Chapter 1: Organization, Overview, Neuroanatomical Background

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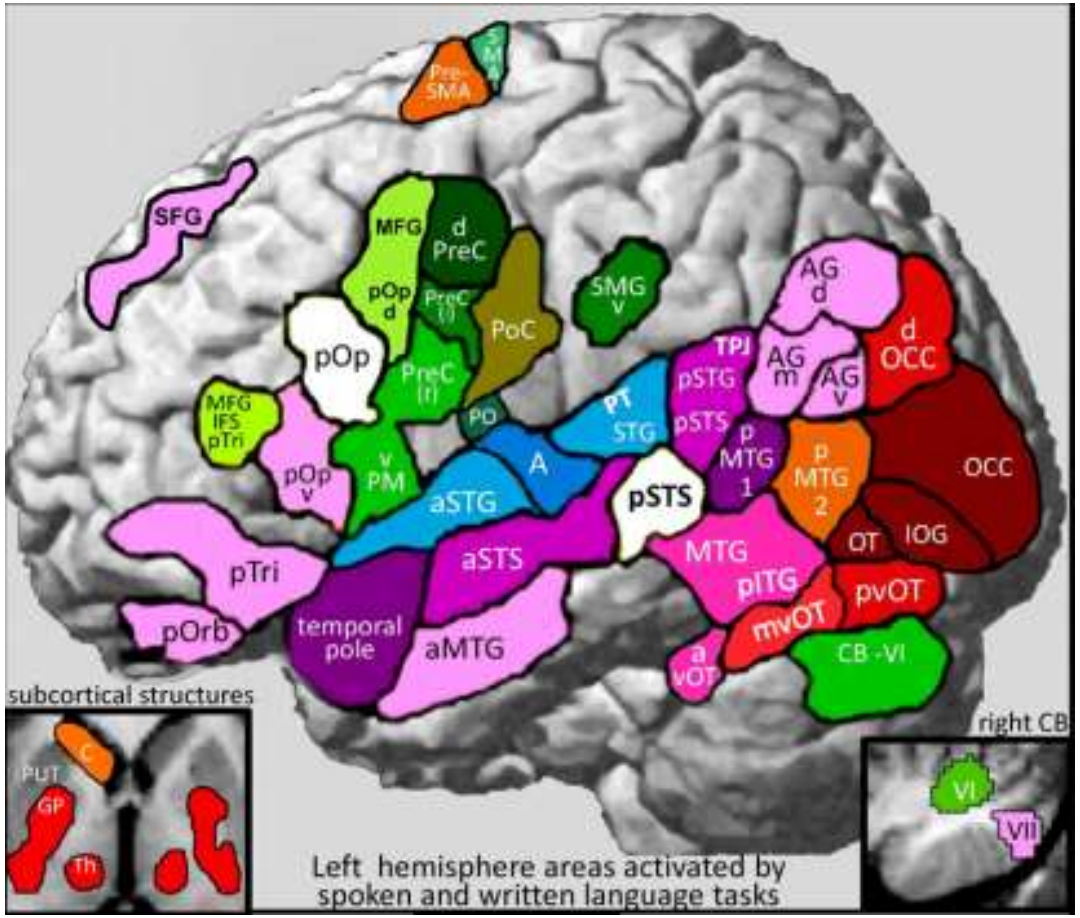
1.1 Course Contents

