Development & Organization of the Nervous System
Layout of the Nervous System

A “system of twos”
Phases of Development

Ovum + Sperm = Zygote
Cell division (multiplication)

There are five phases of neurodevelopment:
• Induction of neural plate
• Neural proliferation
• Migration and aggregation
• Axon growth/synapse formation
• Synapse refinement
The germinal stage of embryogenesis refers to the time from fertilization to implantation in the uterus. The germinal stage takes around 8-10 days.

Potency: the ability to develop into different cell types
- totipotent: morula
- pluripotent (embryonic stem cells): blastocyst
- multipotent; unipotent

End of stage: “Baby in a Compact Disc”
The second phase of development is gastrulation, a migration of blastocyst cells inward, leading to multiple distinct layers of tissue called germ layers.

Cells of the inner cell mass begin to differentiate as the amnion forms.

A gastrula develops when cells begin to migrate inward, forming an indentation.

The cells continue to push inward, forming the endoderm. Cells that remain on the outer surface of the gastrula are called ectoderm.

The mesoderm is formed, as additional cells migrate inward between the endoderm and ectoderm.
Neurulation

The third phase of development is neurulation, the stage at which the nervous system emerges. In the third week of development, a neural plate forms in the ectoderm – the outermost germ layer – of the embryo. The edges of this plate elevate and meet at the mid-line forming a neural tube. This tube is the precursor of the central nervous system.

Neurulation stage
- Neural tube: CNS
- Inside tube: fluid-filled cavities in the brain (ventricles) and spinal cord (canal)
- Neural crest: PNS
- Somite: skull and vertebrae
Proliferation (~4000 cells/s) causes the neural tube to change its size and shape (morphology).

Shape changes are large at the head end of the tube (future brain), whereas they are small at the tail end (spinal cord).

In temporal order, the head end of the tube shows:
- first, three swellings which will give rise to the forebrain, midbrain and hindbrain
- second, five swellings which give rise to major divisions of the brain.
Neural stem cells (radial glial cells) are generated at the inner (ventricular) surface of the neural tube. They begin moving to their “addresses” to form structures.

Migrating cells are immature; i.e., somas only. There are two ways for a cell to migrate:
• radial
• tangential

Cells align themselves with others cells in a variety of ways including via cell-adhesion molecules like desmosomes.
Axon Growth and Synapse Formation

Once positioned, neurons extends processes that will ultimately become their axon and dendrites. The growing tip of a neurite is called the growth cone; it consists of thin spikes called filopodia that extend and retract in response to guidance molecules (chemoaffinity hypothesis).

Formation of new synapses is a multi-step process including chemical signal exchange between axons and dendrites (pre- and post-synaptic neurons). This process is aided by astrocytes.
A diffuse pattern of synaptic contact is characteristic of early development.

A more focused pattern is present after synaptic refinement.

Two mechanisms:
• Neuron death (apoptosis of extra inputs – red – due to a lack of neurotrophins received from targets)
• Neural activity ("neurons that fire together, wire together")
Anatomical References

All vertebrates (including humans) have the same basic body plan — they are bilaterally symmetrical.

Descriptive terms are with respect to the organism in its standard anatomical position.
• anterior/rostral: towards the front/nose
• posterior/caudal – towards the back/tail
• dorsal/superior – towards the top
• ventral/inferior – towards the bottom
• medial – towards the middle
• lateral – towards the side

Structures on the same side of the body are said to be ipsilateral; if on opposite sides, then contralateral.
In humans, the directions in the forebrain are rotated by $90^\circ$ in comparison to those in the spinal cord (and brain stem) because of the unusual upright posture of humans. Thus, for example, the top of the head and the back of the body are both *dorsal* even though the directions are different.
Planes of Section

To view internal structures, it is necessary to make slices (called sections).

For the brain, there are three standard perpendicular planes of section:

- **sagittal** – left vs right (a midsagittal cut separates the left and right halves of the brain)
- **horizontal** – top vs bottom (parallel to the ground)
- **frontal (coronal)** – front vs back

A cross-section is cut at a right angle to a long narrow structure (e.g., the spinal cord)
The Brain

Visual inspection of the brain (lateral view) reveals three parts common to all mammals:

- the **cerebrum** – telencephalon, top-most, highly convoluted, split into two cerebral hemispheres that each receive sensory input from and control motor output to the opposite side of the body.
- the **cerebellum** – behind/below the cerebrum, also highly folded, primarily a motor control center, two hemispheres each concerned with movement of the same side of body.
- the **brain stem** – forms the stalk from which the cerebrum and cerebellum sprout, fibers of passage, cranial nerves, basic functions (e.g., breathe rate).
The spinal cord is a long, thin, tubular bundle of nervous tissue that extends from (is continuous with) the brain stem.

The spinal cord is divided into regions (colors) based on location in the body. 31 pairs of nerves (communication from/to the body; PNS) are attached to the cord.

The spinal cord is shorter than the vertebral column; the lower nerves run down the canal before exiting (cauda equina, “horse’s tail”).
Each spinal nerve attaches to the spinal cord by means of two branches or roots:

- the dorsal root brings sensory information from the body into the spinal cord (afferent), cell bodies in dorsal root ganglion
- the ventral root carries motor commands from cord to body (efferent), somas in cord

In cross section, the spinal cord comprises two areas:

- inner H-shaped core of gray matter (cell bodies) organized into sensory (dorsal) and motor (ventral) nuclei;
- outer area of white matter (myelinated axons; ascending and descending tracts)
The brain and spinal cord are the most protected organs in the body. They are encased in bone (skull and vertebrae) and covered by three meninges or membranes: dura mater; arachnoid mater; and pia mater.
Cerebrospinal fluid (CSF; like the liquid part of blood) fills the sub-arachnoid space covering the brain and spinal cord.

CSF is produced by a special tissue (choroid plexus) in the lateral and third ventricles. It then flows into the central canal of the spinal cord and the sub-arachnoid space. It is finally reabsorbed into veins.

CSF supports the CNS and provides cushioning against injury.
The brain (and spinal cord) have substantial nutritional requirements, and thus receive a rich blood supply. However, the CNS requires a constant environment to function properly.

Barriers, in the form of tightly packed endothelial cells lining blood vessel walls, maintain this environment by impeding passage into the CNS of:

- "foreign substances"
- proteins/other large molecules
- highly charged molecules
- hormones and neurotransmitters

Glucose is actively transported.

The barrier is weak in some areas in the brain to allow monitoring of the chemical composition of blood.
Peripheral Nervous System

Somatic

The branch of the NS of which we are conscious. It provides sensory and motor innervation to all body parts except organs, smooth muscles and glands. It is involved in sensations that we are aware of such as light and pain, and our voluntary movements.

Autonomic

The branch of the NS of which we are unconscious. It regulates the visceral (organ) functions that maintain homeostasis within the body, including heart rate, blood pressure, digestion, etc. It has two efferent components in balance: sympathetic and parasympathetic.
Somatic spinal nerves innervate a particular region of skin.
Autonomic Nervous System

Second-stage neurons are far from the target

Second stage neurons are near the target organ
The Cranial Nerves

“Some Say Marry Money, But My Brother Says Big Brains Matter Most”