- Cell proliferation
- Cell specialization
- Cell interactions
- Cell movement

→ All these processes happen at once in a developing embryo

==> To understand basic strategies, we need to narrow our focus

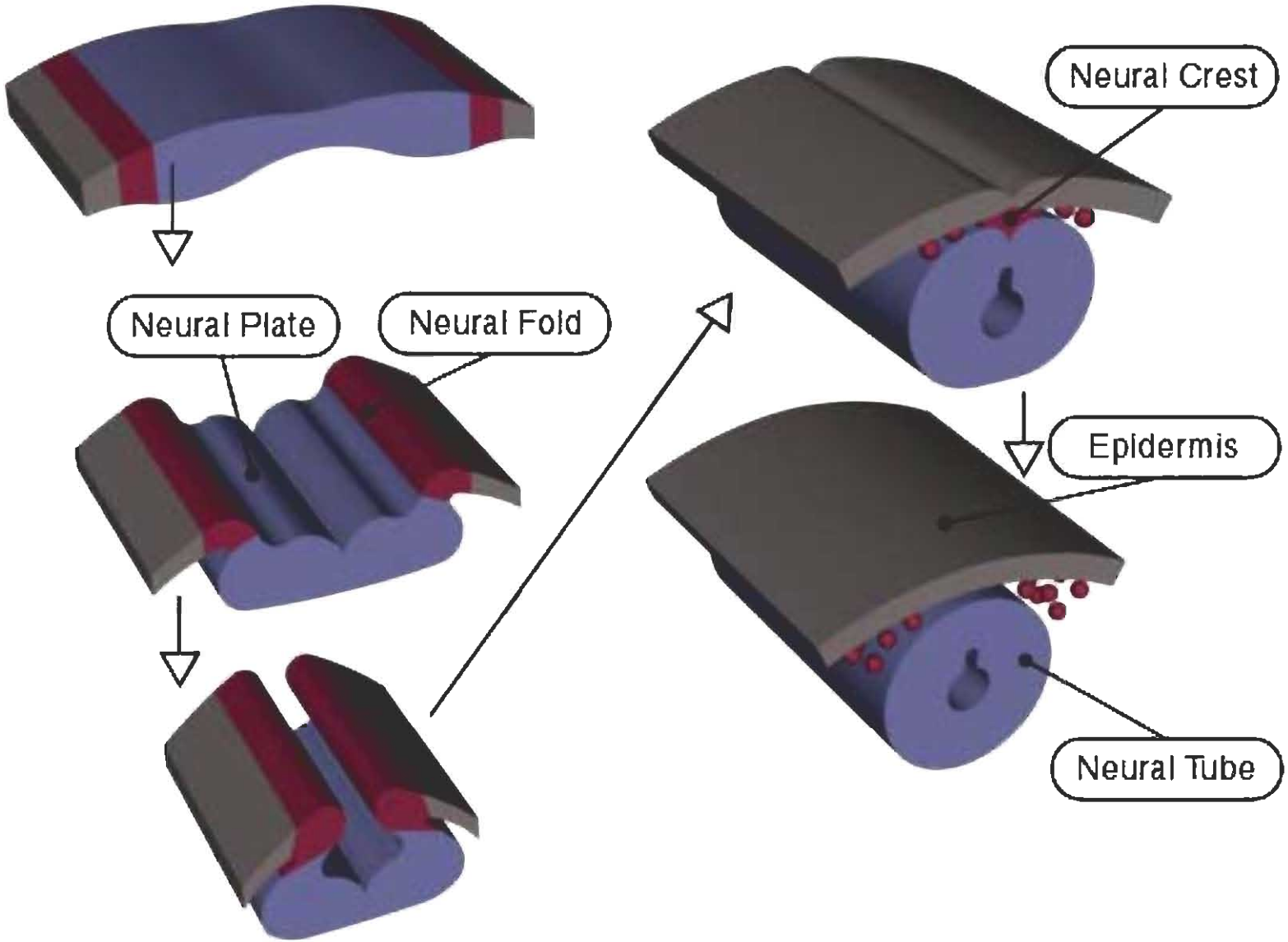
Gastrulation
Neurulation
Later Development

See Gilbert, Developmental Biology, Sinauer

The result of the Gastrulation is the creation of the three germ layers:

Ectoderm
Endoderm
Mesoderm

Neurulation -> the formation of the nervous system from the ectoderm


Neural Plate
Neural Fold
Neural Crest
Epidermis
Neural Tube

Blastula --> Gastrulation --> Neurulation --> Later development

- Ectoderm - CNS
- Endoderm
- Mesoderm

When and where does the ear originate?

