Nervous system development

- Part of the ectoderm differentiates into the neural plate, from which a neural tube and neural crest form.
- Neural tube becomes brain and spinal cord.
- Neural crest becomes peripheral nervous system (and facial cartilage).

Neurulation

- Neurulation is when the neural tube and neural crest form (early organogenesis).
- Neurulation is the end global interactions in chordate development.
  - Up until this point the number of global interactions within the embryo has been increasing.
  - After this point, global interactions decrease, and local interactions predominate.
Neural migration

- Neurons migrate further and faster than other cell types. Speeds up to 40 m/hr!
- Follow both other cells (glia) and molecular gradients
- Can travel over 1m to precisely specify target

Neural cells

- Neurons and Glia are the two major cell types that make up the nervous system
- Neurons transmit messages from cell to cell
  - Sensory neurons transform stimuli (e.g. light, sound, or joint position) into messages sent to other neurons
  - Interneurons integrate information from many cells; particular interneurons are sensitive to complex features of the world; networks of interneurons are responsible for cognition and (presumably) consciousness.
  - Motor neurons transmit messages to muscles, controlling their action.

The Neuron

- Neurons consist of
  - Soma, the cell body.
  - Axon, which sends signals on to the next cell. Each neuron has one axon; it can be very long.
  - Dendrites, tree-like structure which receives signals from the axons of other cells. Often very highly branched, but doesn't go far from soma
Many kinds of neurons

Even within a particular anatomic type, there is a great functional diversity. Organization of neurons is highly diverse as well.

Neurons communicate at synapses

The axon of one neuron sends its message to the dendrites of the next (or to muscle) by sending neurotransmitter molecules across a synapse.

There are more than 300 kinds of neurotransmitters known to date, e.g. glutamate, serotonin, adrenaline, dopamine, acetylcholine, GABA. Each has a specialized set of receptors.

Resting neurons maintain a voltage gradient

The process of integrating inputs from dendrites and sending that message down the axon depends on manipulating voltage differences over regions of the cell membrane.

- Voltages are controlled by managing concentrations of Ca⁺, K⁺ and Na⁺ ions across the membrane.
- At "rest" a neuron actively maintains a voltage (- inside) by pumping ions with ATP: 3 Na⁺ out for 2 K⁺ in.
Action potentials

- **Excitatory inputs** at the dendrites locally depolarize the membrane, called EPSPs.
- **Inhibitory inputs** at the dendrites locally hyperpolarize the membrane, called IPSPs.
  - Inputs propagate toward soma, where they are integrated
- When soma depolarization exceeds a threshold, the cell sends a positive current down the axon, called an action potential.
  - Action potentials are an "all or none" phenomenon.

Action Potential Propagation

- When the axonal membrane becomes depolarized, it depolarizes its neighbor by opening voltage-gated \( \text{Na}^+ \) channels.
- It then repolarizes and is insensitive to depolarization for a brief inactivation period.

Speed of transmission

- Electrical properties of neurons allow messages to be transmitted fast.
- **Nodes of Ranvier**
  - Myelination makes transmission even faster
  - Myelin is lipoprotein
  - Inside myelin, diffusion is fast, but fades out
  - At nodes, new action potentials are triggered
- >120 m/s (200+ mph)
Presynaptic transmission

When an action potential reaches a synapse on the axon (called a presynaptic terminal), it causes the release of neurotransmitters.

- Action potential causes Na⁺ influx, which in turn causes Ca⁺ influx.
- Ca⁺ ions cause vesicles containing neurotransmitter to fuse with membrane, releasing the neurotransmitter.

Molecular Synaptic Transmission

- Neurotransmitter stored in vesicles in axon of presynaptic cell is released into synaptic cleft as a result of depolarization (action potential).
- Neurotransmitter diffuses across cleft, binds to receptors, and causes a postsynaptic effect.
- Neurotransmitter is taken back into the presynaptic cell ("reuptake") so that its effect has a time limit.
  - Prozac and relatives are “Selective Serotonin Reuptake Inhibitors” so it slows the reuptake of the neurotransmitter serotonin, increasing duration of its effects in the synapse.

Ion channels

- Change in membrane voltage is mediated by three kinds of ion channels:
  - Voltage gated: open by change in local voltage; the mechanism of action potentials
  - Ion gated: binding to neurotransmitter opens the channel
  - Metabotropic: binding to neurotransmitter causes secondary message (through G proteins) which opens an associated channel.
Changes in synaptic properties are a key mechanism in learning.

- Basic mechanism is Long-term potentiation (LTP).
  - A neuron which is multiply activated by several axons simultaneously becomes more sensitive.
  - After long term potentiation, the same presynaptic input produces a larger postsynaptic potential.
- Others include growth and removal of entire synapses.

One kind of LTP is driven by calcium ion concentrations, mediated by the NMDA glutamate receptor.

When a postsynaptic region is already depolarized and additional glutamate is transmitted, NMDA receptor opens, allowing calcium to flow into the cell.

- NMDA is both voltage- and ligand-gated.
- Glutamate alone does not open NMDA channel, due to Mg blocking it; Mg is released when the region is depolarized.

Calcium influx causes more receptors (called AMPA) to move to the membrane in that region, making it more sensitive.

Change is mediated by Ca²⁺ binding to Calmodulin, which causes the autophosphorylation of Calmodulin Kinase II, which releases AMPA receptor which can migrate to membrane.
Presynaptic changes

- Retrograde (in the opposite direction of the signal) transmission changes the presynaptic terminals.
  - Mechanism is Nitric Oxide (also others, e.g. arachadonic acid.)
  - NO effects the transport and exocytosis of vesicles
- May be just short term; long term mechanism unknown

Neurons form circuits

- Reflexes are simplest circuits (0 or 1 interneurons).
- Retina is next step up
  - Cells inhibit neighbors, for a “center on, surround off” response.
  - Detects edges, shape

Cortical organization

- Signals converge on the cortex.
- Signals are integrated to identify more complex phenomena in inputs.
  - E.g. Individual visual cortex neurons are sensitive to color, motion, orientation, location, etc.
- Most cortex has 6 layers (some 3)
Nervous system

Peripheral nervous system (sensory and motor nerves)
- Sympathetic (involuntary, fight or flight)
- Parasympathetic (involuntary, opposite of sympathetic)

Central nervous system (spinal cord, brain, and cranial senses)