Neurons are similar across phyla. Thus, many different model systems are used in developmental neurobiology.
EVOLUTION OF METAZOAN BRAINS

GASTRULATION
MAKING THE 3rd GERM LAYER AND INDUCING NEURAL TISSUE
Neural tissue derives from ectoderm - *How do we know that?*

**C. elegans** cell lineage

**Step 1**
- Proliferation
- Differentiation

**Step 2**
- Gastrulation
- Cellular movements
- Origin of mesoderm
- Induction of ventral neural tissue
- Delamination of neural tissue from ectoderm

http://www.youtube.com/watch?v=M2d6XH5YVaw

Fig. 1.2

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**C. elegans** neural lineage

Fig. 1.3
Fig. 1.4

Drosophila neural lineage:

- Gastrulation
- Cellular movements
- Origin of mesoderm
- Induction of ventral neural tissue
- Delamination of neural tissue from ectoderm

http://www.youtube.com/watch?v=c5X6rJiFGBo

Fig. 1.5

Drosophila neural lineage:

- Delamination of neuroblasts
- Production of GMCs
- Proliferation
EVO-DEVO

The disciplines of evolutionary biology and developmental biology are intertwined. Small alterations in the developmental program can cause profound changes in phenotype!

"... evolution is the control of development by ecology."
- Leigh van Valen, U of Chicago, Committee on Evolutionary Biology

"YE HAVE MADE YOUR WAY FROM THE WORM TO MAN, AND MUCH WITHIN YOU IS STILL WORM."
- NIETZSCHE

Example:
Tunicate larvae share many features with frog tadpoles, revealing their common evolutionary history with all Chordates

Amphioxus (Chordata)
ONTOGENY RECAPITULATES PHYLOGENY?

More accurately, the embryonic morphology of different vertebrates reveals a basic, common blueprint, or “Bauplan”. This is especially true early in development.

Embryonic development shares many common elements across Vertebrates

Fish

Chick

Pig

Human

http://www.pbs.org/wgbh/nova/odyssey/clips/
Vertebrates (Frog):
- Gastrulation
- Origin of mesoderm
- Induction of neural tissue from ectoderm
- Neural plate
  - Neural tube
  - Neural crest

http://www.youtube.com/watch?v=dXpAbezdOho

Neural crest formation
- Skin, bone, muscle
- Peripheral nervous system
  - Autonomic NS
  - Sympathetic
  - Parasympathetic
- Sensory ganglia
Zebrafish development

Fig 1.8

Chick Development

Fig 1.9

http://www.youtube.com/watch?v=Ah-gT0hTio
CHICK GASTRULATION

Fig. 1.10

Human embryo gastrulation resembles avian discoidal pattern

http://www.youtube.com/watch?v=UgT5rUQ9EinQ
When is the fate of neural tissue determined?

Fig. 1.11

Spemann & Mangold
Where does neural tissue originate?
Heterotopic transplant experiments
1939 Nobel Prize

*Fig. 1.12
What induces mesoderm?

Fig. 1.13

Test alternate hypotheses for inducer action:
Direct or indirect neural induction?

*Fig 1.14
What is the Neural Inducer? “Noggin”

Other inducers include chordin and follistatin.

Figs. 1.15, *1.16

How do inducers work?

Follistatin blocks activin receptors. The TGF-β protein family member activin is a mesoderm inducer. Blocking activin action should thus inhibit mesoderm induction. It does, but... Surprise! It also led to neural induction!

Perhaps neural tissue is the default fate of dorsal ectoderm?

*Fig. 1.17
Contact-mediated inhibition?

Note BMPs are TGF-β protein family members.

Thus, preventing action of TGF-β family members leads to neural tissue, by *inhibiting an inhibitor.*

*Fig. 1.18*

Functional homologs in Drosophila. Chordin = sog, BMP4 = dpp.

Inhibiting an inhibitor of neural tissue is an ancient solution to making a nervous system! Saint-Hilaire proposed a body axis inversion in a common ancestor, and molecular evidence supports the idea.

*Fig. 1.19*
Noggin inhibits the BMP4 inhibitor of neural fate

Cerberus, chordin, & follistatin also interfere with BMP binding and are found in the IMZ (dorsal lip of the blastopore)

Chordin+Noggin knockout

Fig. 1.21
Ascidean neurulation requires FGF

TGF-β receptors are membrane-bound kinases that work through Smads to affect gene transcription in the nucleus. Most neural inducers inhibit this pathway. FGF works downstream on Zic genes.

Fig. 1.22
Now that neural tissue is made, how are neurons and glia generated?

Production of neuroblasts from neural tissue by delamination. Neuroblasts can make more neuroblasts, or make neurons or glia, through proneural genes.

The proneural genes code for the bHLH family of transcription factors e.g. achaete-scute (asc).
Lateral inhibition of neural fate:
Proneural clusters give rise to only 1 neuroblast.
How & Why?

Fig. 1.23

Fig. 1.24

Wild type
Proneural mutant (no proneural genes (asc), so no neurons)
Neurogenic mutant (no neurogenic genes (Notch/Delta), so no lateral inhibition)

Testing Lateral Inhibition

Fig. 1.26

Notch-Delta signaling

Notch/Delta binding blocks neural fate in neighboring cells by blocking asc.

Fig. 1.27
Fig. 1.28

Notch-Delta signaling suppresses neuroblast fate through lateral inhibition

If 1 cell randomly produces a little more Asc, Asc production in the neighbor is reduced through Notch-Delta signaling (negative feedback)

Fig. 1.29

Greater expression of the proneural genes Asc in one cell represses their expression in neighboring cells, through lateral inhibition caused by Delta binding to Notch.