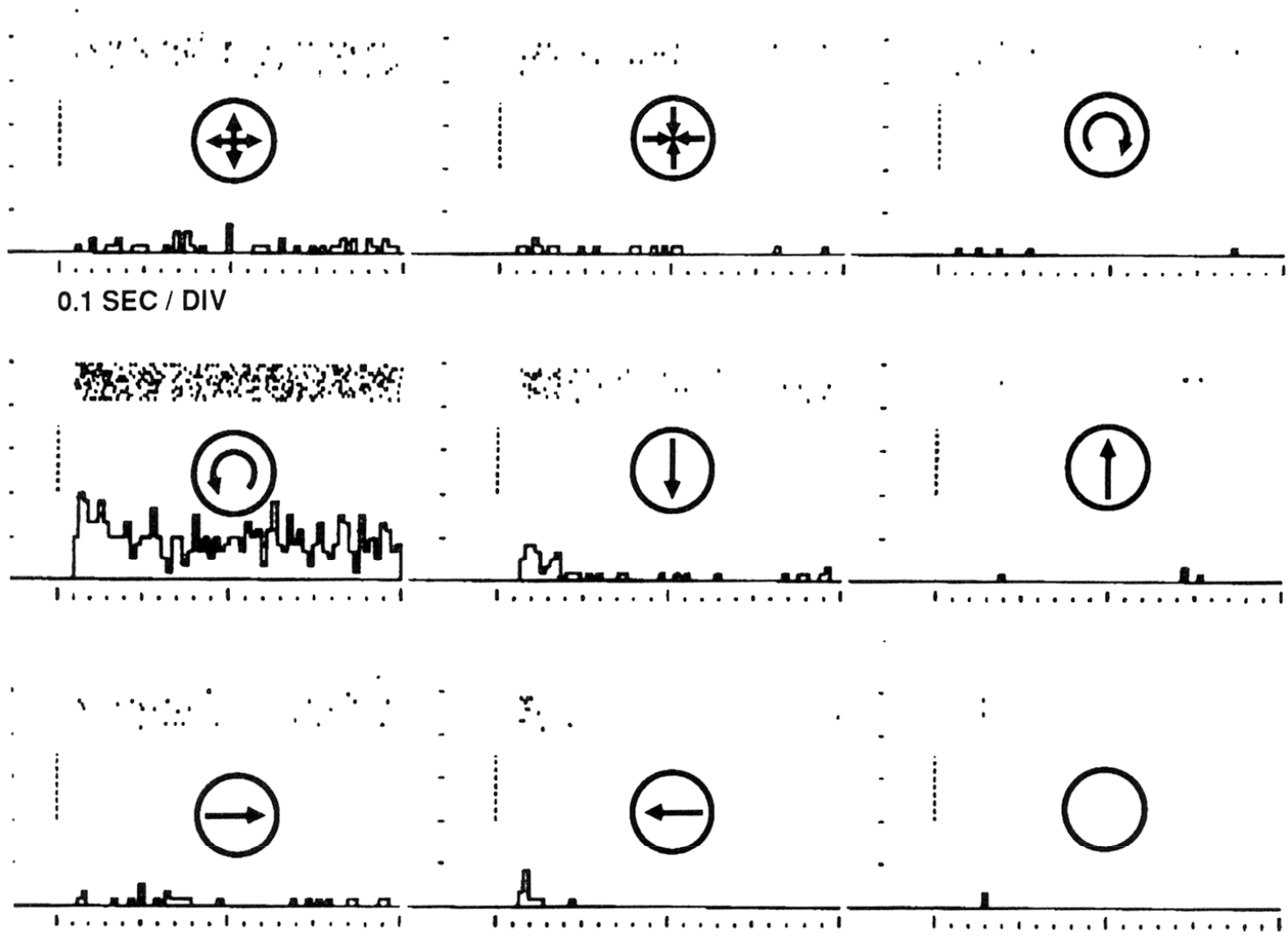


Cells in area MST often respond best to more complex types of motion.



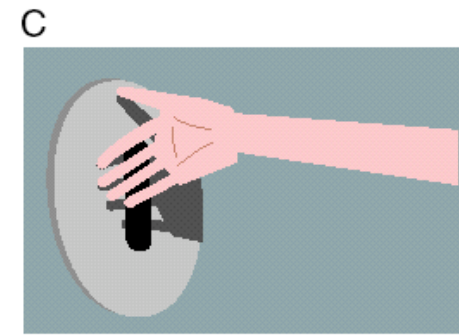
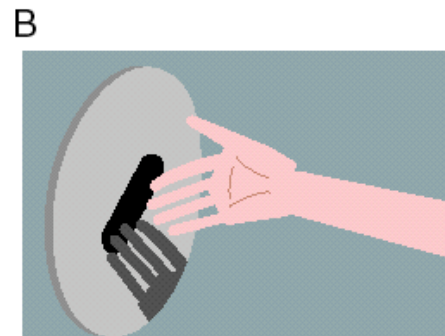
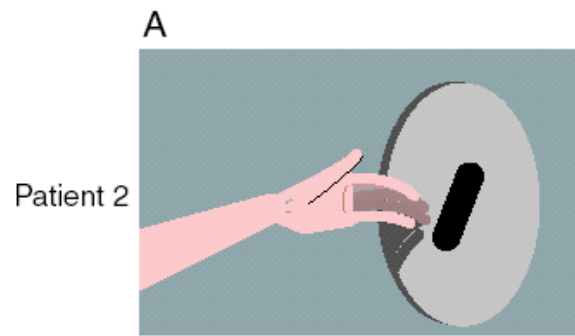
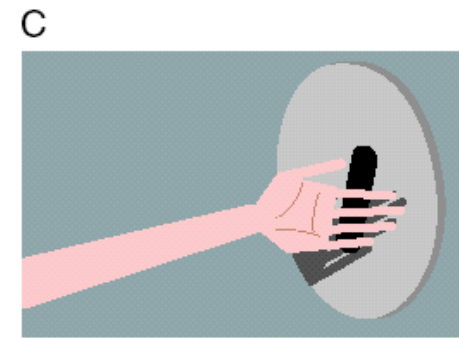
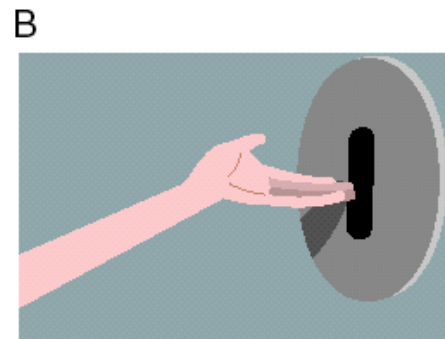
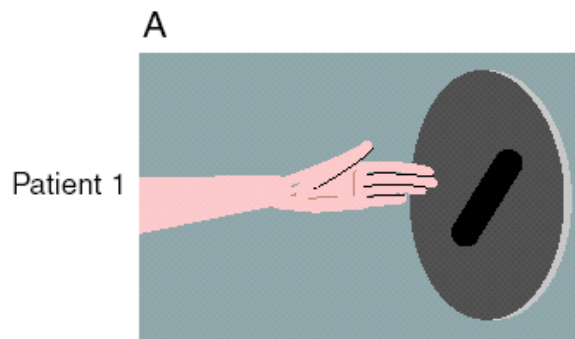
20 SPIKES / DIV

0.1 SEC / DIV



## Lesions of the “where” stream

- loss of speed motion perception
- visual neglect in peripersonal space
- loss of ability to follow moving objects
- loss of ability to use visual information to grasp objects



Ipsilesional field  
Accurate reaching

Orientation errors  
Contralesional field

Directional errors

## The “what” stream

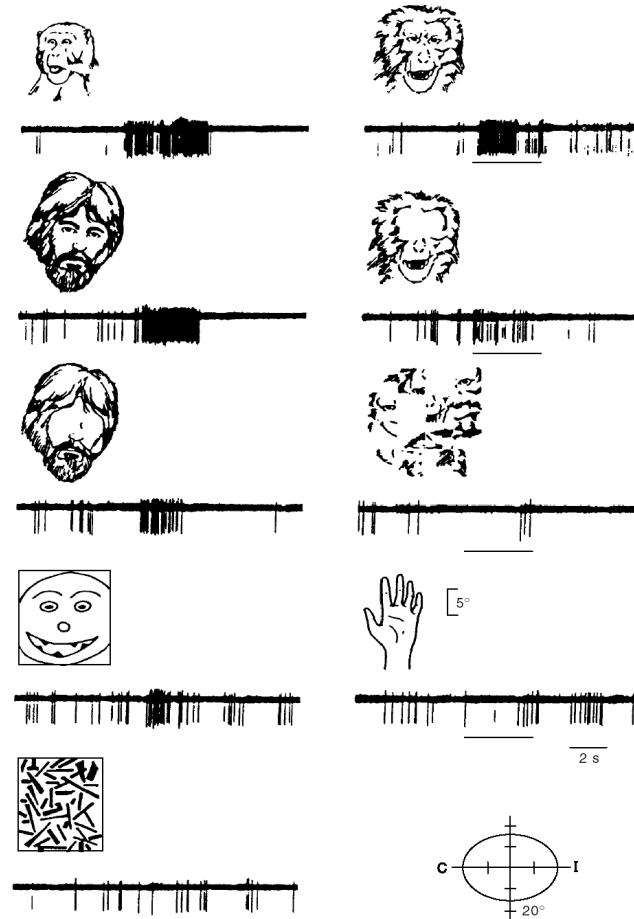
- Some areas have many cells that are color-selective.
- Some areas have cells that respond to complex shapes.
- Some areas are particularly important for face perception.



## Lesions of the ventral stream

- Achromatopsia: loss of color vision
- Prosopagnosia: loss of face recognition
  - Some regions have cells that respond best to objects such as particular faces.

# Example of a ventral occipito-temporal cell that responds best to faces

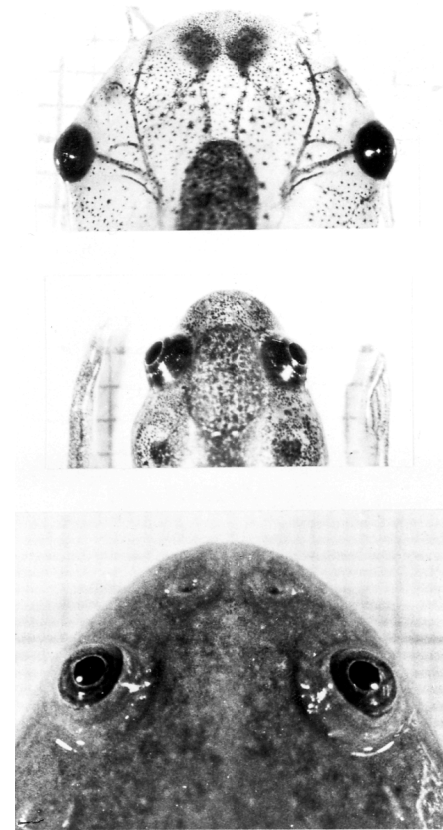






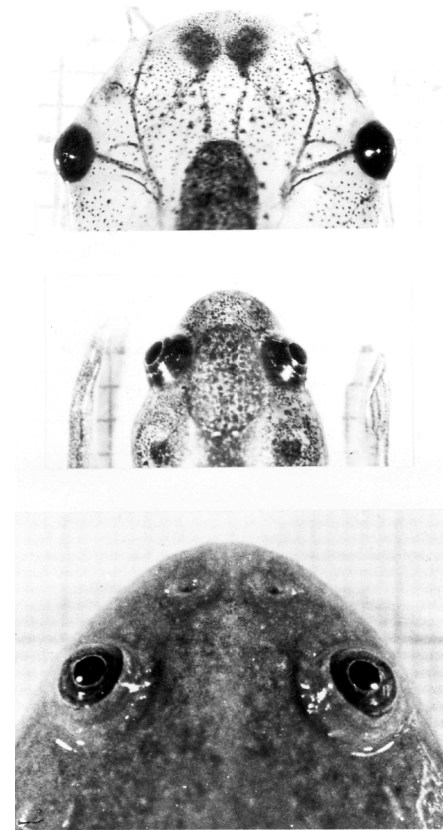
# Binocular development in *Xenopus tectum*

- Proper alignment of the projections from the two eyes requires binocular visual input during a critical period.



# Binocular development in *Xenopus* tectum

- Proper alignment of the projections from the two eyes requires binocular visual input during a critical period.
- Abnormal visual input leads to altered connections.



# Mechanisms

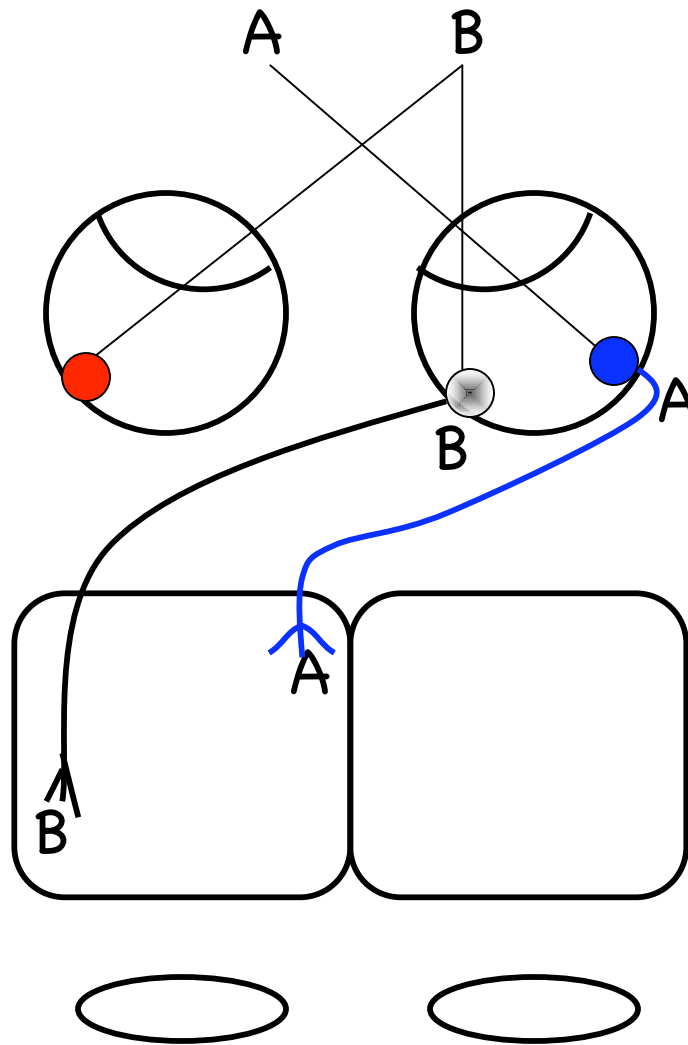
- At least two kinds of transmitter receptor are essential for matching of the connections from the two eyes.
- Correlated activity brings the inputs into register.
- The circuitry is complicated.
- When proper connections form, they are stabilized by release of a “retrograde messenger.”