→ The first morphological manifestation is a thickening of the ectoderm near the hindbrain = otic placode

→ Does this mean that the process starts with placode formation?
-> check out Groves and Bronner-Fraser (2000)

“Later Development”

Asymetric cell division

Cell signaling:

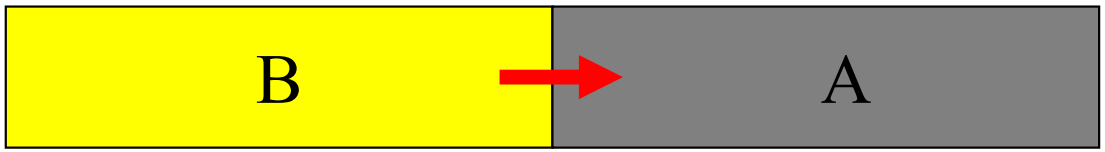
- Inductive signal
- Morphogen
- Lateral Inhibition

- Cell survival
- Cell death

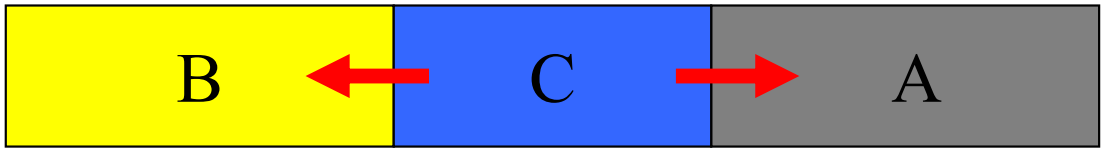
- Axonal migration

Sequential induction

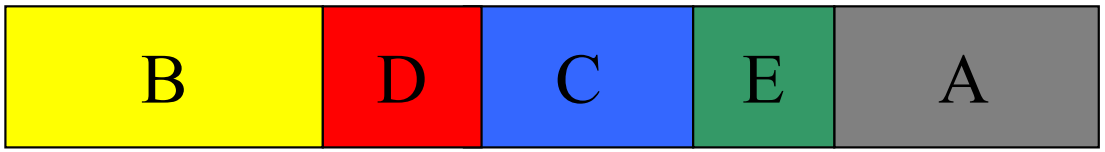
Simple pattern



C is induced by signal
From B acting on A

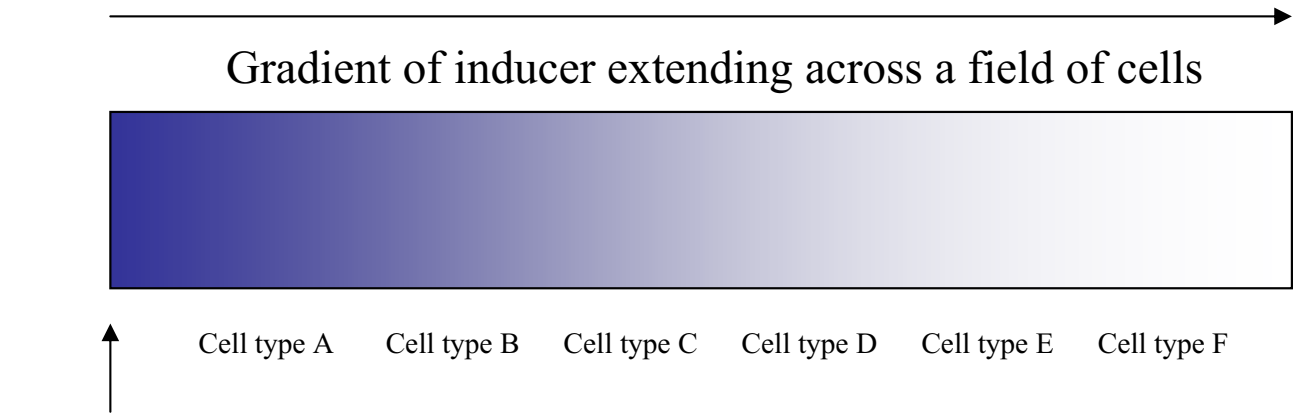


D and E are induced by
Signal from C acting on