Neuroimaging and Brain Function

MR response to flashing visual stimulus

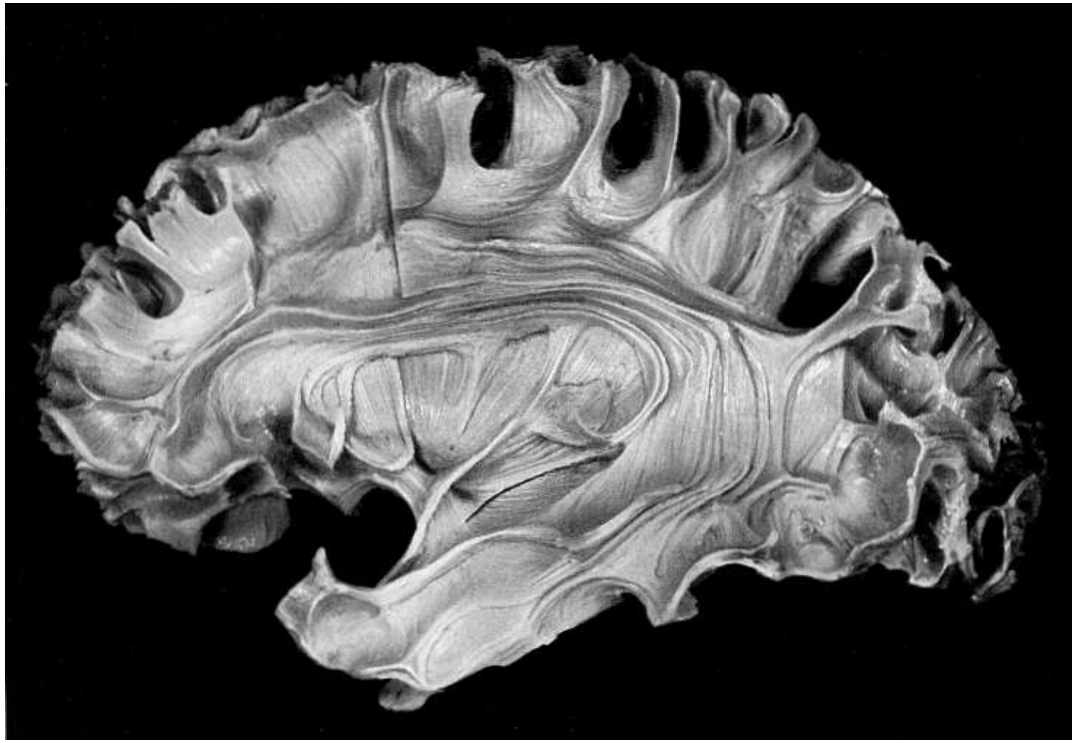
Red: Increased **Blue:** Decreased MR Signal



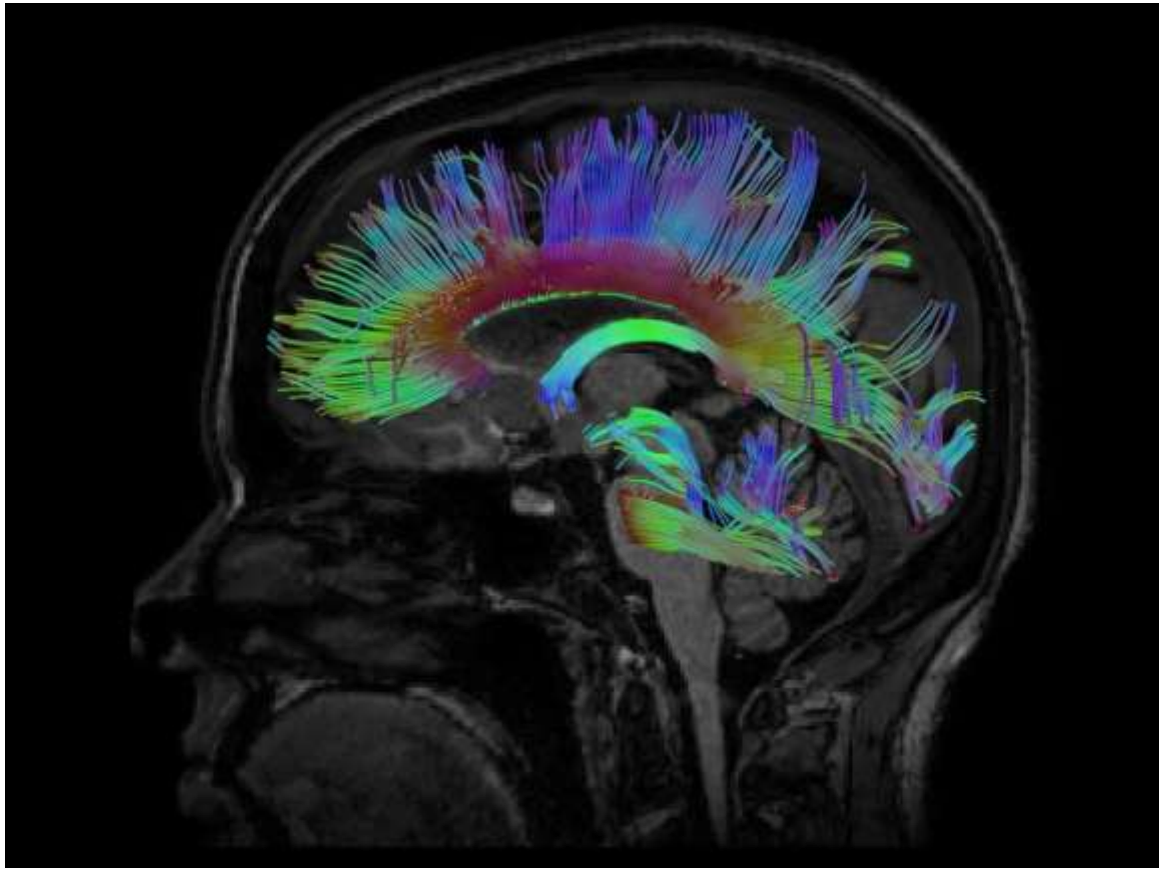
A detailed map of brain regions involved in understanding and producing language