Visual field

retina

tectum

Nucleus isthmi



The  
retinotectal  
"map"

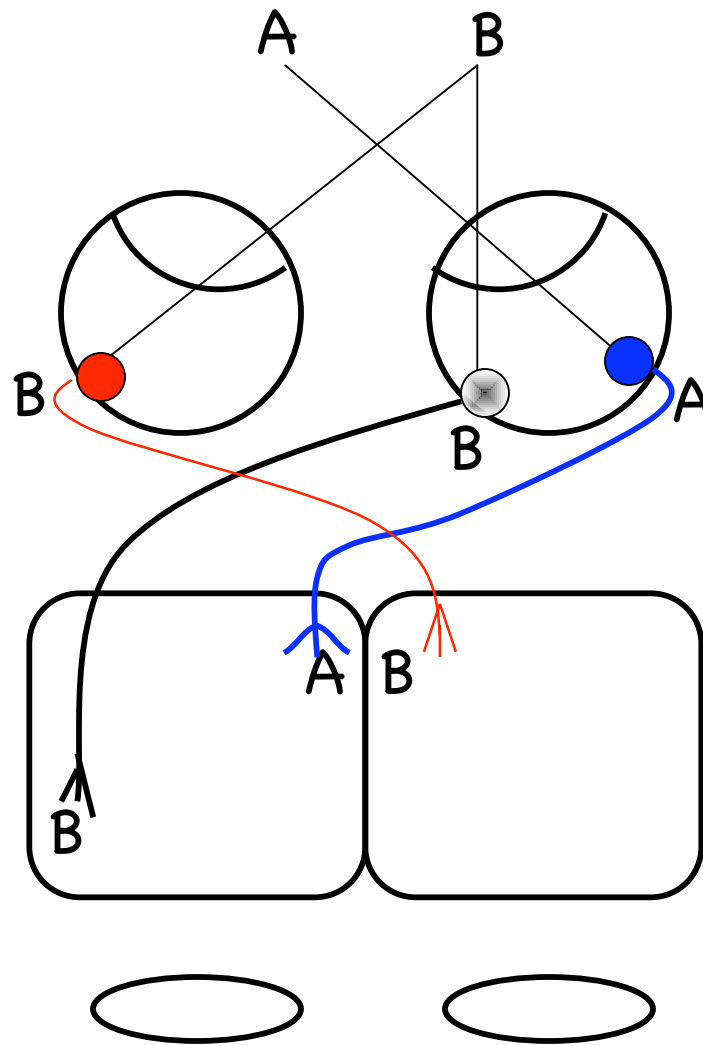


Visual field

retina

tectum

Nucleus isthmi

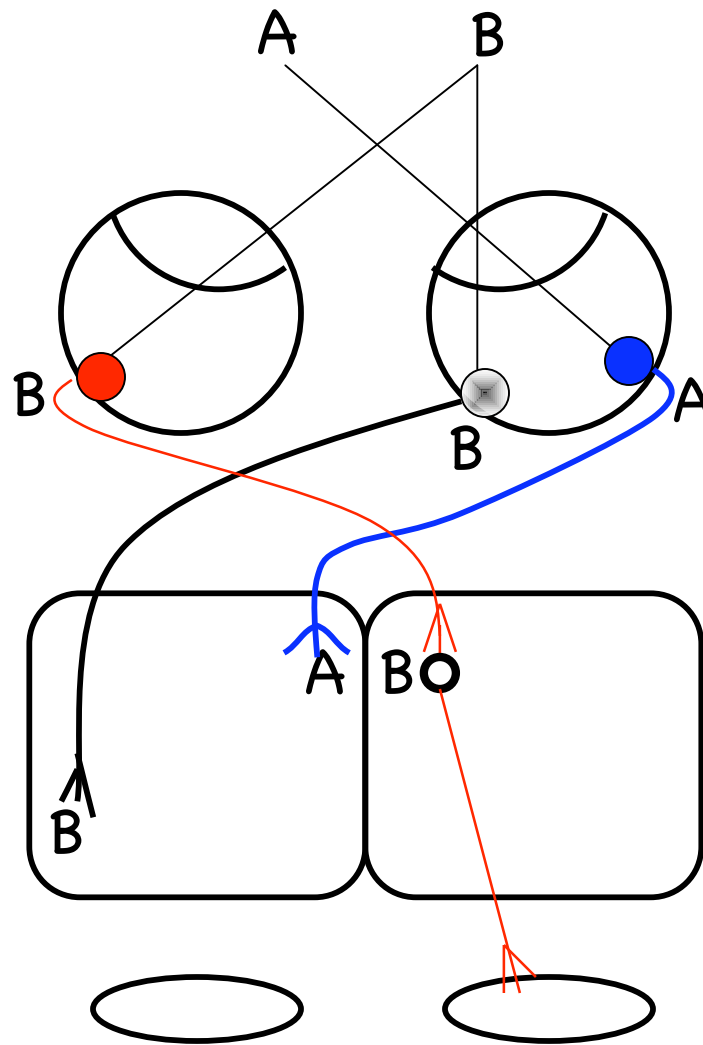


Visual field

retina

tectum

Nucleus isthmi

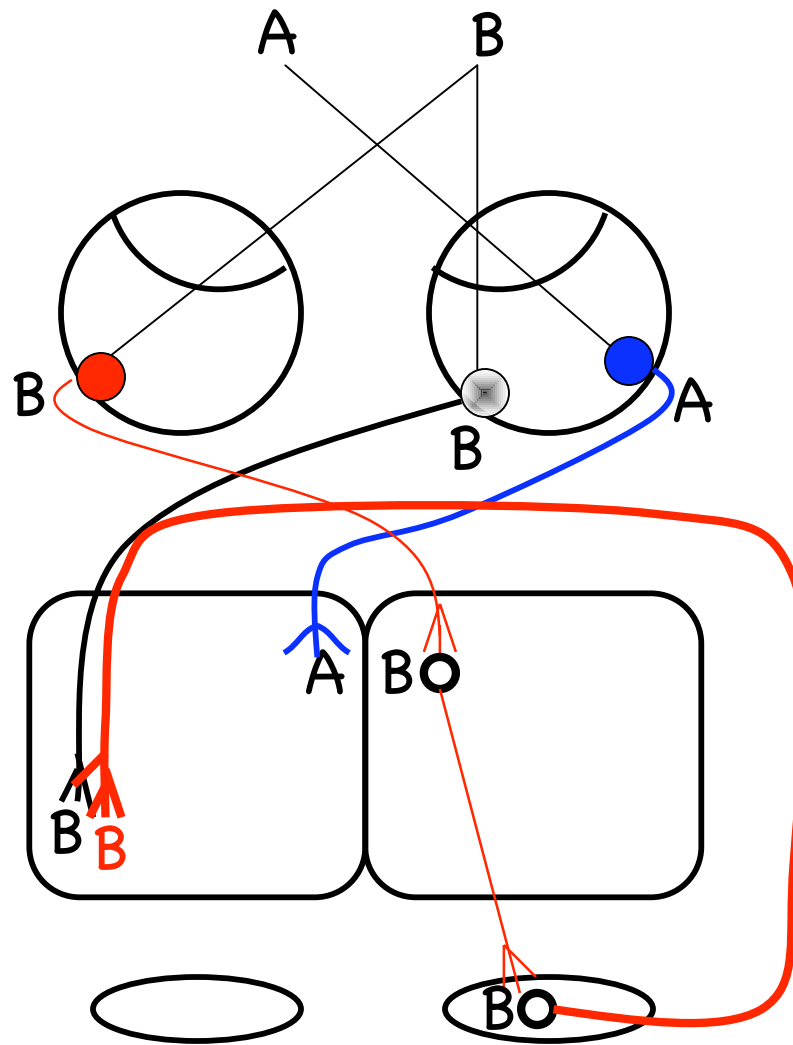


Visual field

retina

tectum

Nucleus isthmi

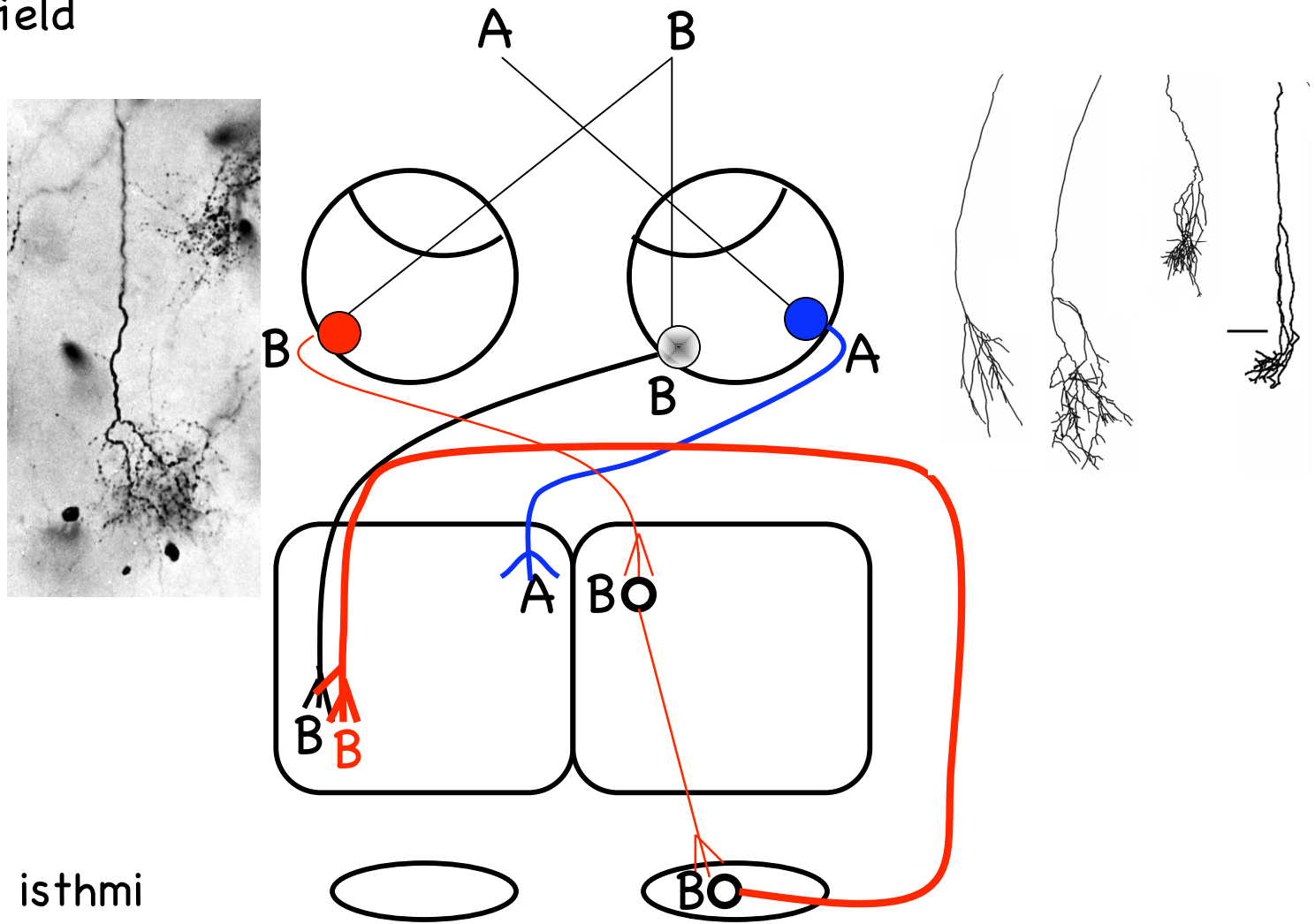


Visual field

retina

tectum

Nucleus isthmi