A and B, respectively

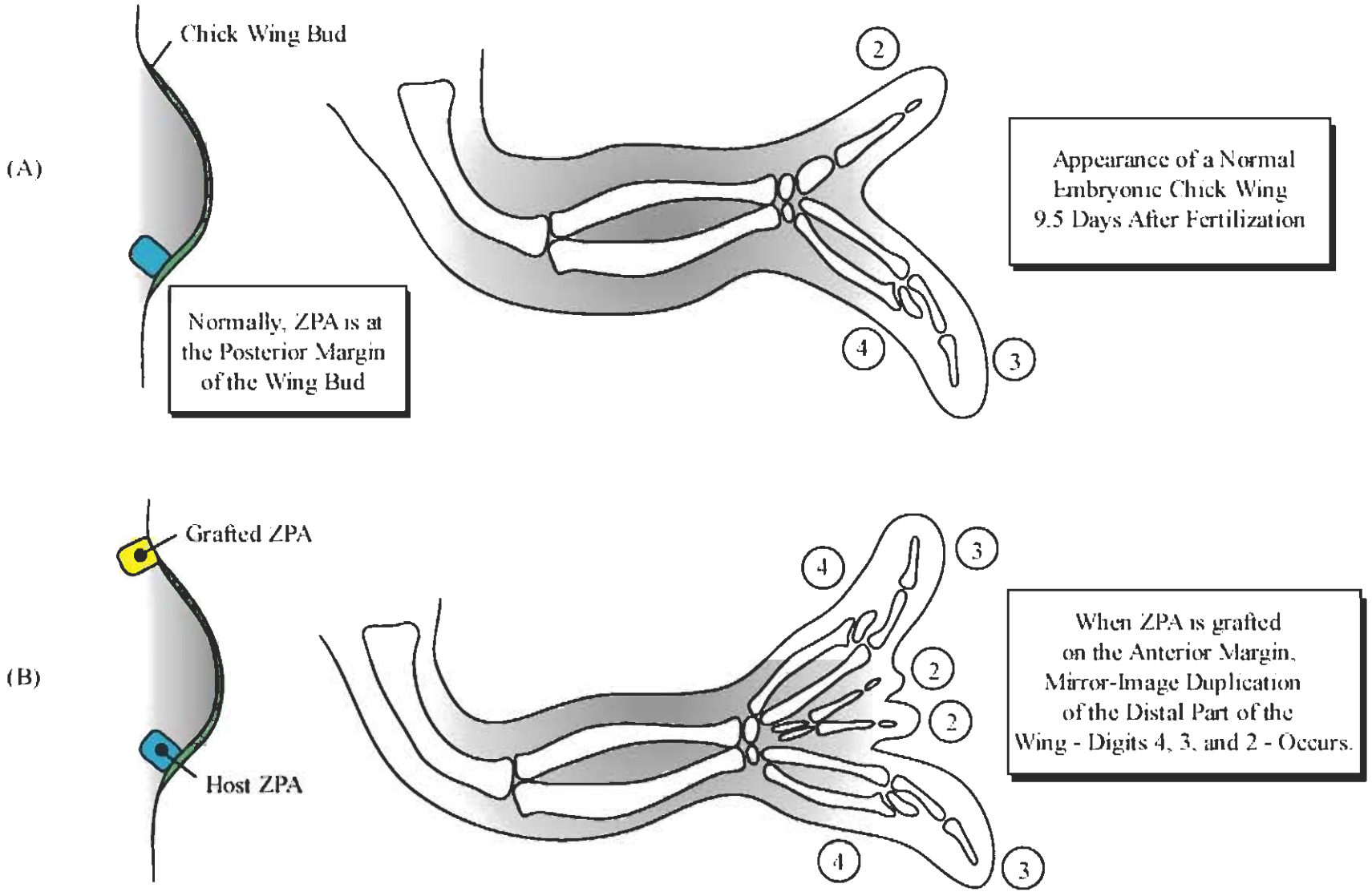


Progressively more
complicatedp attern

Morphogen: A signaling molecule that imposes a pattern on a field of cells. This means that the morphogen induces different responses depending on its concentration.



ZPA = Zone of Polarizing Activity



Gallus gallus (Chick) Limb Development-Retinoic Acid and Sonic Hedgehog (SHH)

To the left is a chick embryo (sans shell) with normal wing development.
Courtesy of Dr. Fallon, Univ. of Wisconsin

Courtesy of Dr. Tickle, Univ. of Dundee A bead soaked in Retinoic Acid was implanted into the anterior margin of the early wing limb-bud. Note the mirror-image duplication of the digits.