Images from Hu et al., 1997 / Price 2012

Neuroimaging and Brain Structure

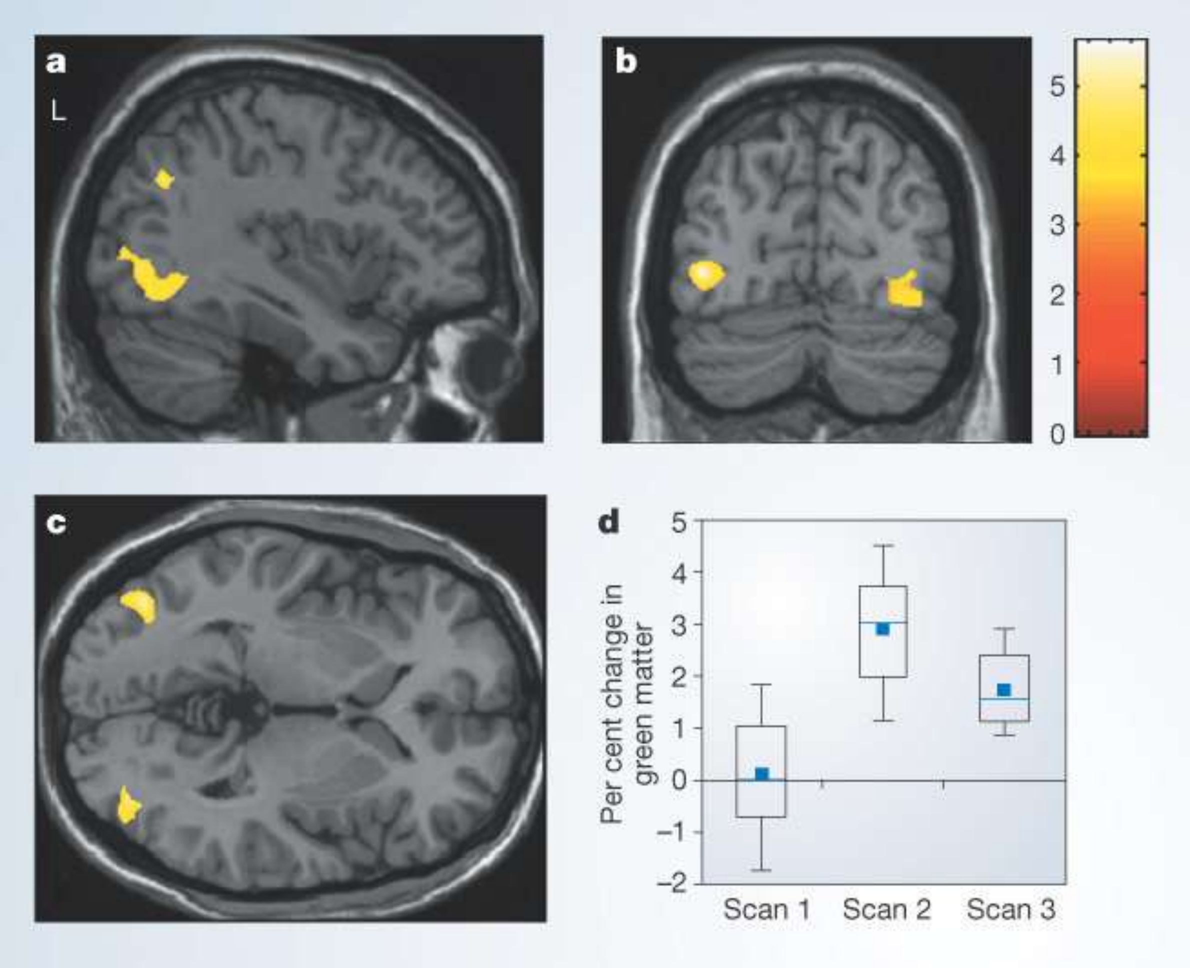


Photograph of a Klingler Dissection