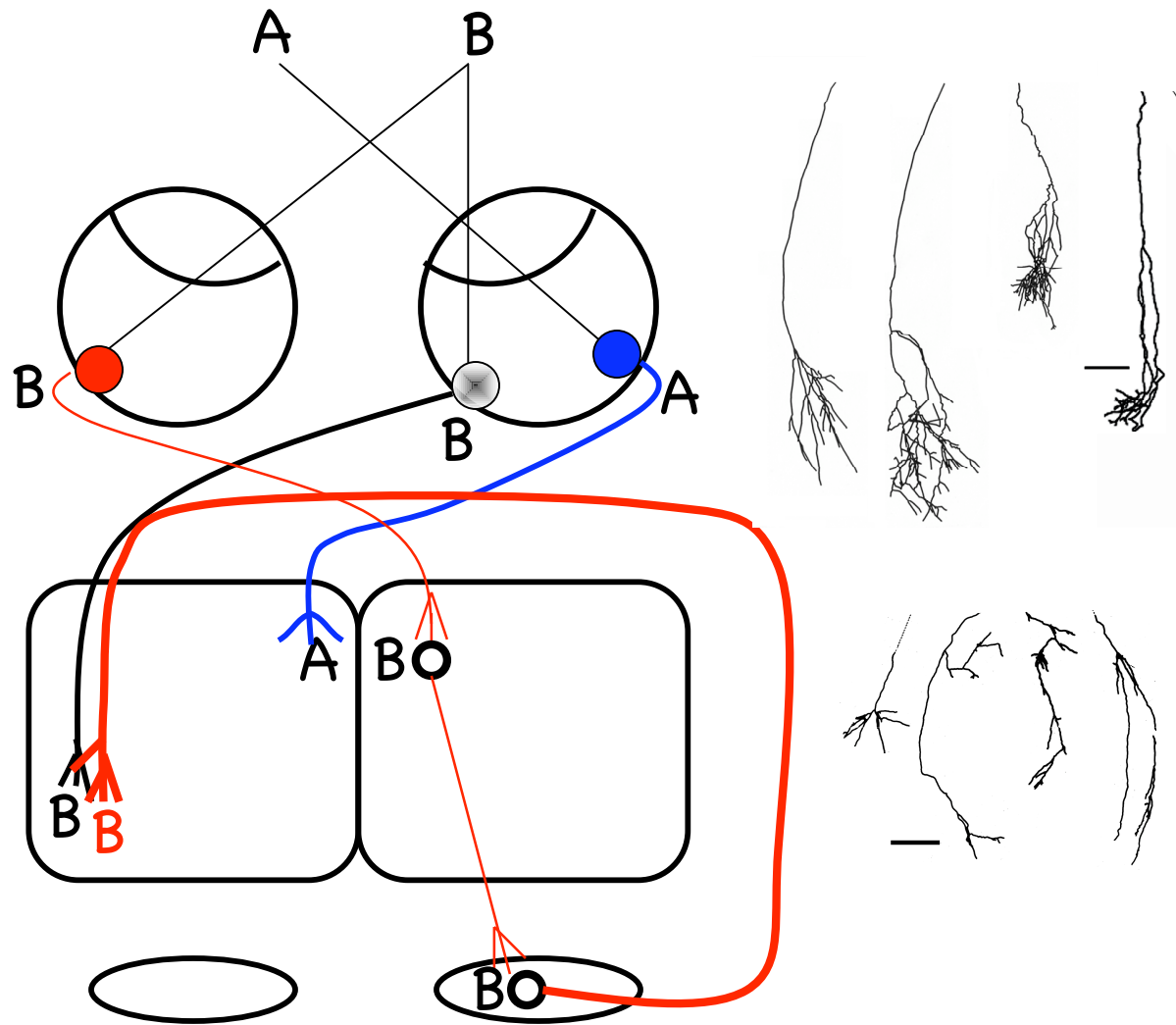


Visual field

retina

tectum

Nucleus isthmi

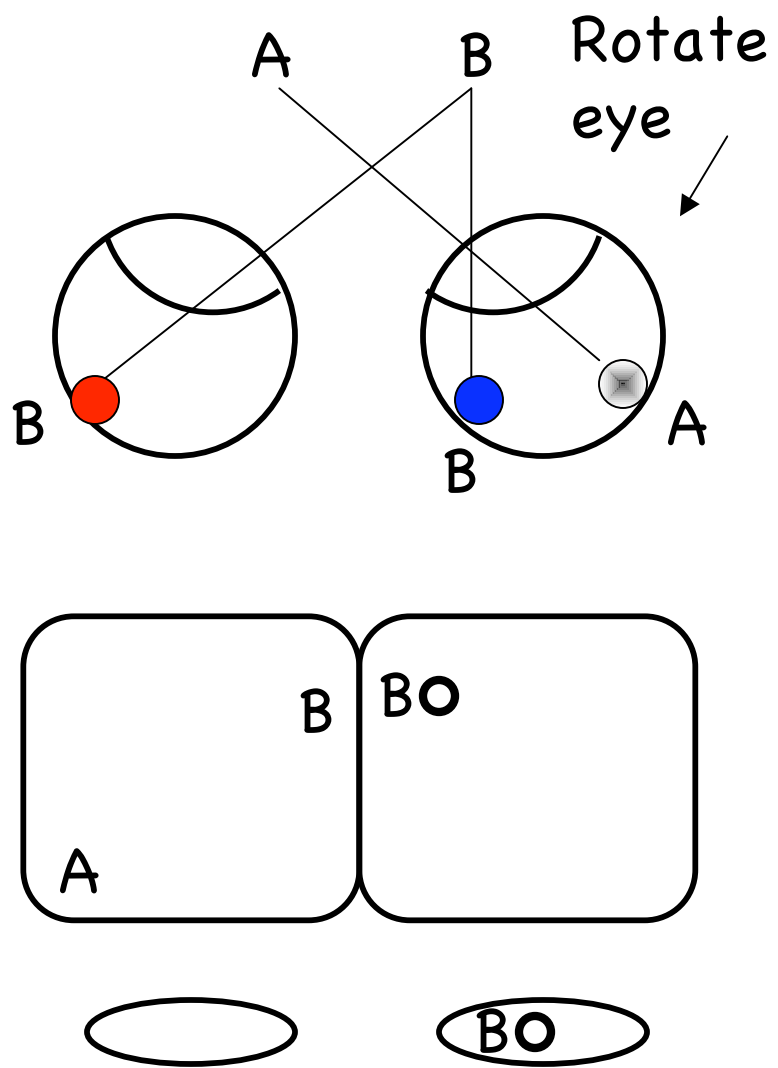
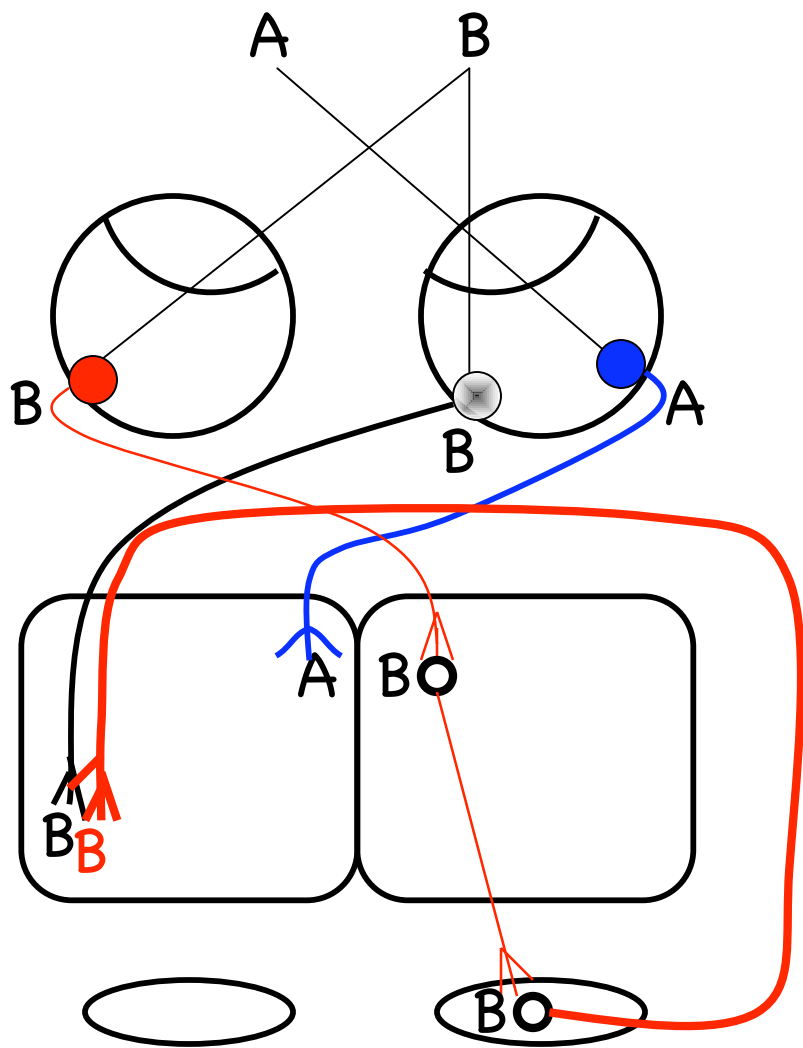


# Eye rotation

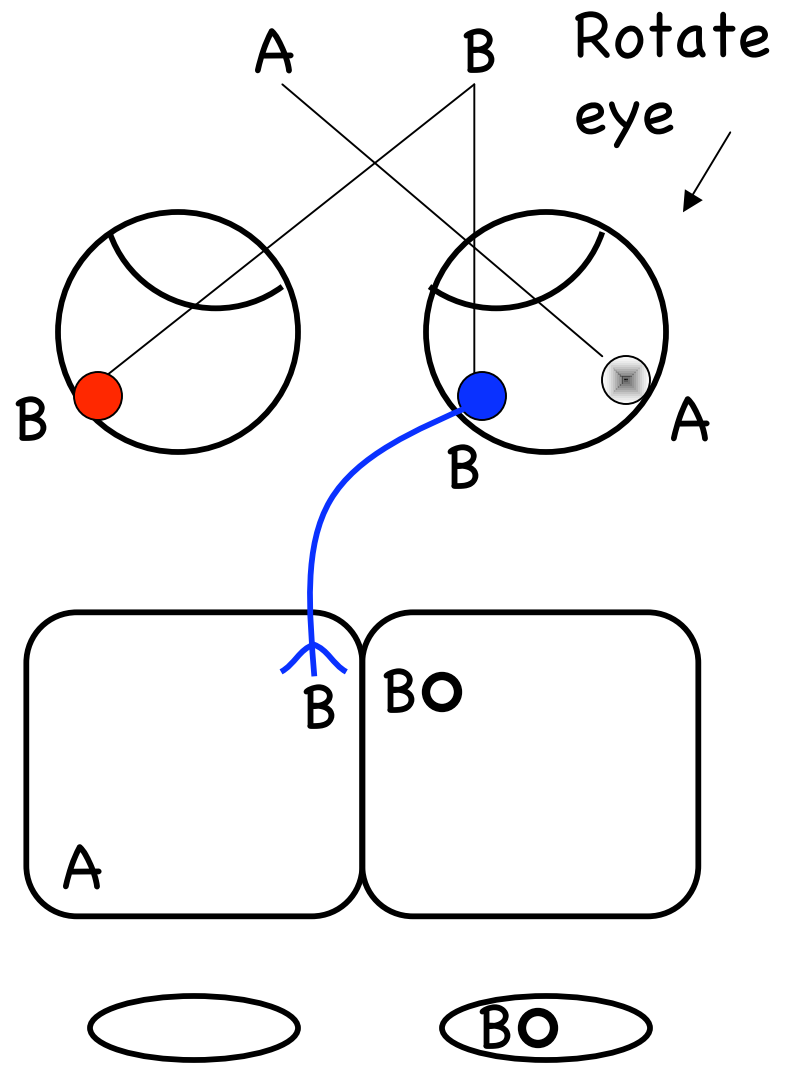
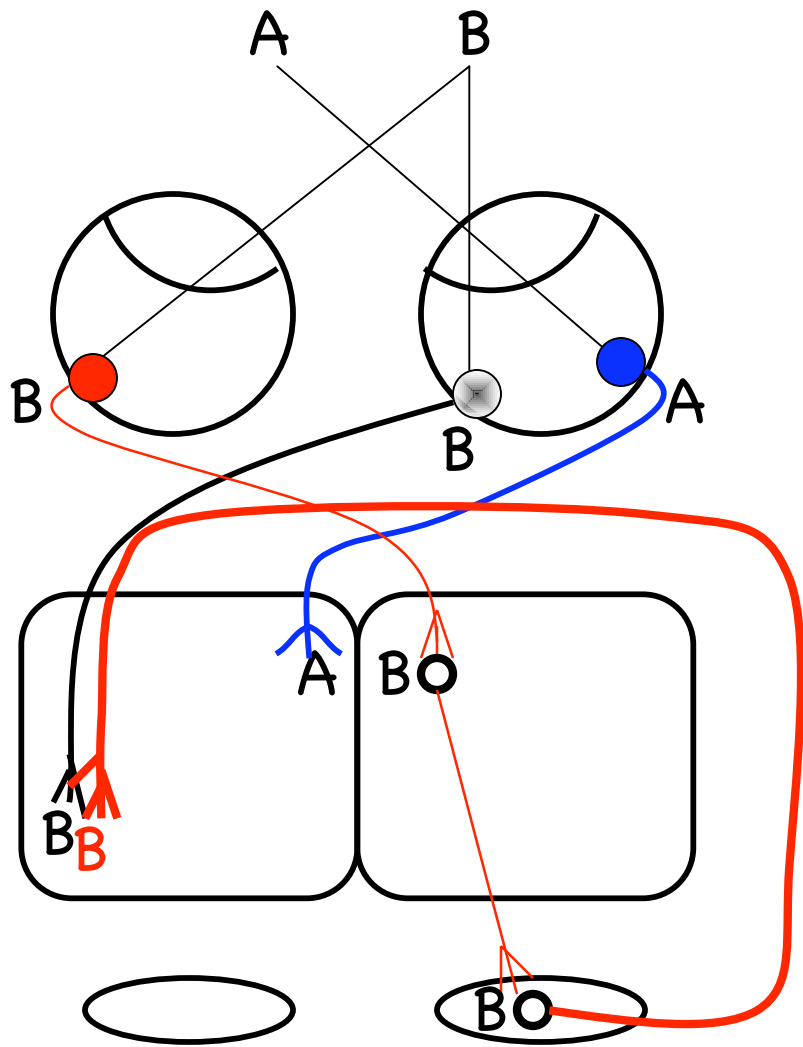
- Eye rotation experiments show that visual input is essential for binocular maps.

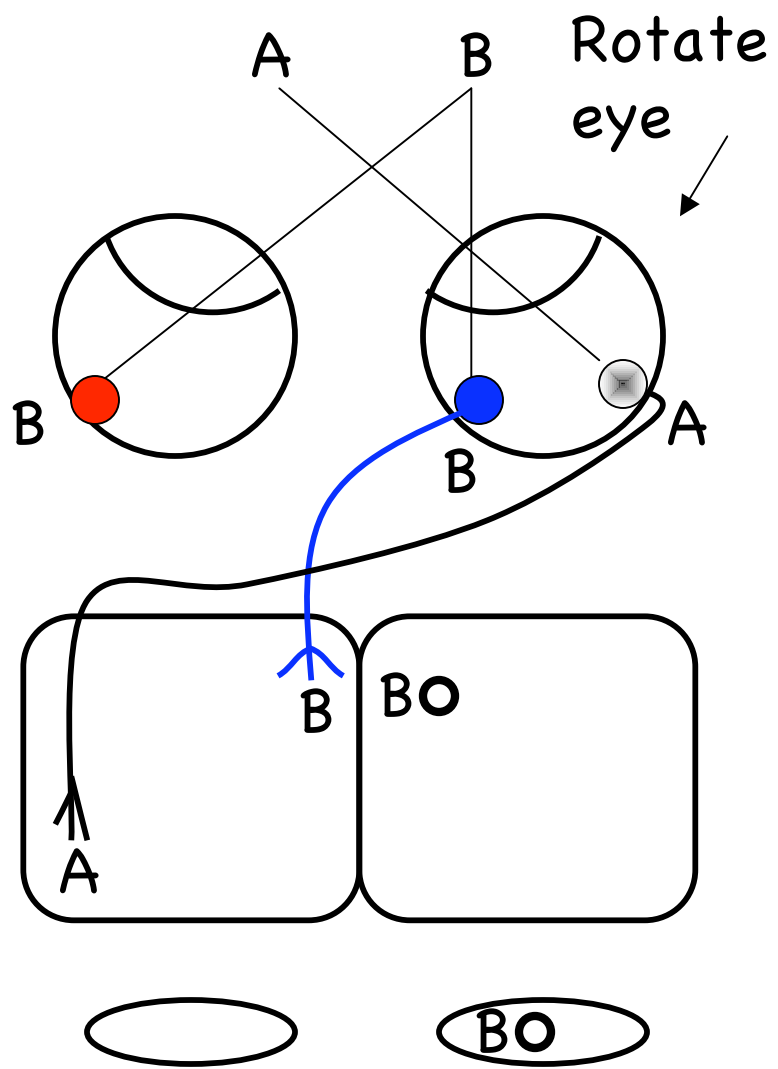
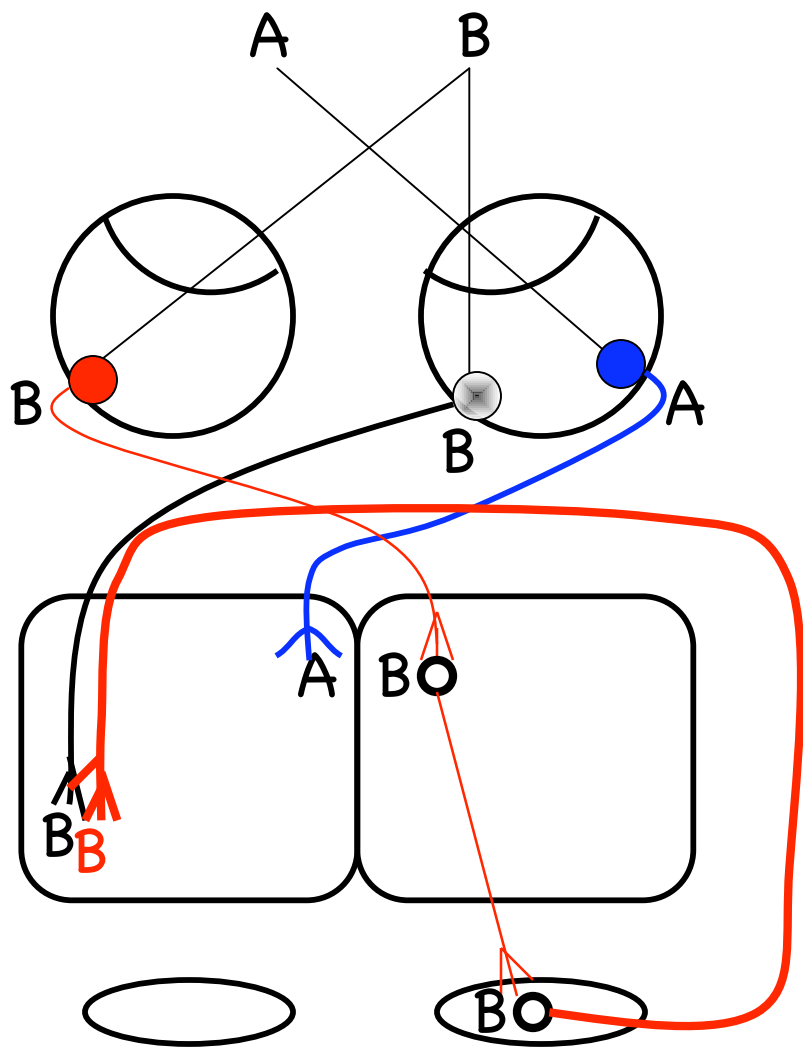
# Eye rotation