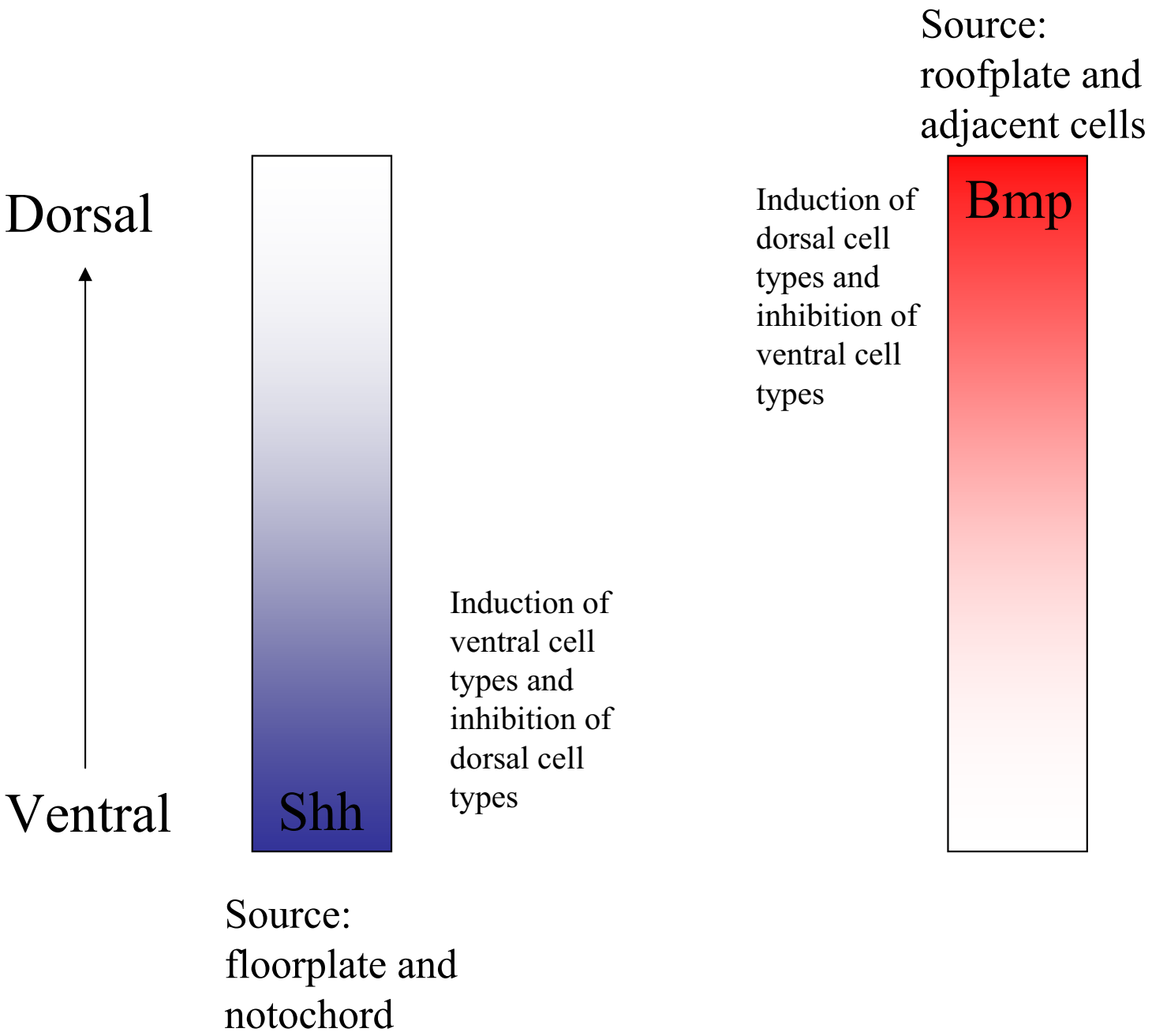
IV
III
II

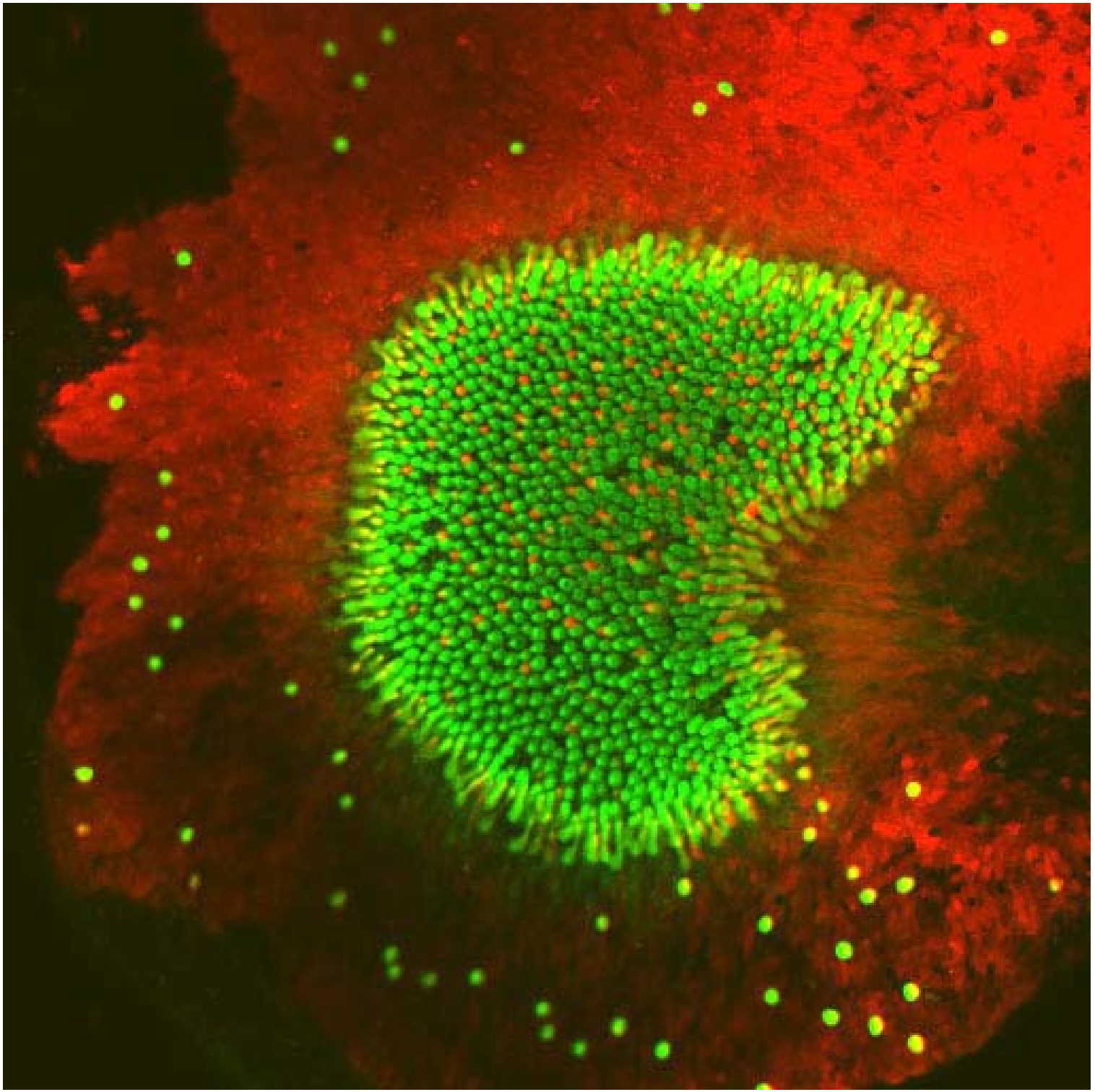
II
III
IV

ZPA graft can be mimicked by implantation of a bead soaked in retinoic acid

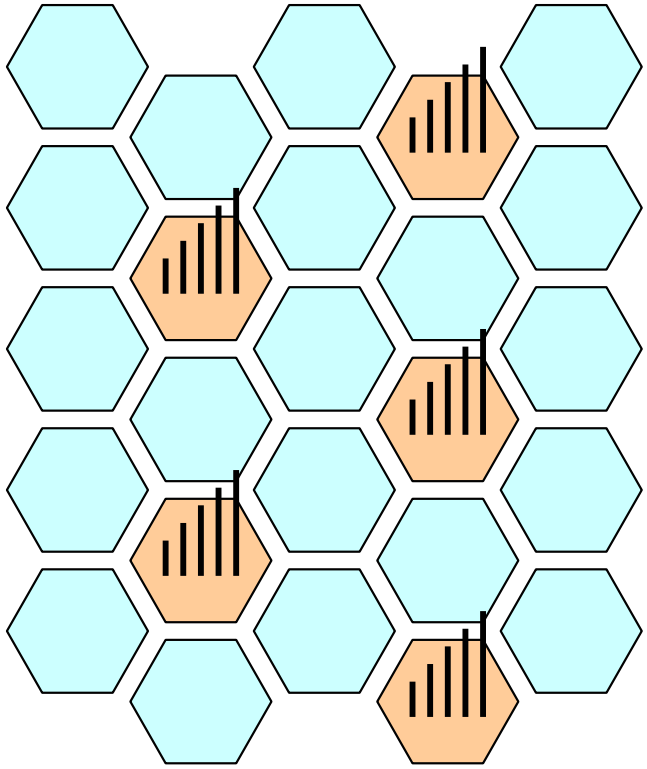
Digit IV represents a posterior limb structure. The ectopic release of Retinoic Acid from the bead leads to ectopic expression of **Sonic Hedgehog (SHH)**, forming a secondary ZPA.