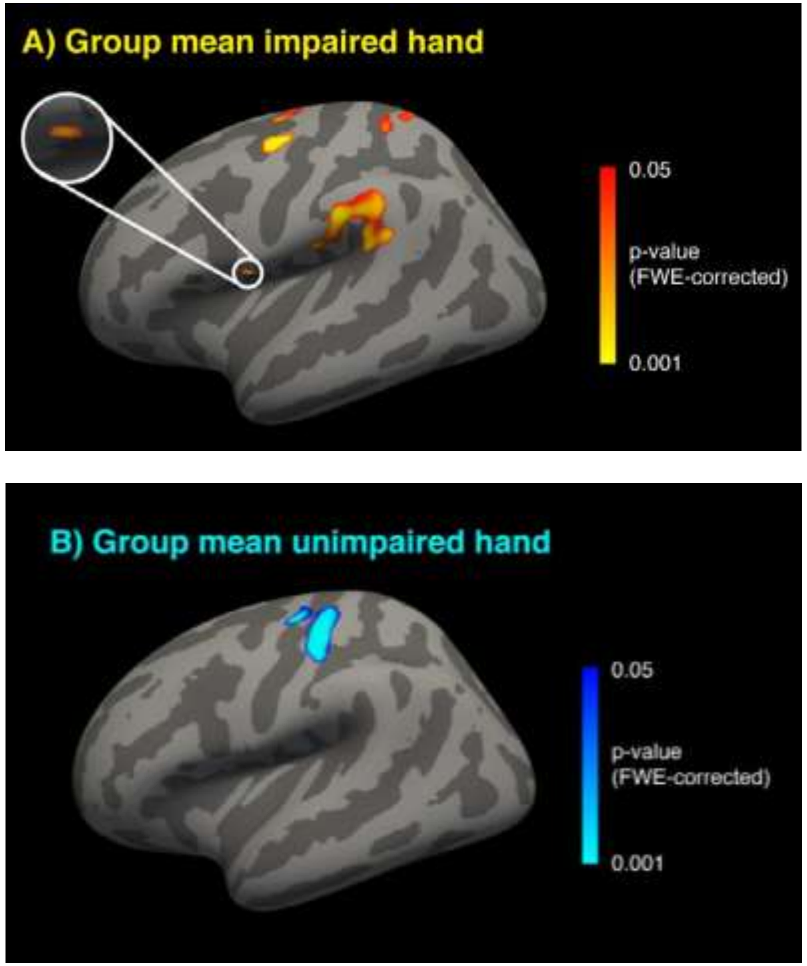


Tractography of my sister's brain

Neuroimaging and Plasticity / Learning



Gray matter increase when learning how to juggle

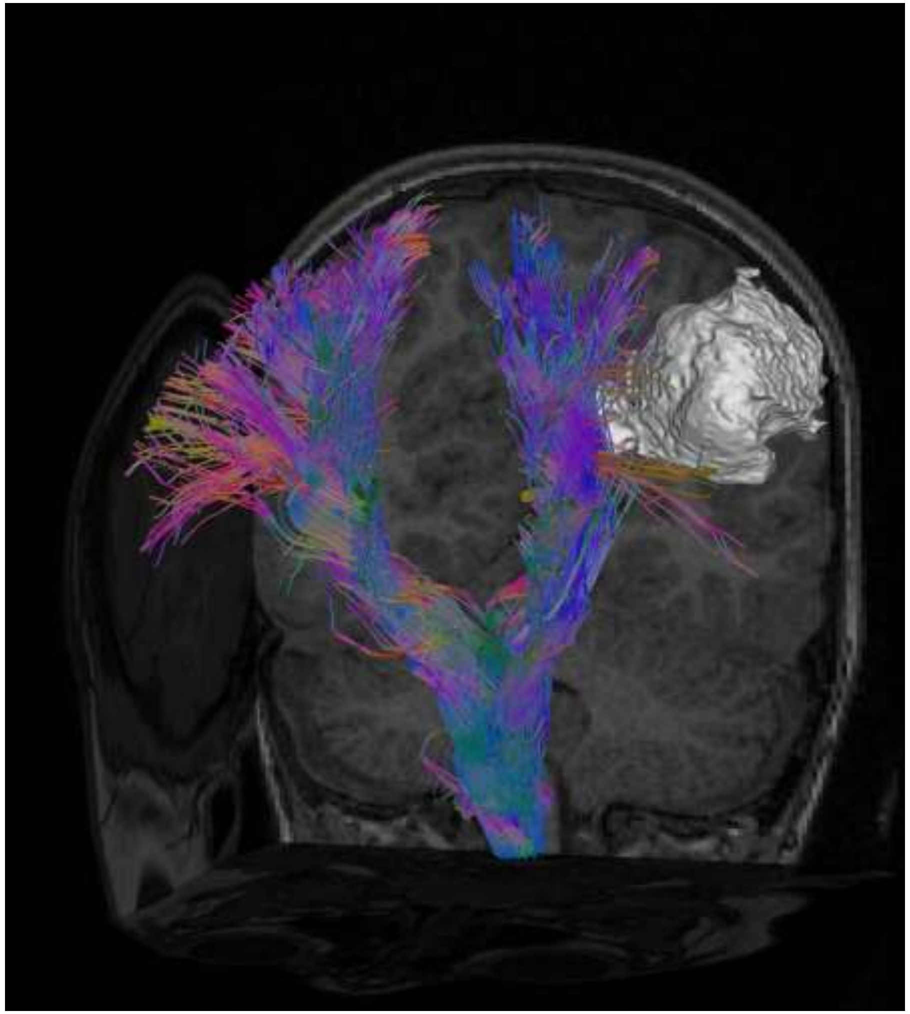