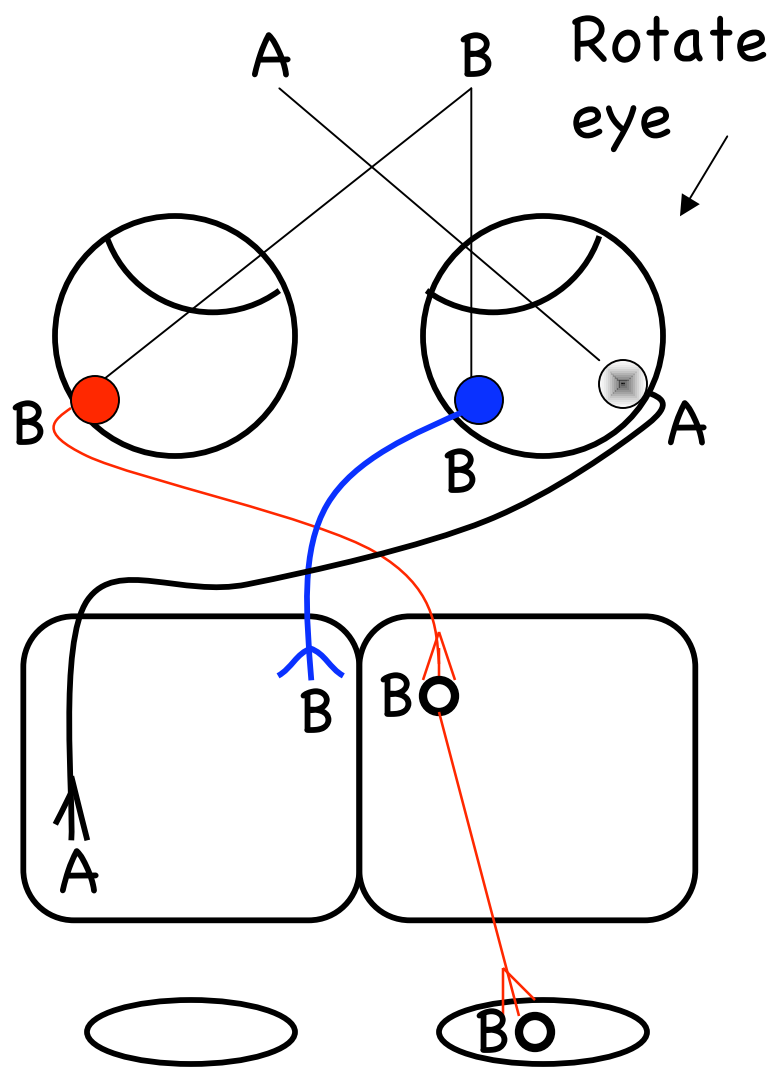
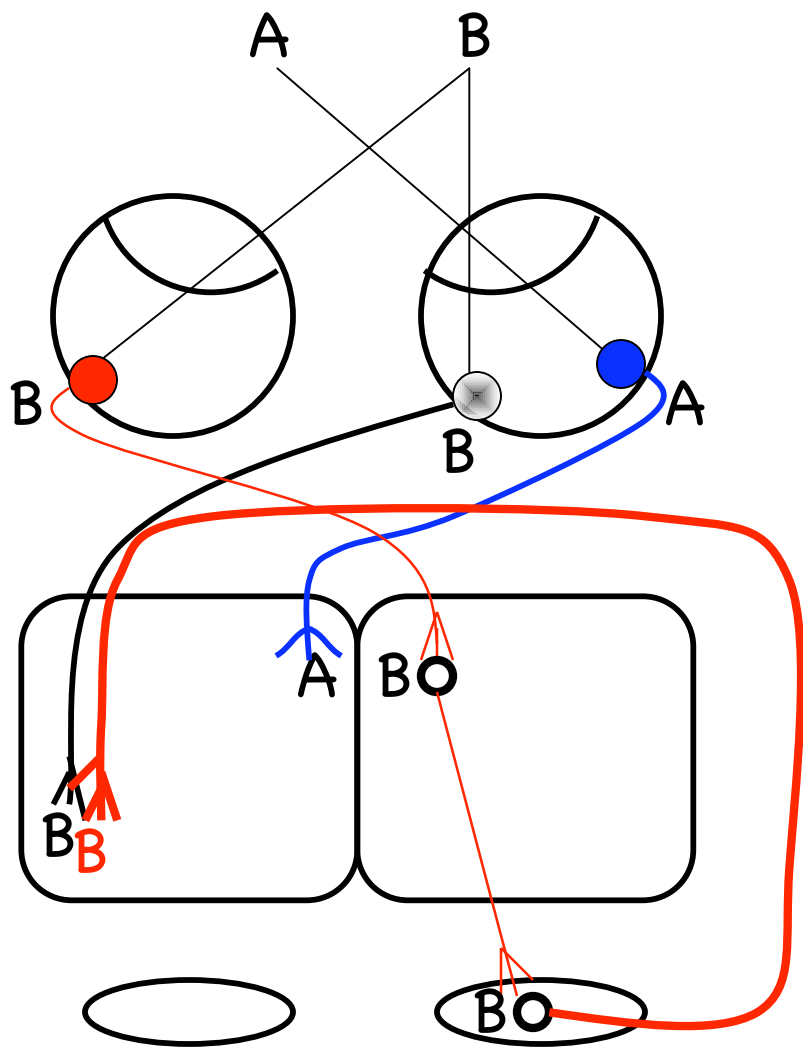
- Eye rotation experiments show that visual input is essential for binocular maps.
- Rotating one eye in a tadpole leads to rewiring of connections.

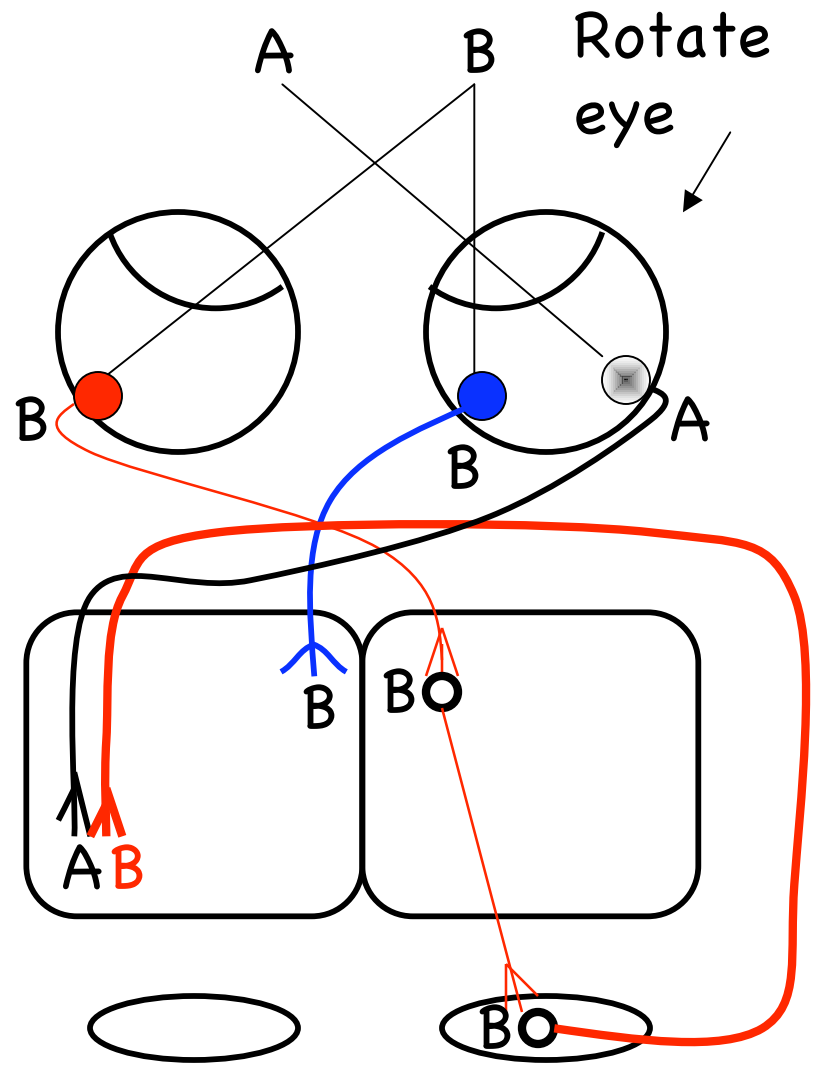
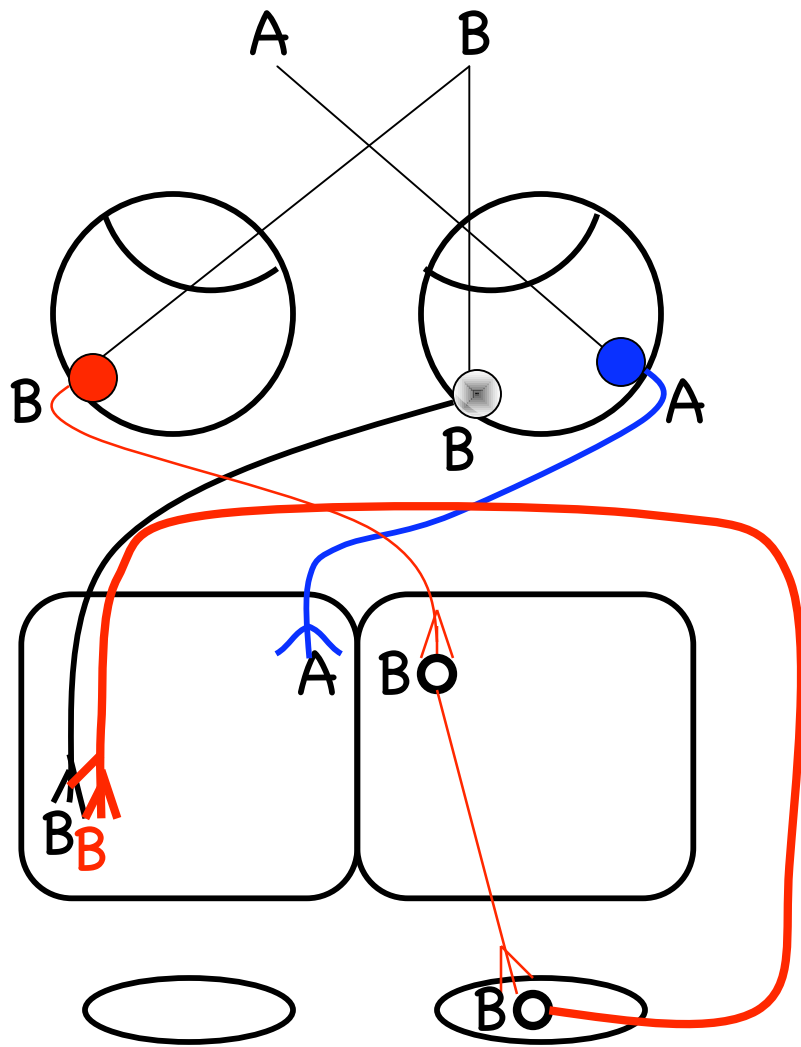


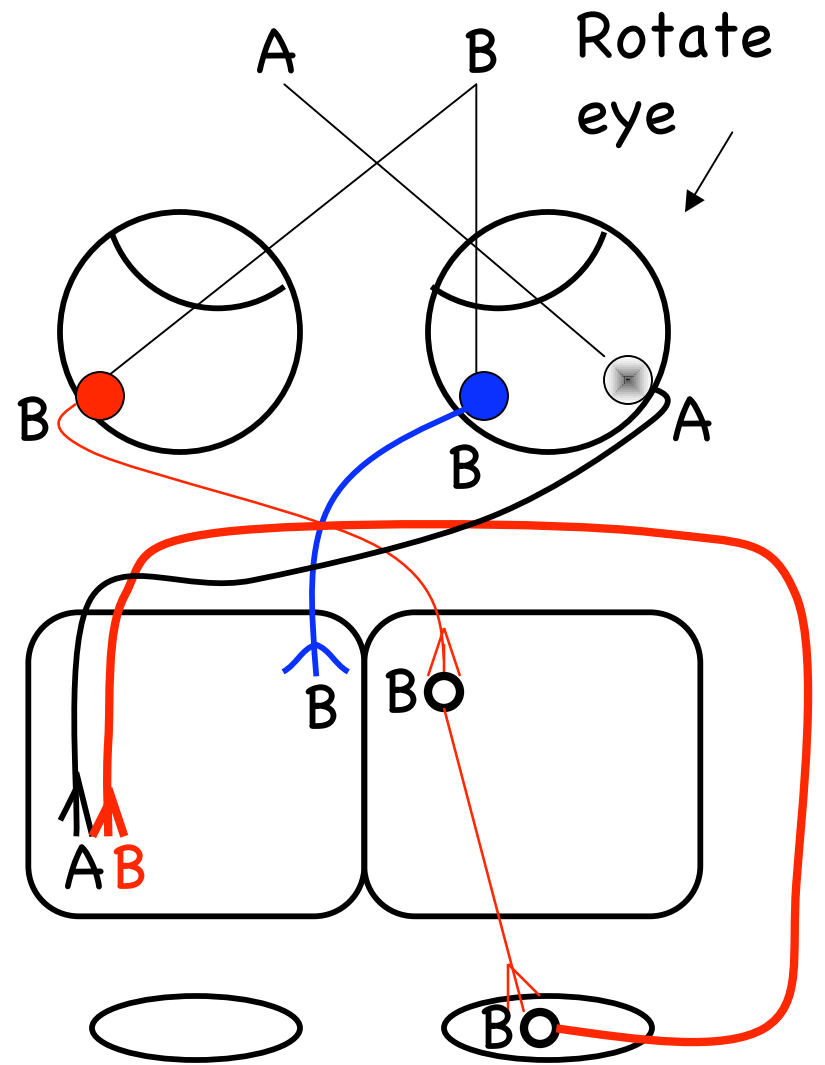
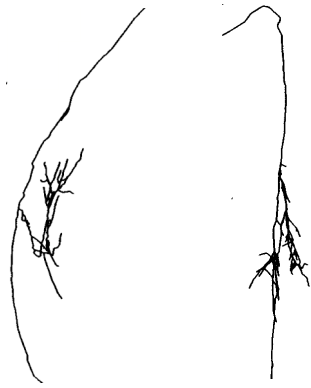