Spinal cord cell type induction by morphogenic gradients of inducers and inhibitors.





Hair cells always occur in a mosaic with supporting cells



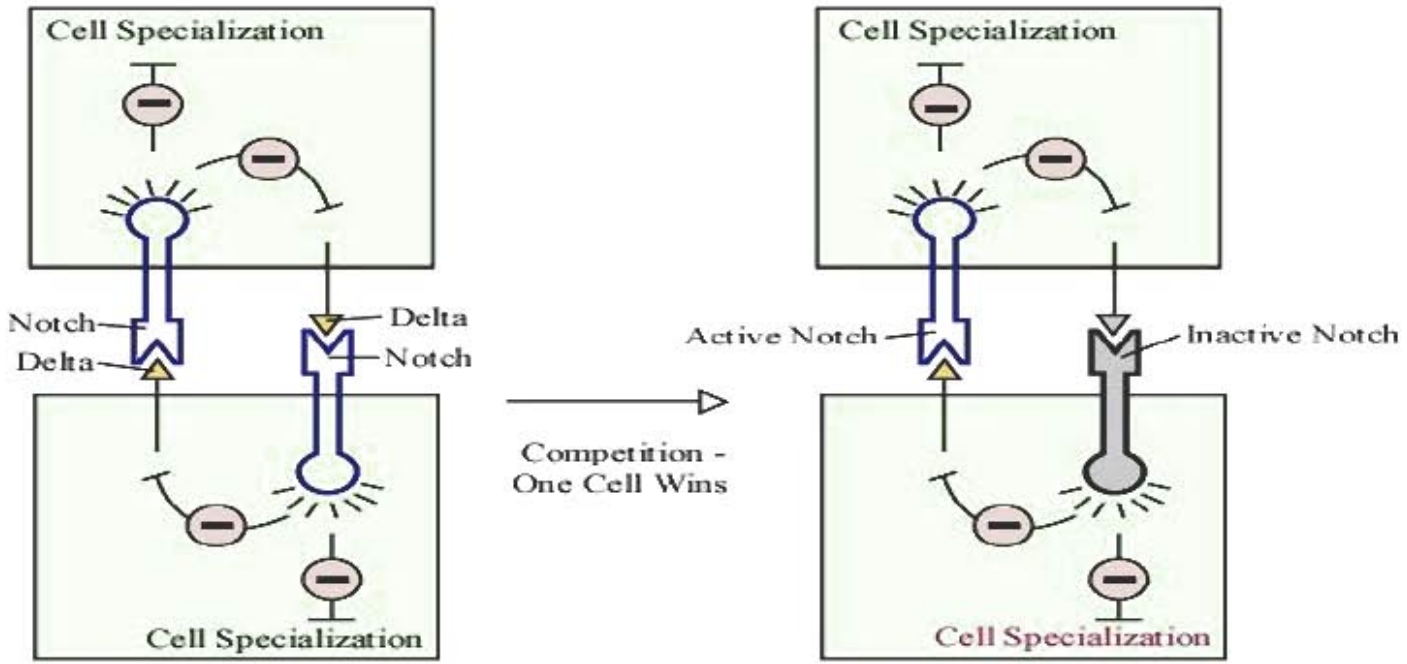
Lateral Inhibition?

Rigging the Competition:

Numb Protein Biases Lateral Inhibition:

Numb Blocks Notch Activity
→ the Numb-Containing
Cell Cannot Be Inhibited by
its Neighbor.

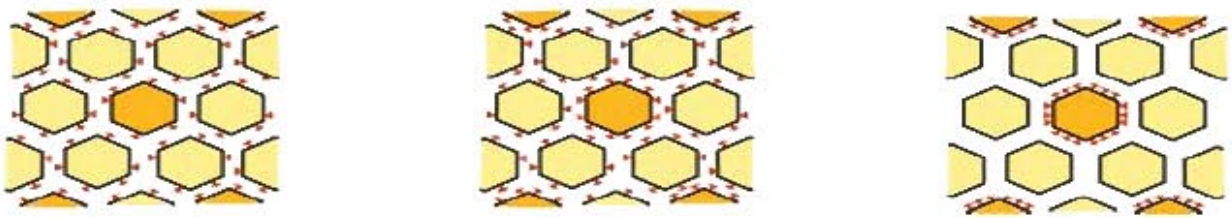
(A)