Motor areas in epilepsy patients after hemispherotomy

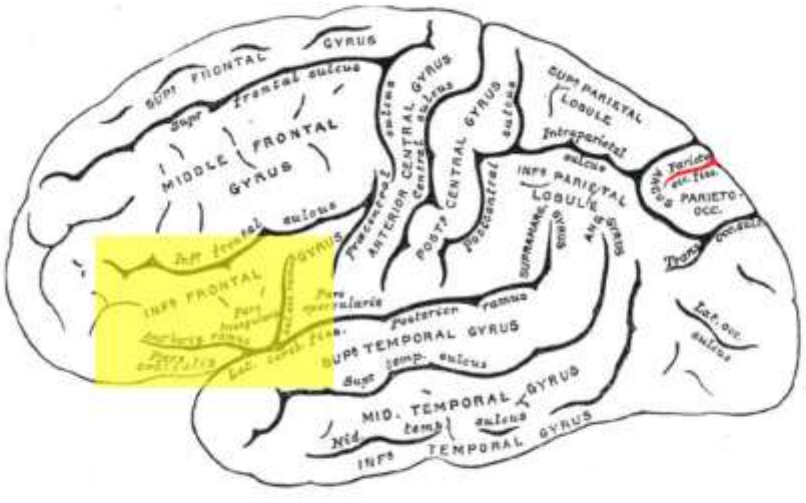
Images from Draganski et al., 2004 / Prillwitz et al. 2021