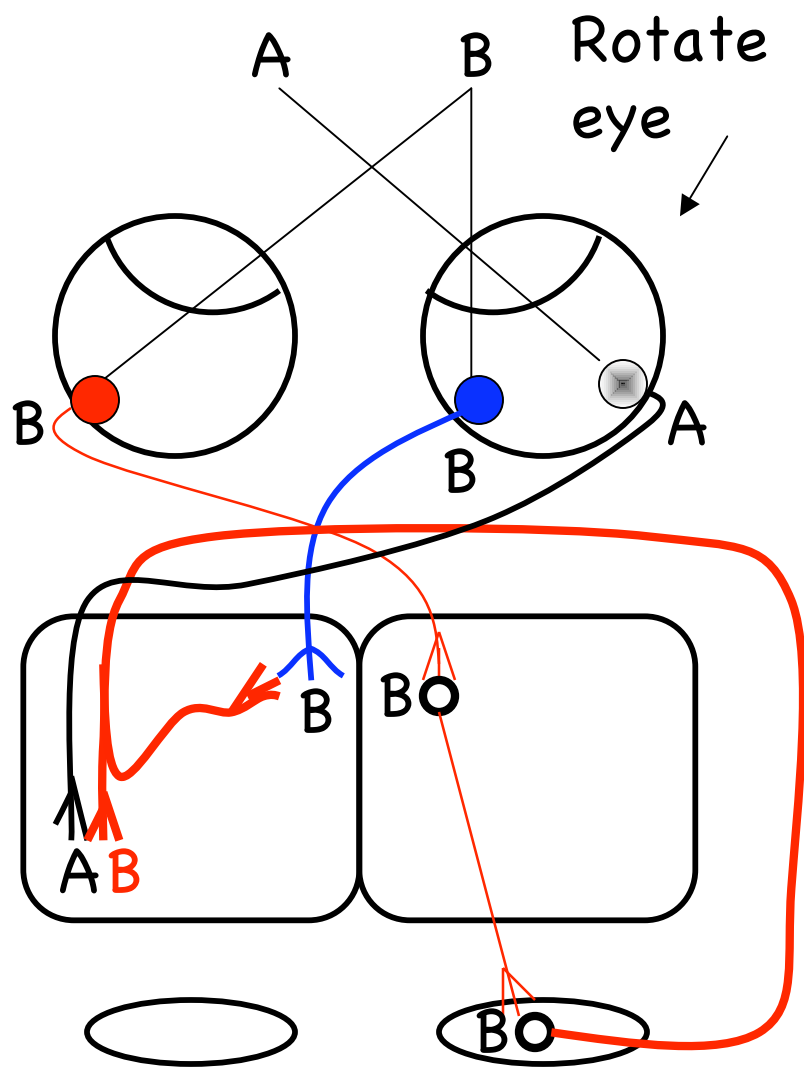


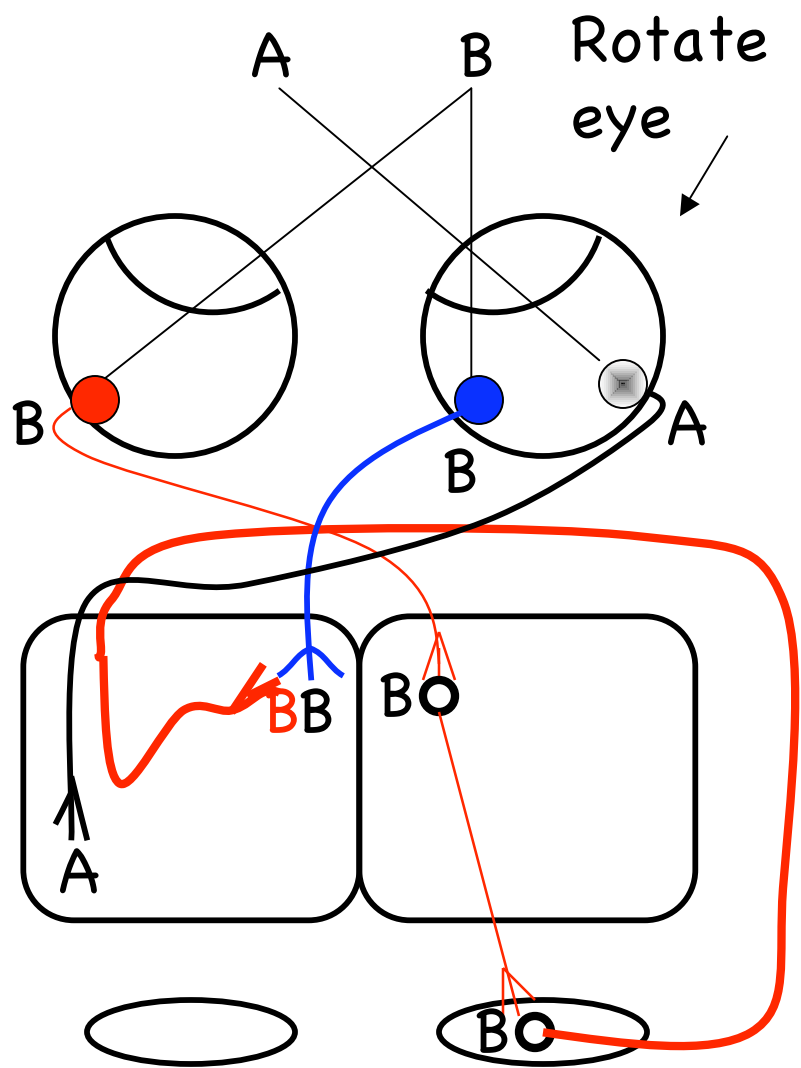












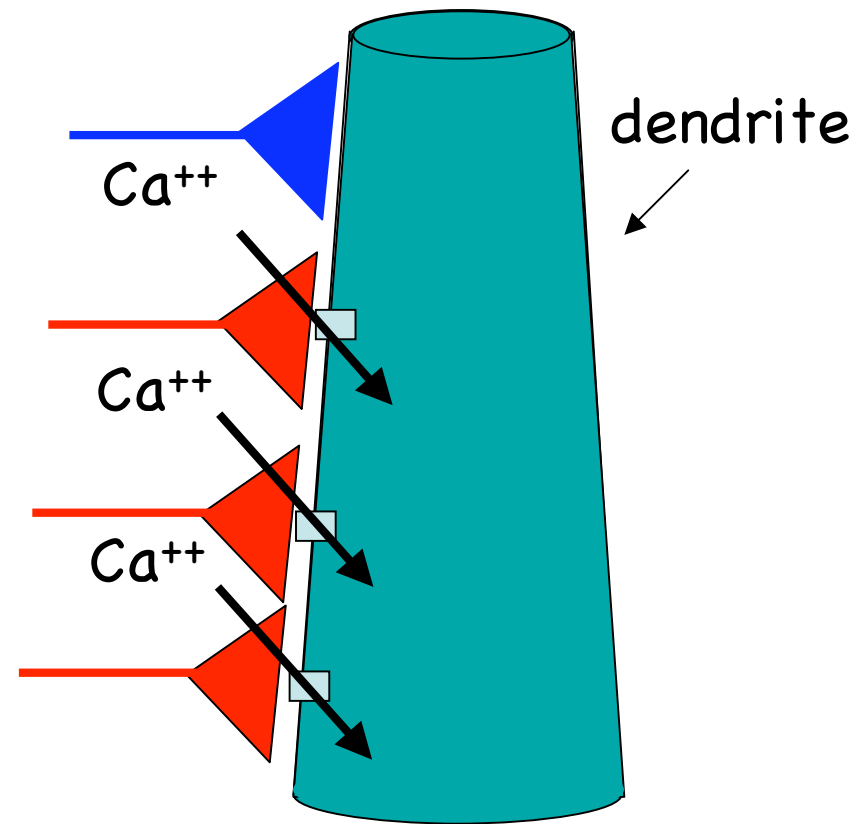
# What are the mechanisms?

- NMDA-type glutamate receptors are essential.



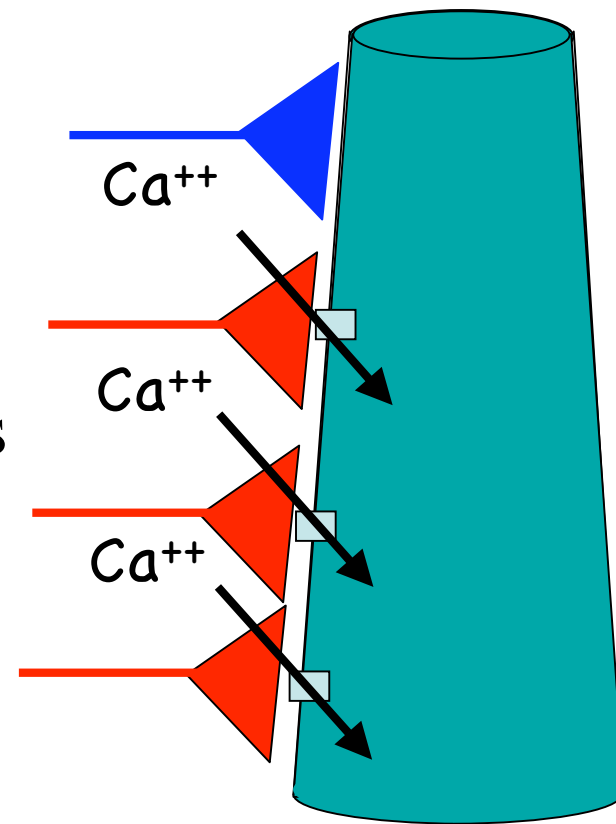
# Why are NMDA receptors important?

- Retinotectal axons release the neurotransmitter glutamate.



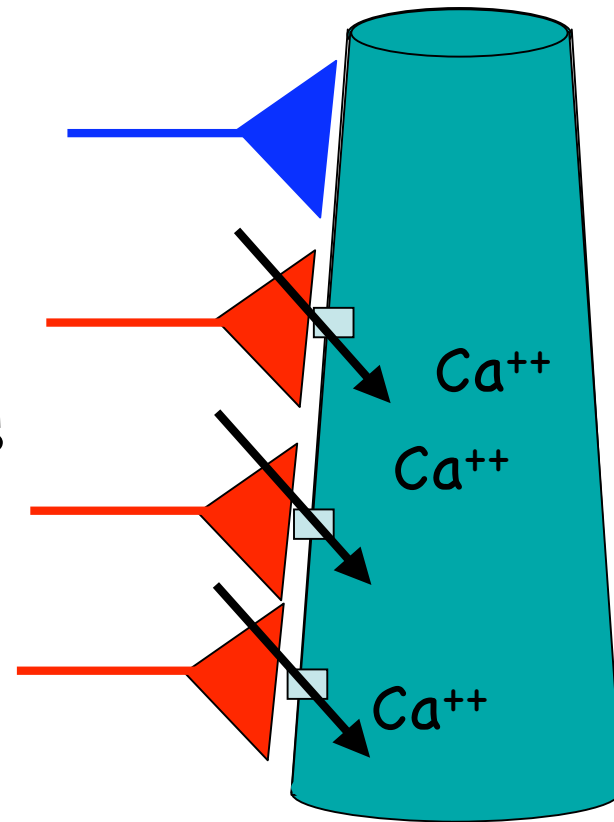
# Why are NMDA receptors important?

- Retinotectal axons release the neurotransmitter glutamate.
- Strong excitatory synaptic activity opens up NMDA-type glutamate receptors, which admit calcium.



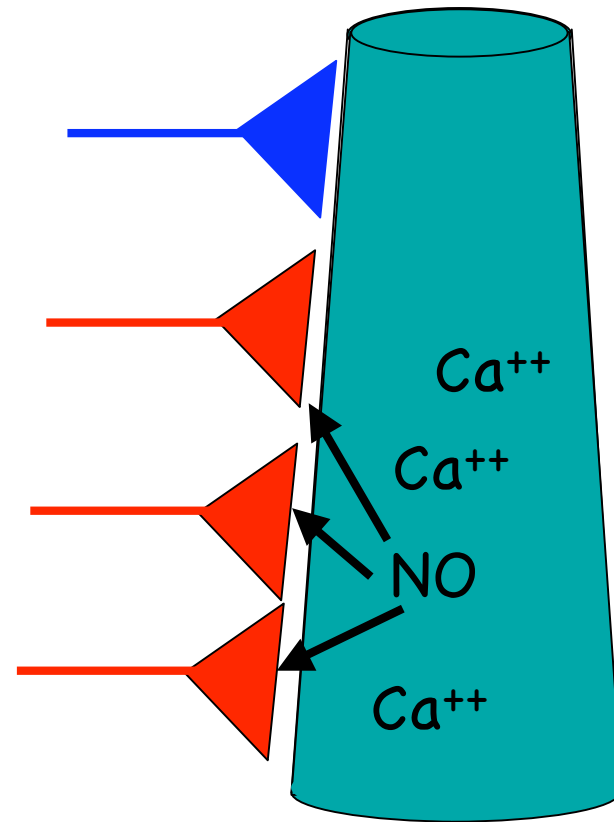
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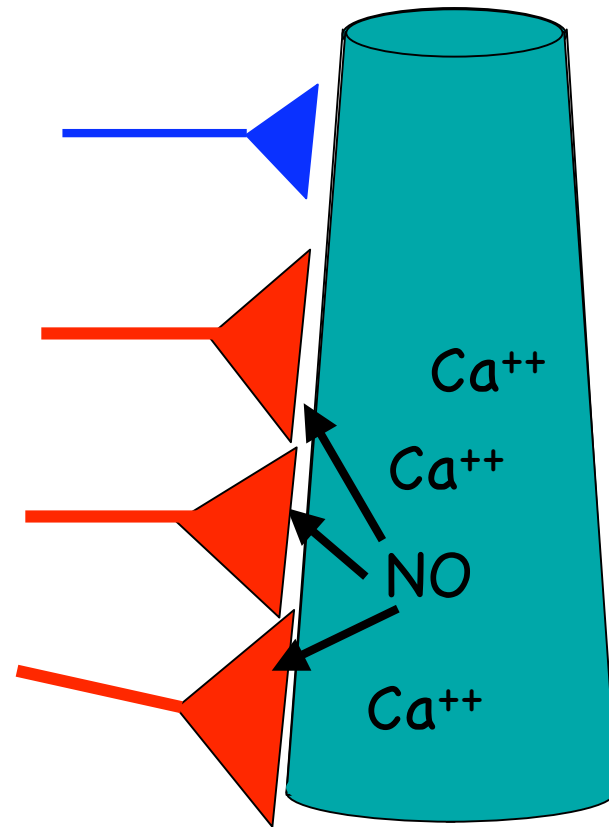
# Why are NMDA receptors important?

- If there's enough calcium, it triggers production and release of a retrograde trophic factor such as nitric oxide.