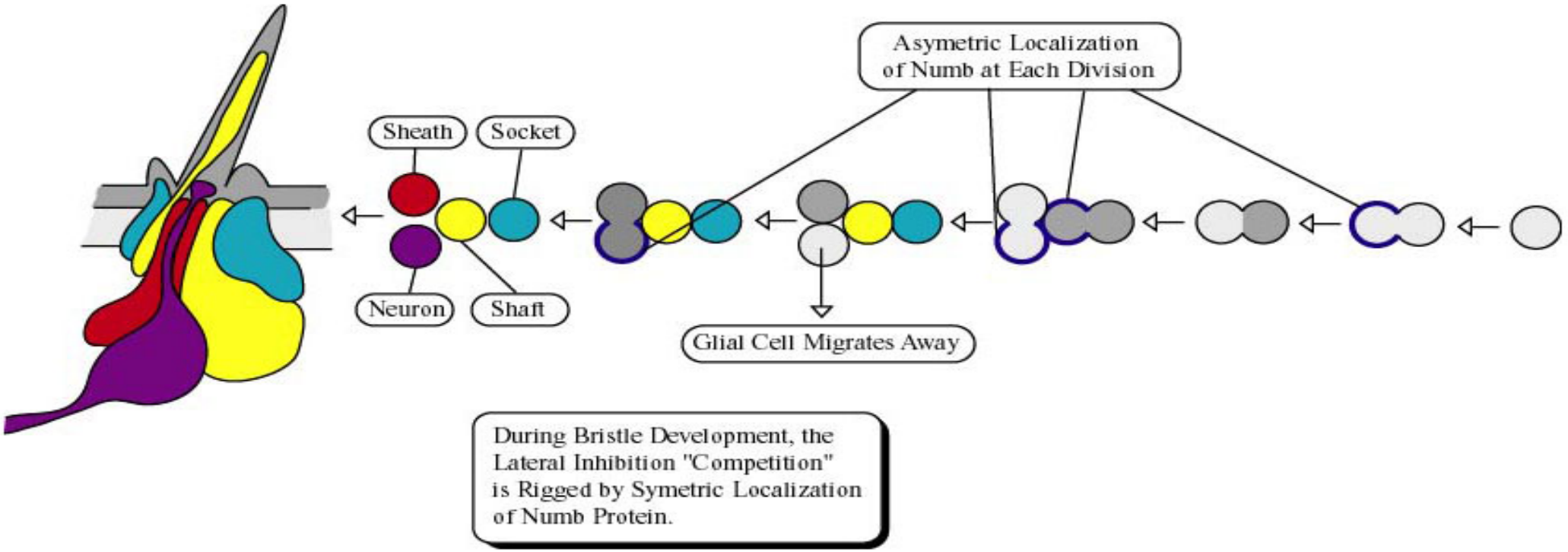
Each Cell Tends to Inhibit Its Neighbor

Cell with Active Delta Specializes and
Inhibits Its Neighbor from Doing Likewise

(B)



During bristle development, the lateral inhibition “competition” is rigged by asymmetric localization of Numb protein.



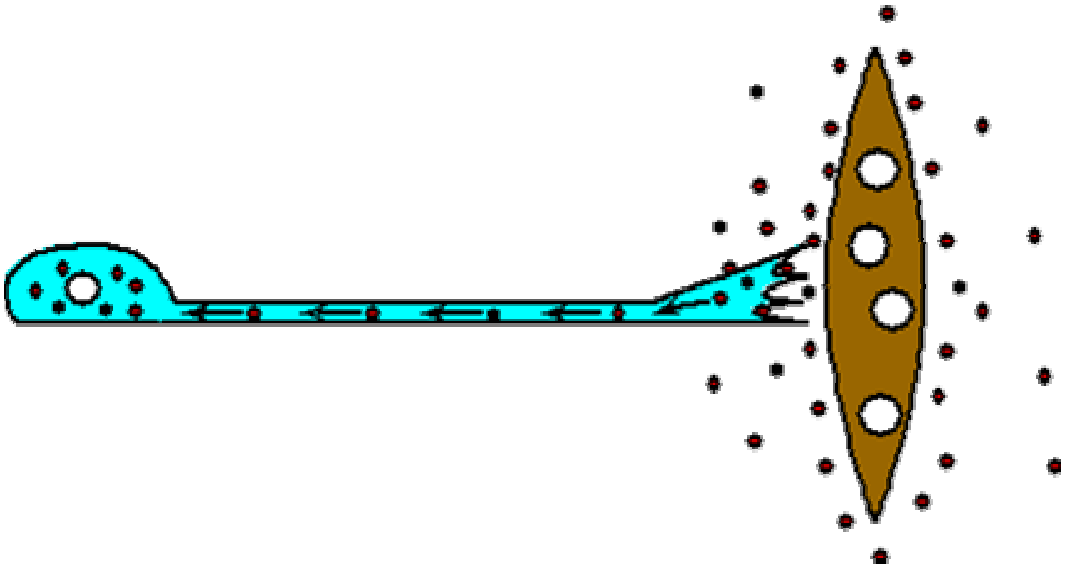
“Later Development”

