• 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
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”

Asymmetric cell division

Cell signaling: Inductive signal
Morphogen
Lateral Inhibition

Cell survival
Cell death

Axonal migration
Sequential induction

Simple pattern

B → A

C is induced by signal
From B acting on A

B ← C → A

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

B → D → C → E → A
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.

Gradient of inducer extending across a field of cells

Source of inducer

Cell type A  Cell type B  Cell type C  Cell type D  Cell type E  Cell type F
ZPA = Zone of Polarizing Activity

(A) Chick Wing Bud

Normally, ZPA is at the Posterior Margin of the Wing Bud

Appearance of a Normal Embryonic Chick Wing 9.5 Days After Fertilization

(B) Grafted ZPA

When ZPA is grafted on the Anterior Margin, Mirror-Image Duplication of the Distal Part of the Wing - Digits 4, 3, and 2 - Occurs
**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*

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.

*Courtesy of Dr. Tickle, Univ. of Dundee*  

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.

ZPA graft can be mimicked by implantation of a bead soaked in retinoic acid.
Spinal cord cell type induction by morphogenetic gradients of inducers and inhibitors.

- **Ventral**
  - Source: floorplate and notochord
  - Induction of ventral cell types and inhibition of dorsal cell types

- **Dorsal**
  - Source: roofplate and adjacent cells
  - Induction of dorsal cell types and inhibition of ventral cell types

Indicators:
- **Shh**
- **Bmp**
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) Cell Specialization

Notch
Delta

M
Notch

Active Notch

Inactive Notch

Cell Specialization

Competition - One Cell Wins

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”

Asymmetric 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

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”

Asymmetric cell division

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<thead>
<tr>
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</thead>
<tbody>
<tr>
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</tr>
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</tbody>
</table>

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