

Overview of steps in neural development

1. Induction
2. Neurulation
3. Regionalization/Patterning
4. Differentiation
5. Migration
6. Axon outgrowth and guidance
7. Synaptogenesis
8. Refinement of synapses
9. Adult neurogenesis/repair

---

---

---

---

---

---

---

---

Cellular/molecular mechanisms of neural development involve:

- Control of gene expression
- Cell-cell signaling
- Cell movements and shape changes

All three of these affect each other.

---

---

---

---

---

---

---

---

How do we study neural development?

1. Model systems
2. Manipulate genes/molecules--genetic methods
3. Imaging--how do cells/molecules behave?

---

---

---

---

---

---

---

---

1. Model Systems

Worms (*C. elegans*)

Flies (*Drosophila*)

Zebrafish

Frogs

Chicks

Mice

In vitro cell culture

Molecules/mechanisms are evolutionarily conserved from worms to humans.

---

---

---

---

---

---

---

---

Factors that make us choose a particular model system

•Ability to do genetics. Very powerful. [best in *C. elegans*, *Drosophila*, zebrafish, mice.]

•Simple systems with identifiable neurons. [*C. elegans*, *Drosophila*, somewhat in zebrafish and frogs.]

•Ability to manipulate and/or image (including microsurgery, introduction of DNA/RNA, pharmacological treatments, accessibility/visibility for imaging). [chick, frog, zebrafish, cell culture]

•Cost/space to maintain animals. [worms, flies, zebrafish, frogs, cell culture]

---

---

---

---

---

---

---

---

2. Genetic Methods

Standard steps to analysis of gene/molecule function:

•Look at where/when gene is expressed--is it in the right place at the right time?

•Gain-of-function experiments/tests of sufficiency.

•Loss-of-function experiments/tests of necessity.

---

---

---

---

---

---

---

---

Examples of gain-of-function methods

- Inducible promoters (e.g. heat shock, hormone inducible).  
Allow temporal control of gene expression.
- Gal4/UAS is one example of method to get spatial control.
- Electroporation--gives some spatial and temporal control.

---

---

---

---


---

---

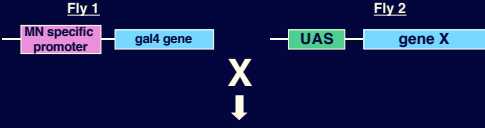
---

---

Gal4/UAS

In yeast: 

Use as a tool in *Drosophila* or zebrafish.  
e.g. Say you want to misexpress gene X in motor neurons:



MNs make Gal4, it binds to UAS and turns on gene X only in MNs.

---

---

---

---

---

---

---

---

Examples of loss-of-function methods

- Mutation or knockdown of gene
  - targeted gene deletion in mice (knockout mice)
  - morpholino antisense
  - RNAi
- Conditional mutations
  - Cre/lox recombinase system in mice to restrict mutation to specific cells
  - mitotic recombination clones in *Drosophila*.

---

---

---

---

---

---

---

---