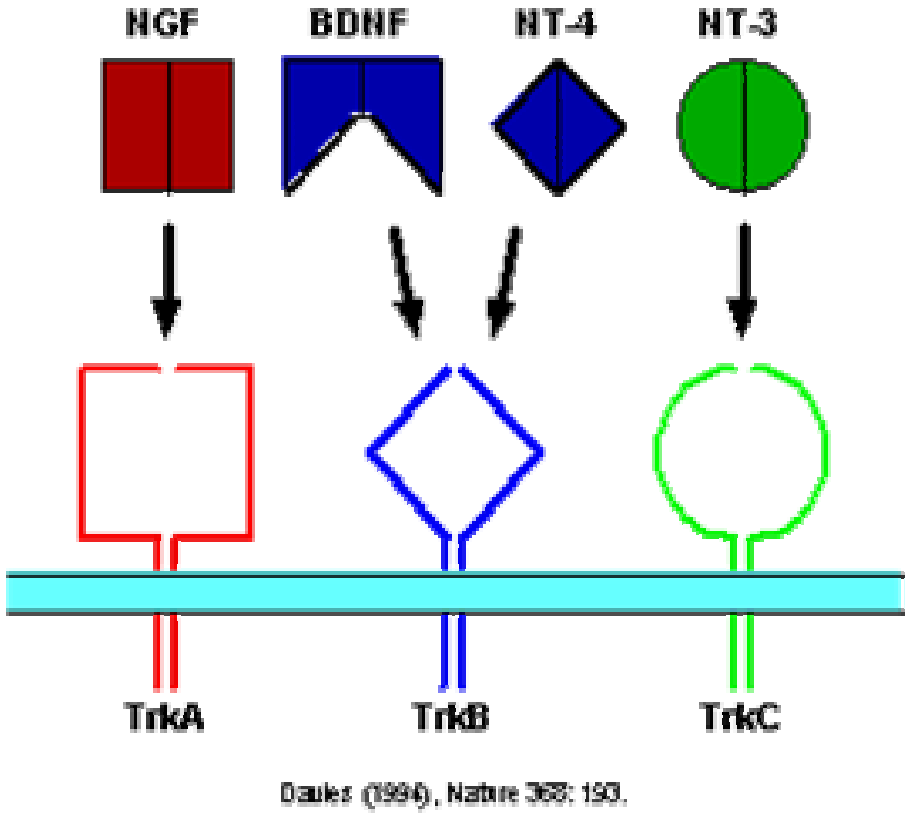
Asymetric cell division

Cell signaling:	Inductive signal	Shh
	Morphogen	Shh, BMP
	Lateral Inhibition	Notch, Numb
	Cell survival and Cell death	
	Axonal migration	

Motorneurons die during development

See Alberts et al., 2002 Molecular Biology of the Cell





Neurotrophic factors are released by the neurons' targets, bind to receptors, and are transported back to the cells' somae. Neurons that receive trophic support survive. Neurons that do not receive sufficient support initiate a suicide, also named programmed cell death or apoptosis.

Neurotrophins in the inner ear:

Cochlear hair cells produce BDNF and NT3 as support for auditory ganglion neurons. Gene defects in either neurotrophin or their appropriate receptors lead to degeneration of auditory ganglion cells.

Programmed cell death during formation of the semicircular canals

See: Bissonnette, John P. and Donna M. Fekete, "Standard atlas of the gross anatomy of the developing inner ear of the chicken." Journal of Comparative Neurology, Vol. 368. Pages 620-630, 1996.

Axons are guided by attraction and repulsion of the growth cone & Axonal/Growth cone guidance in the cochlea

See Alberts et al., 2002 Molecular Biology of the Cell

“Later Development”

Asymetric cell division

Cell signaling:	Inductive signal	Shh
	Morphogen	Shh, BMP
	Lateral Inhibition	Notch, Numb
	Cell survival and Cell death	Neurotrophins
	Axonal migration	Attraction and repulsion of growth cones