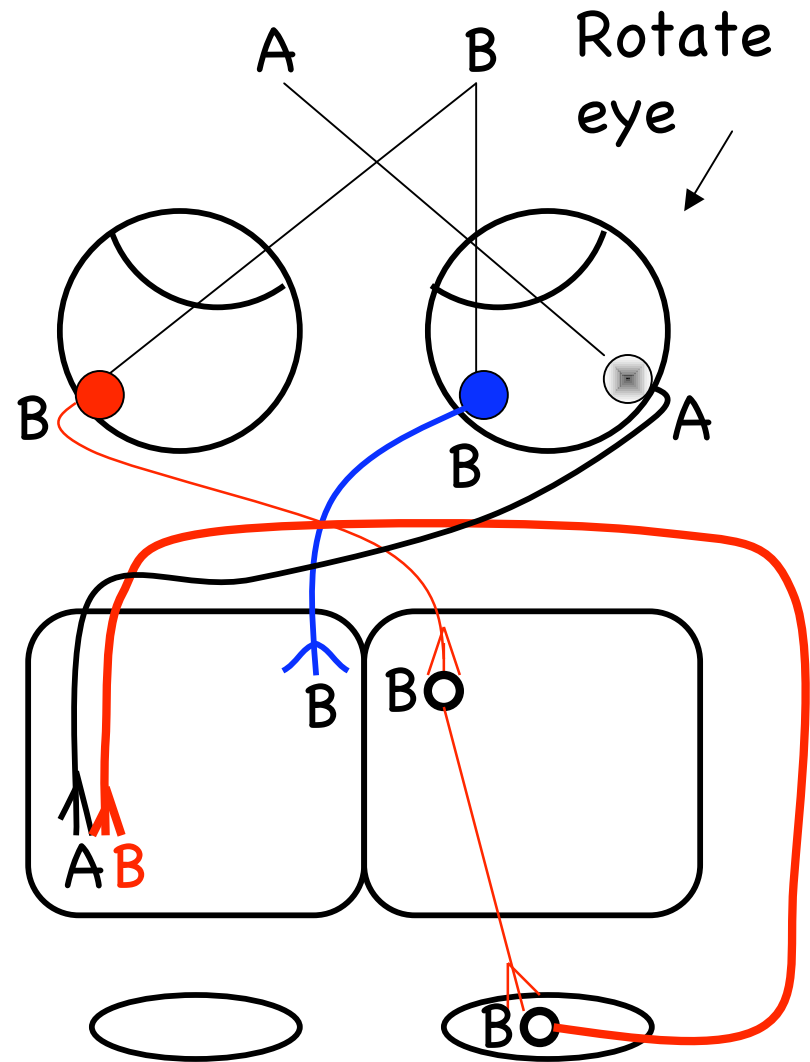


# Why are NMDA receptors important?

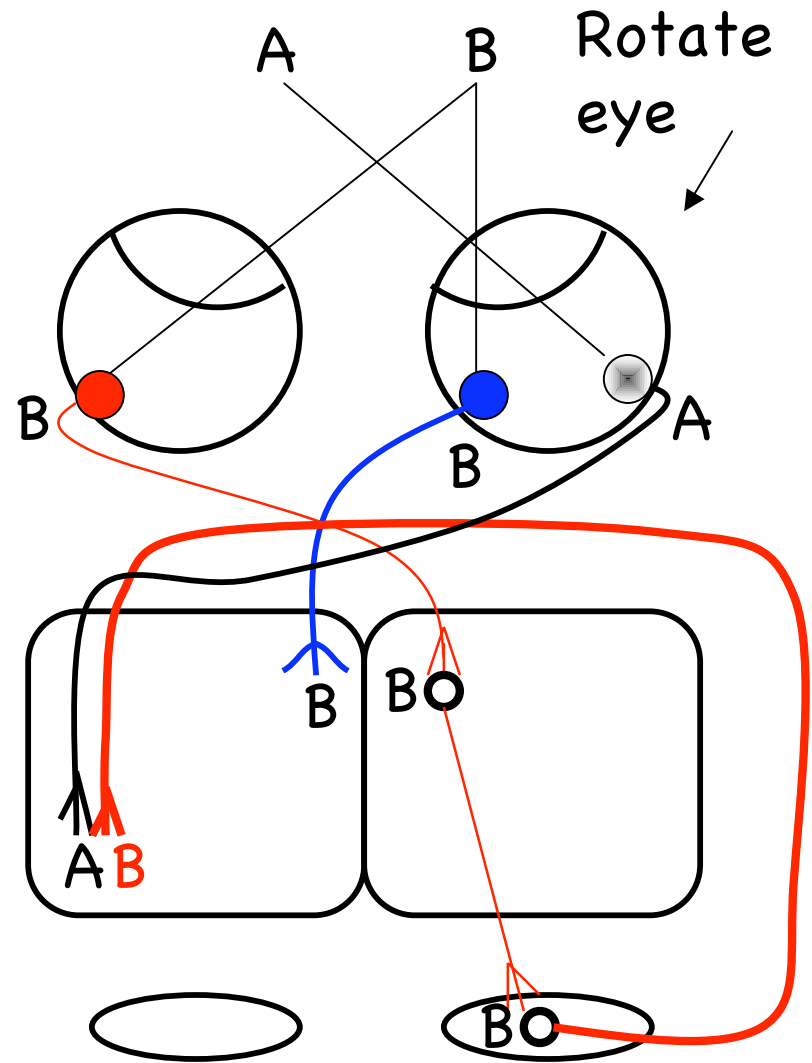
- The **active synapses** get stronger and bigger
- The **other synapses** get weaker and smaller.



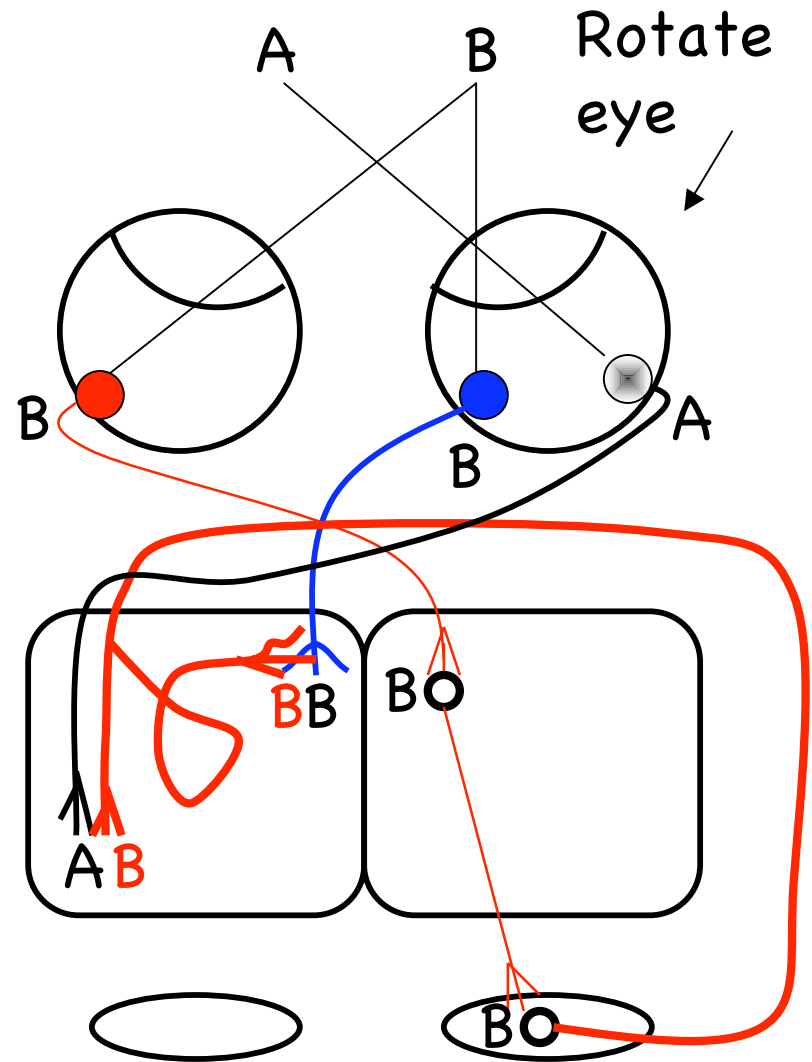
- Blocking NMDA receptors prevents reorganization.



NMDA in adults restores plasticity.

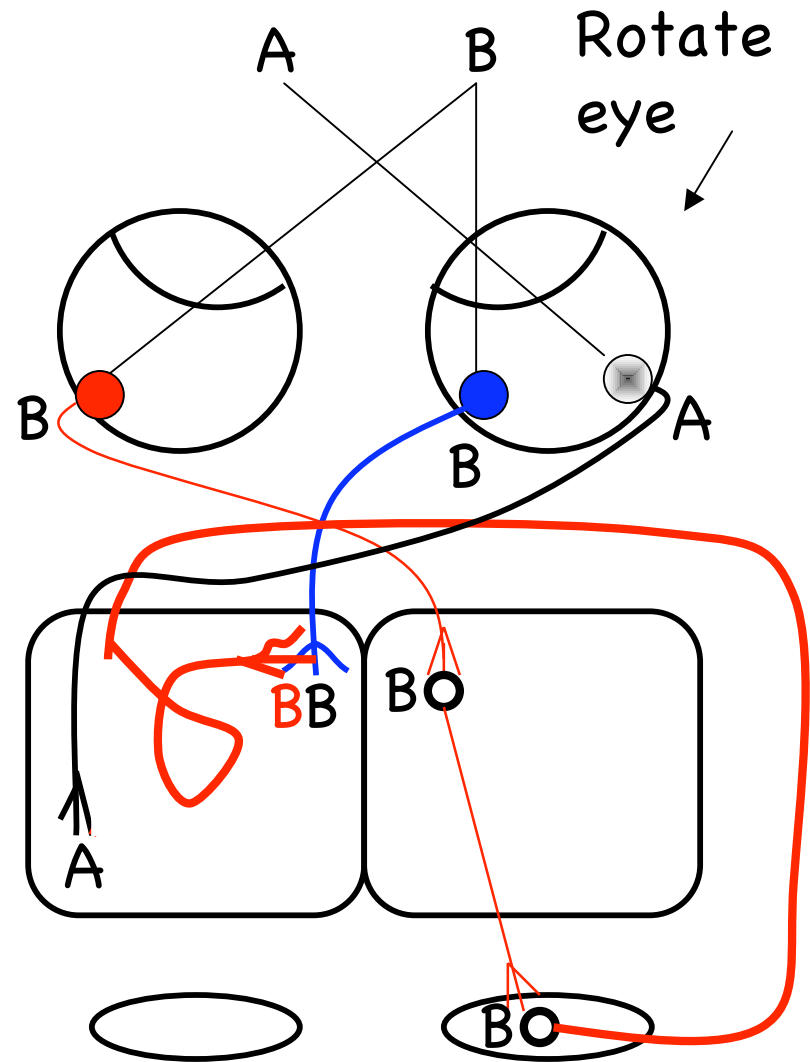


NMDA in adults restores plasticity.



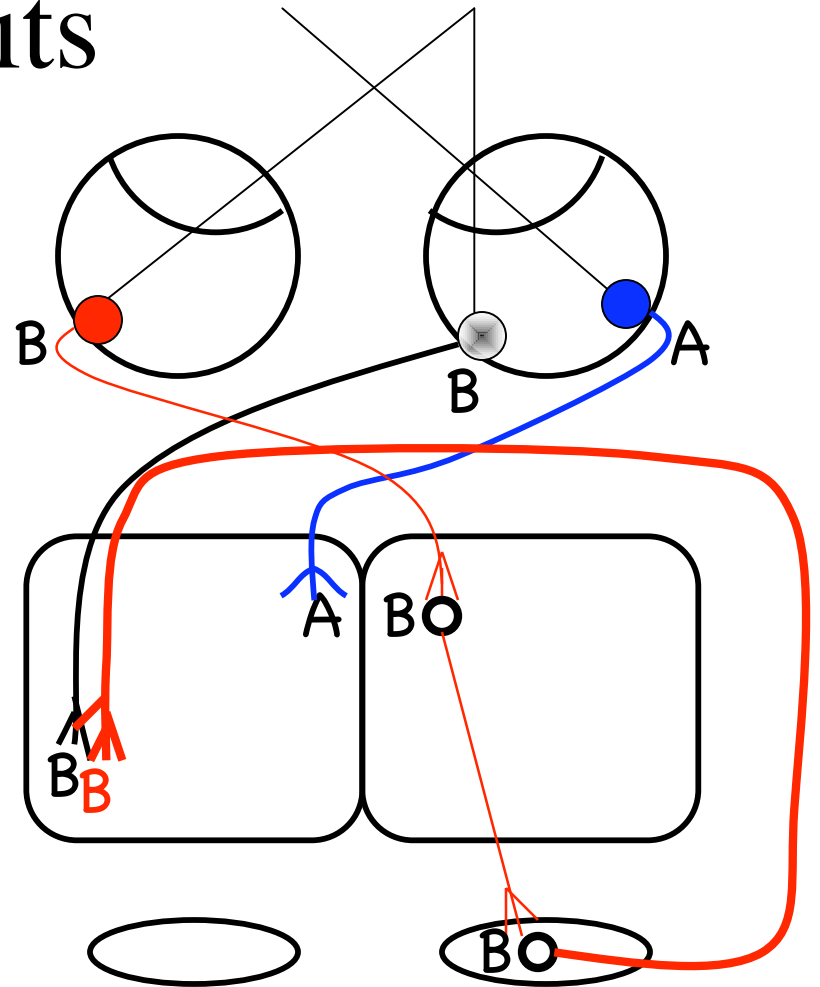


NMDA in adults restores plasticity.



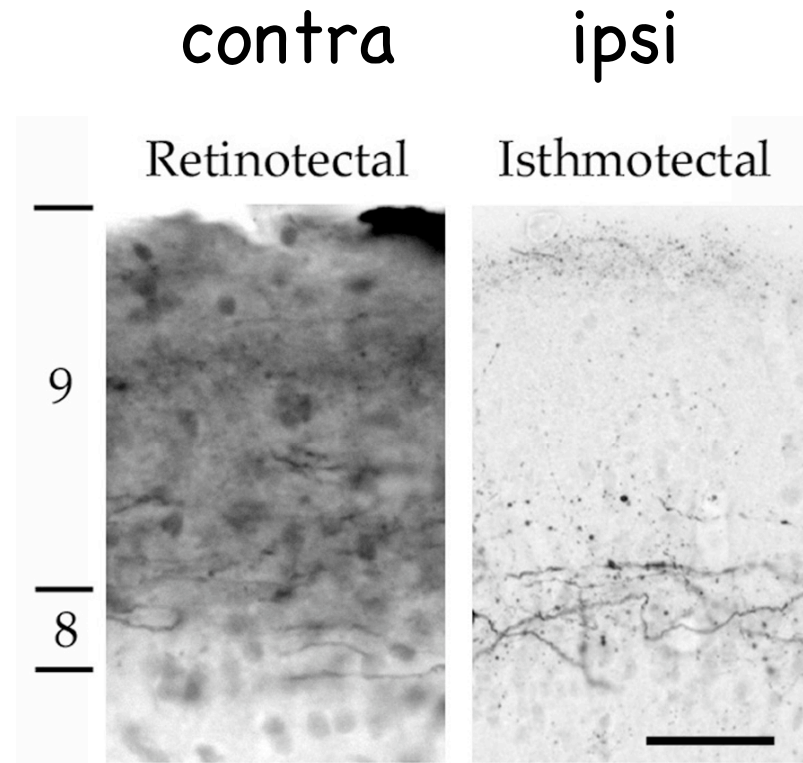
# Circuits

- It seemed likely that the two sets of axons would synapse on the same dendrites, but they don't.



# Circuits

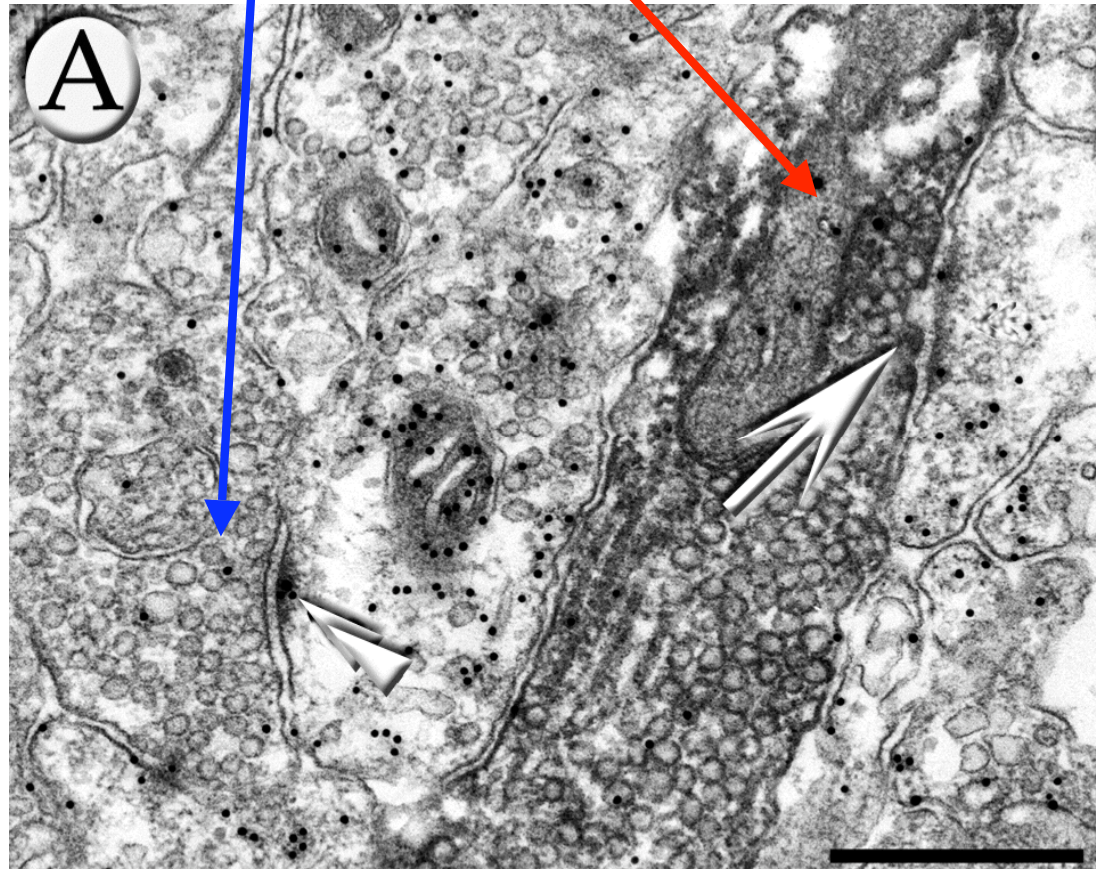
- It seemed likely that the two sets of axons would synapse on the same dendrites, but they don't.



# Connections?

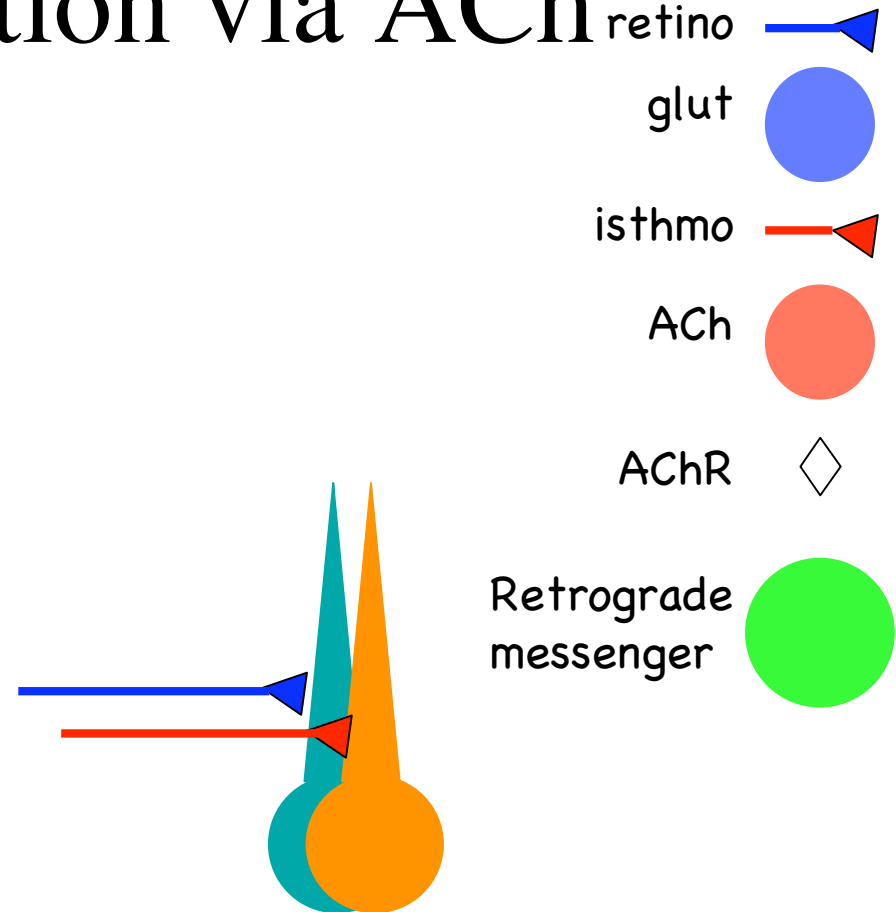
- We used electron microscopy to look for connections from retinotectal and isthmotectal axons onto common dendritic targets.

An **isthmotectal axon** giving a **retinotectal axon** the cold shoulder



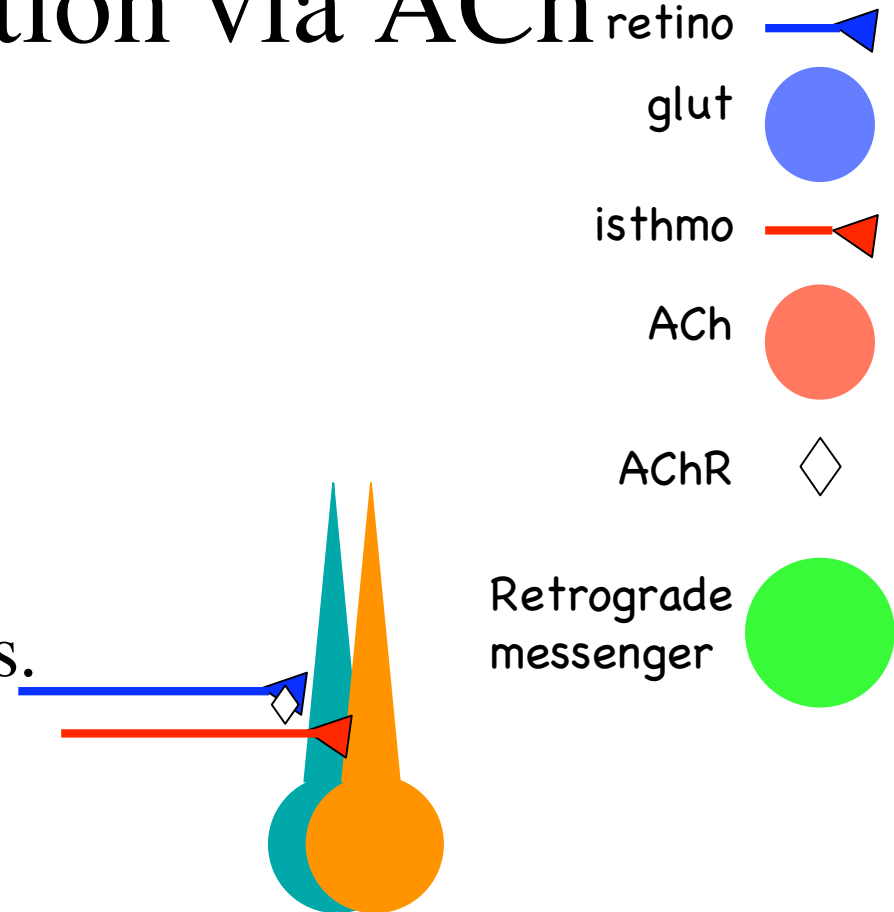
# Model incorporating indirect communication via ACh

- Retinotectal and isthmotectal axons terminate on different cells.



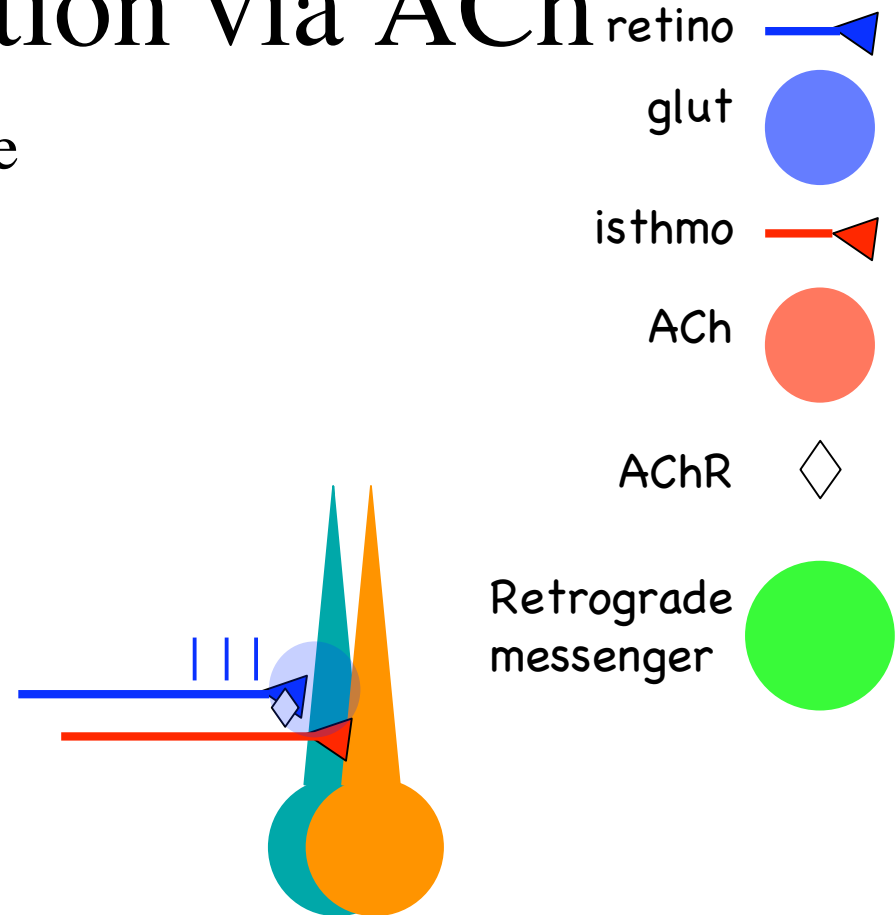
# Model incorporating indirect communication via ACh

- Retinotectal and isthmotectal axons terminate on different cells.
- There are nicotinic acetylcholine receptors on retinotectal terminals.



# Model incorporating indirect communication via ACh

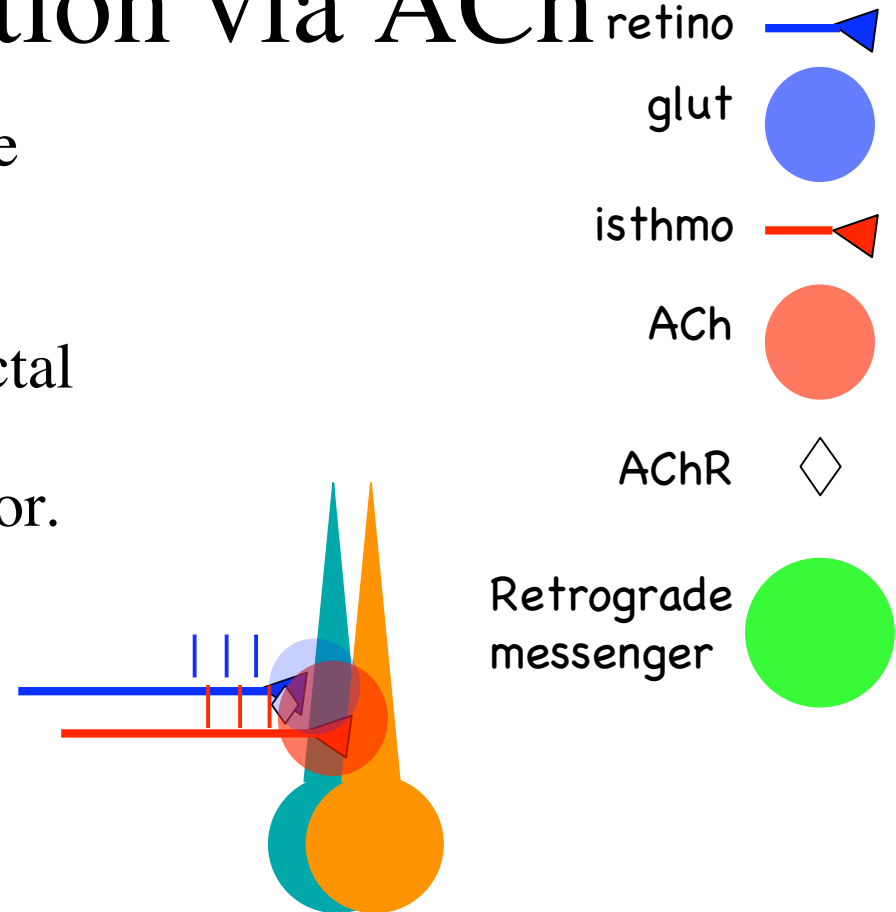
- A visual stimulus causes the retinotectal axon to release glutamate.





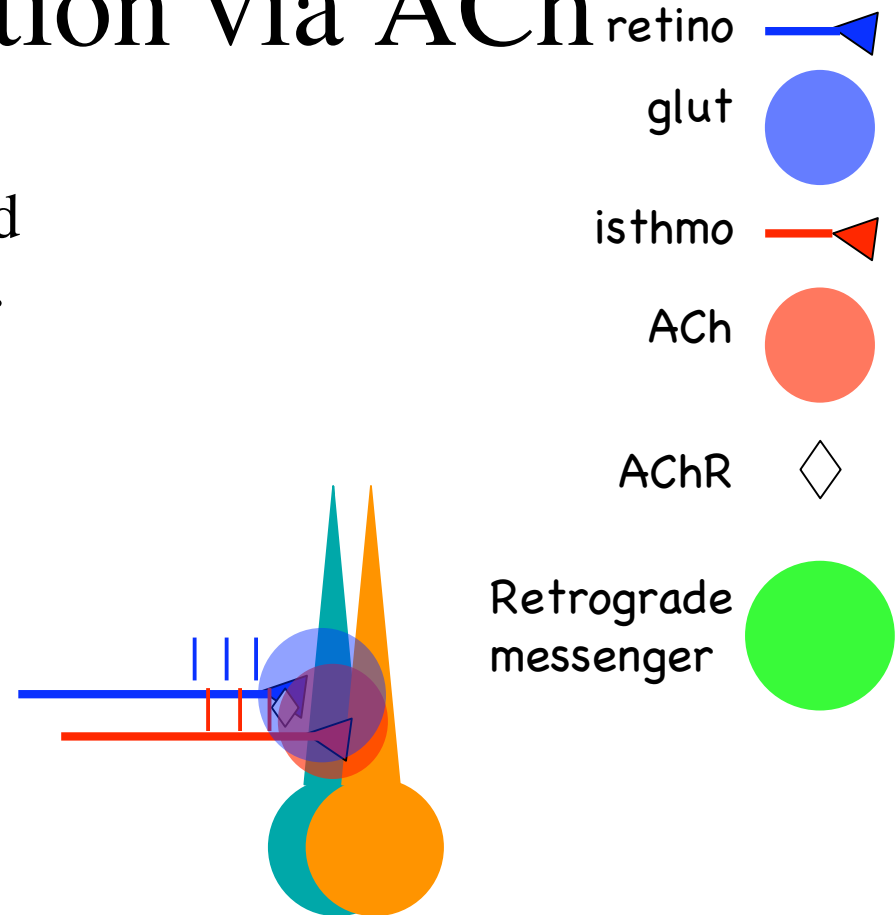
# Model incorporating indirect communication via ACh

- A visual stimulus causes the retinotectal axon to release glutamate.
- 10 msec later, the isthmotectal axon releases ACh, which reaches the nicotinic receptor.



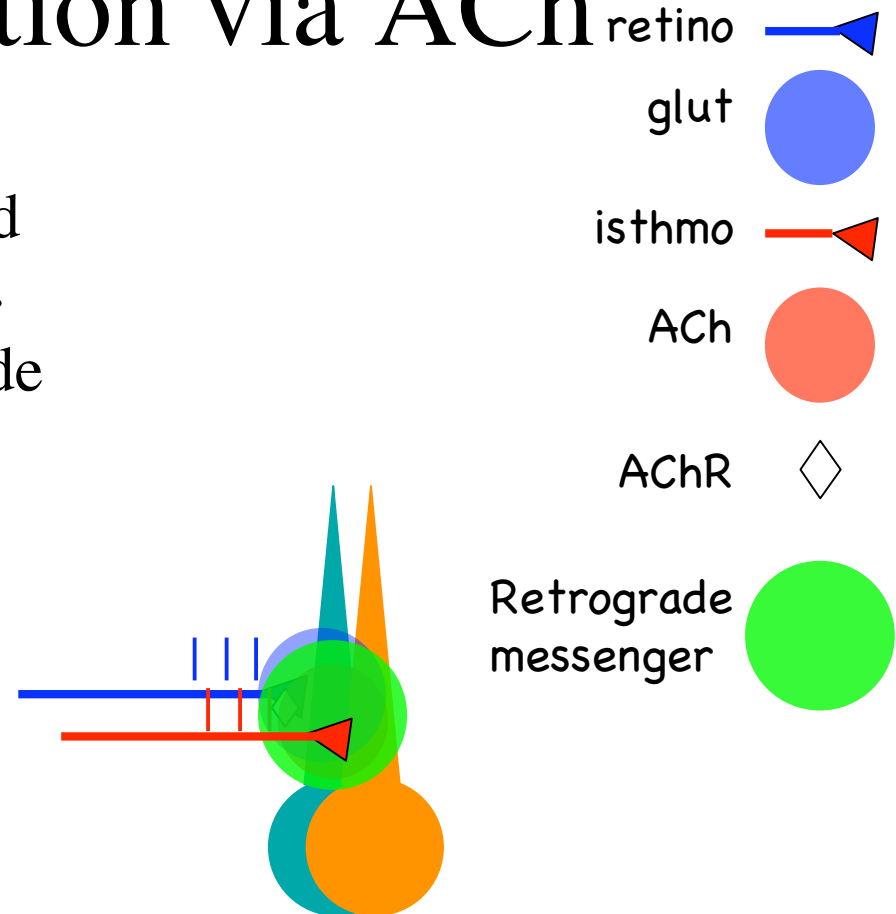
# Model incorporating indirect communication via ACh

- The retinotectal axon then releases more glutamate and NMDAR activity increases.



# Model incorporating indirect communication via ACh


- The retinotectal axon then releases more glutamate and NMDAR activity increases.
- The cell releases a retrograde messenger, stabilizing the isthmotectal axon.



# Model incorporating indirect communication via ACh

- What is the retrograde messenger?

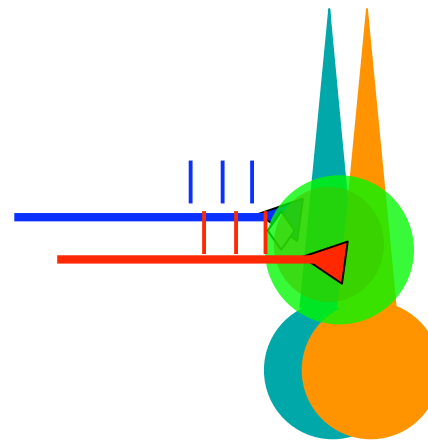
retino 

isthmo 

ACh 

AChR 

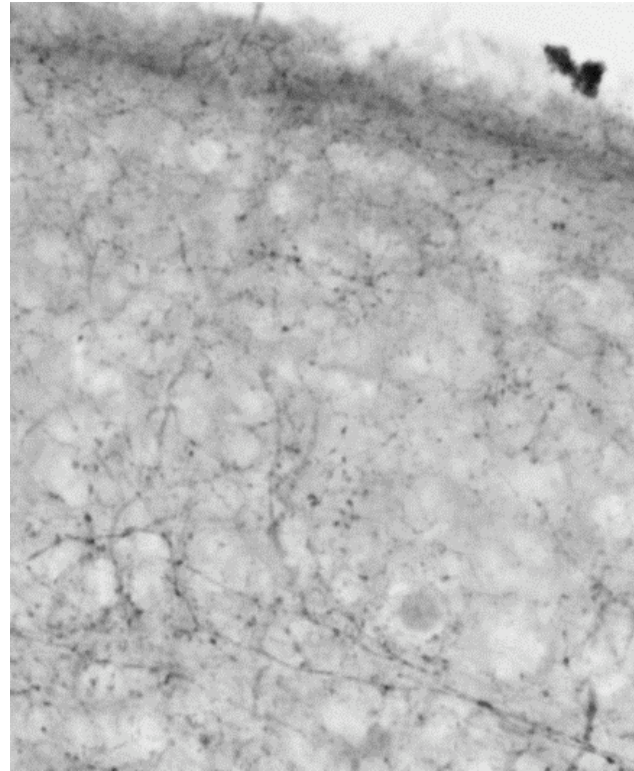
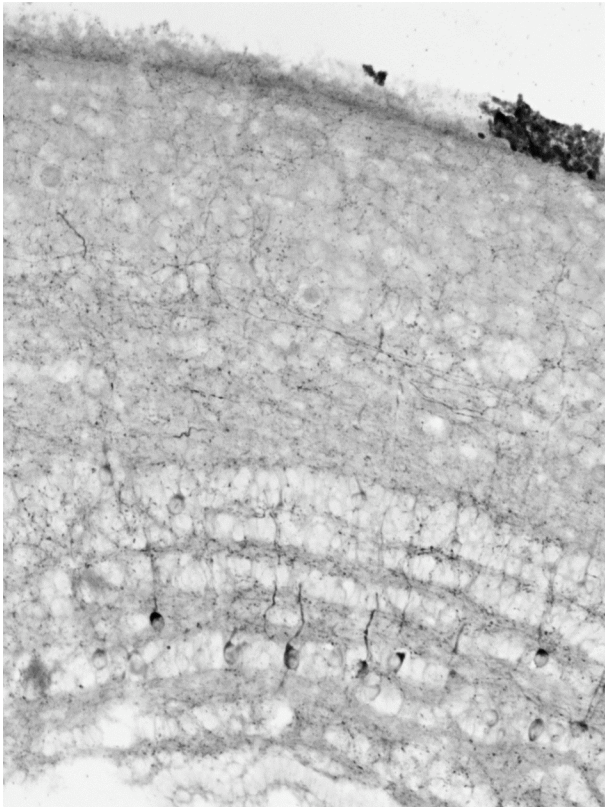
Retrograde messenger 



# Nitric oxide is a good possibility



- It is synthesized by tectal cells.

NO is synthesized by tectal cells.



# One way that axons respond to NO is to produce cGMP

- We used one set of antibodies to label isthmotectal axons (green) and another set of antibodies (red) to label cGMP.
- The yellow color shows that the two stains show up in the same place.
- Therefore, isthmotectal axons can respond to nitric oxide

cGMP      ChAT  
      



# Summary

- NMDA receptors are essential for establishing matching binocular maps in *Xenopus* tectum.



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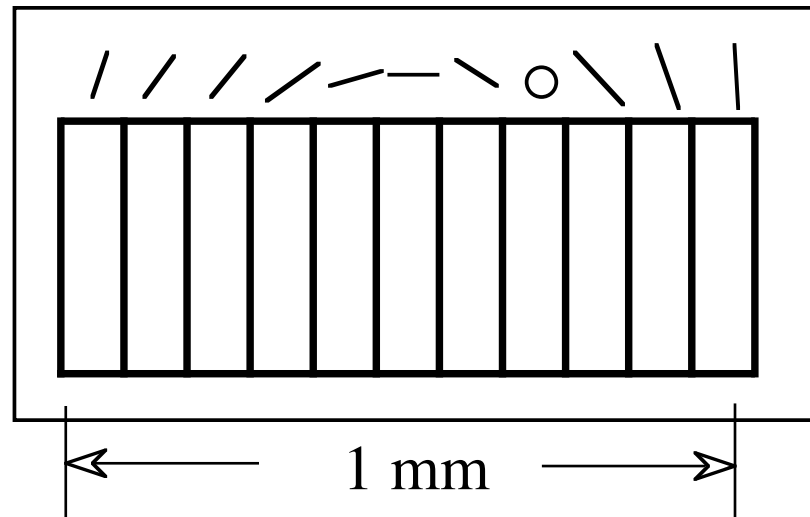
- NMDA receptors are essential for establishing matching binocular maps in *Xenopus* tectum.
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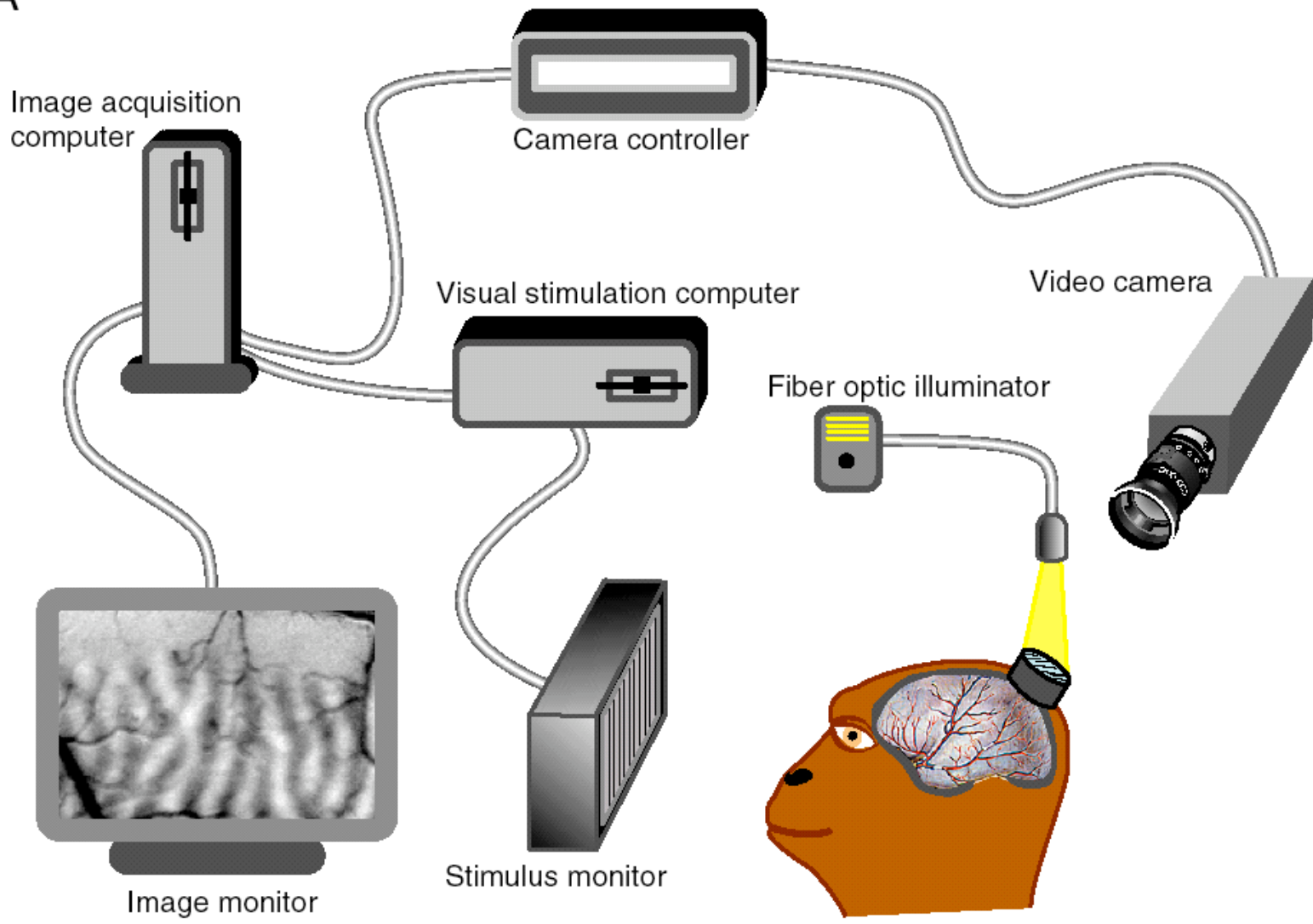
- NMDA receptors are essential for establishing matching binocular maps in *Xenopus* tectum.
- Correlated visual input determines where isthmotectal axons terminate, but the specific timing requirements still need to be discovered.
- The two sets of inputs don't communicate by terminating on the same cells, but probably communicate indirectly.
- Nitric oxide is a good candidate retrograde messenger.

# Organization of orientation columns

- Adjacent columns usually have cells with slightly different orientation preferences.
- This orderly pattern is interrupted by occasional “color blobs” -- columns of color-selective cells with center-surround receptive fields.

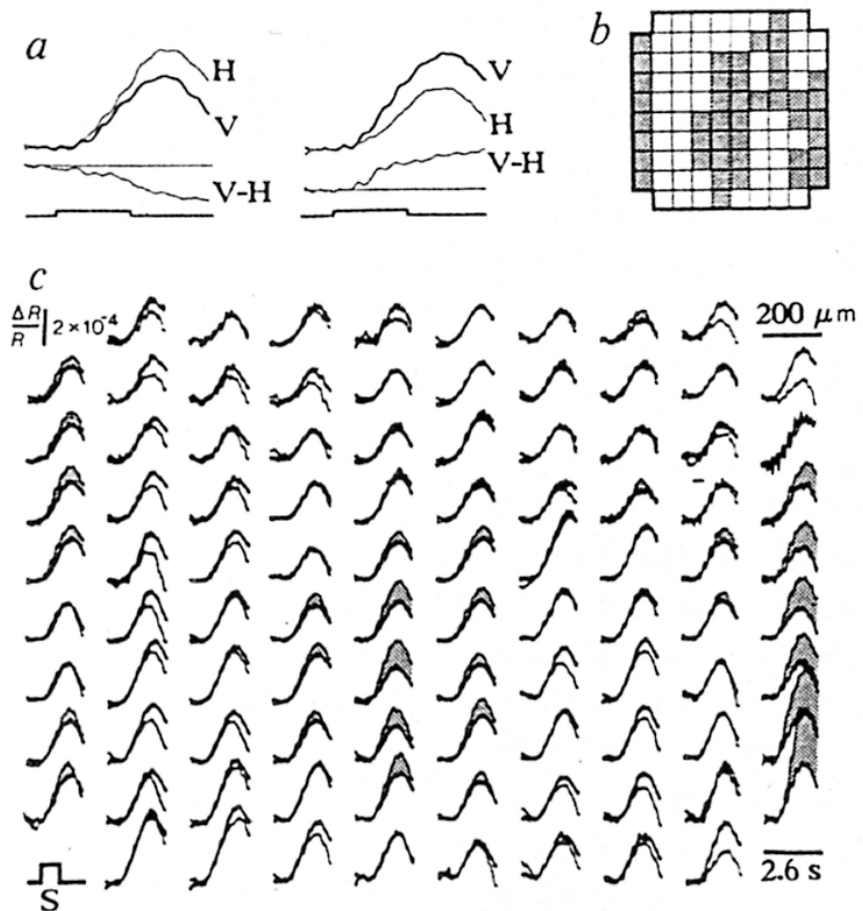


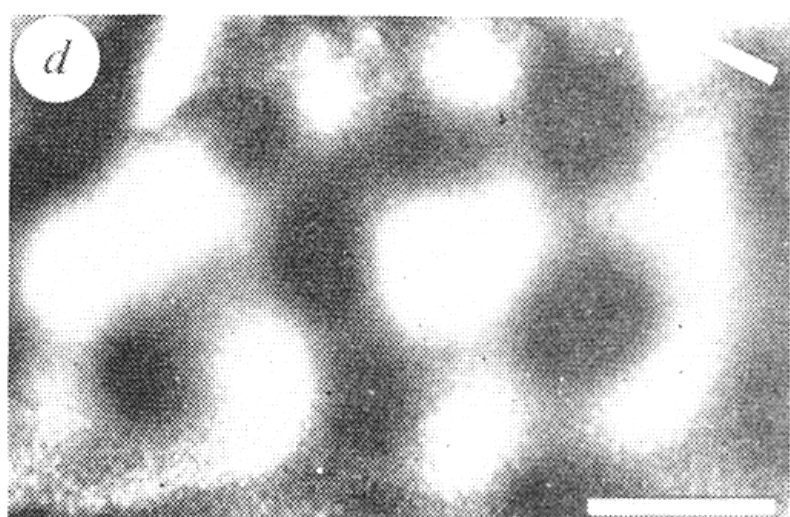
A



# *In vivo* imaging

- Present horizontal bars.
- Collect image intensity data.
- Repeat with vertical bars.
- Subtract the difference on a point-by-point basis.





Orientation columns form a “pinwheels” with 360° of orientations surrounding a zone of non-oriented cells.

Center: non-oriented, color ‘blobs’.