Clinical Applications of Neuroimaging

Images from Grün et al. 2023 / Wikipedia / Khatami et al. 2017



Motor tracts in a tumor patient



0.25	0.25	0.25	0.75	1.33	1.33
0.00	1.00	0.50	0.67	1.25	1.75
0.25	0.75	0.00	0.75	1.33	1.75
0.25	0.25	0.50	0.75	1.00	1.67
0.00	0.50	0.00	0.25	0.33	0.00

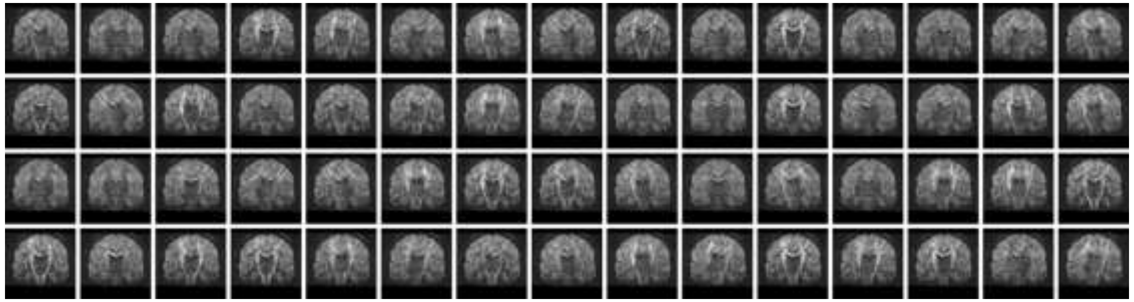
Sample score for one subject

TMS Results

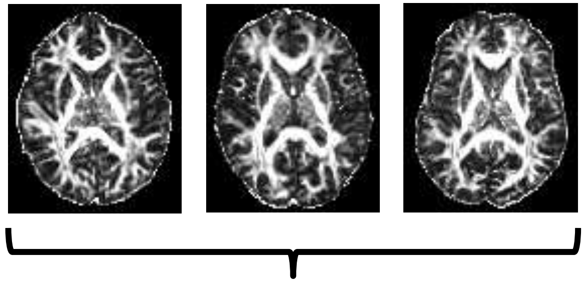
The Computational Neuroimaging Pipeline

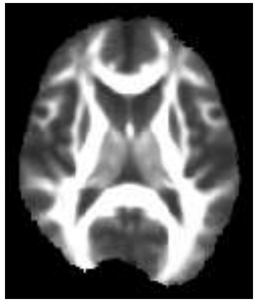
Acquisition

Reconstruction & Artifact Correction



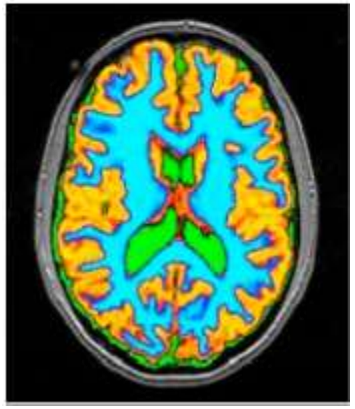
Registration



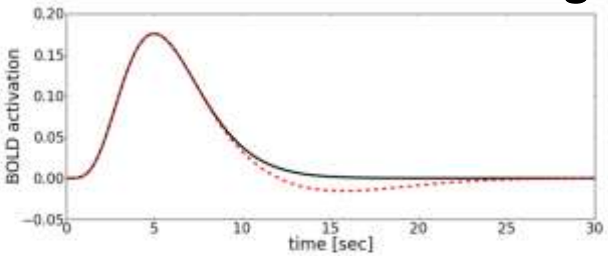


Atlas Construction

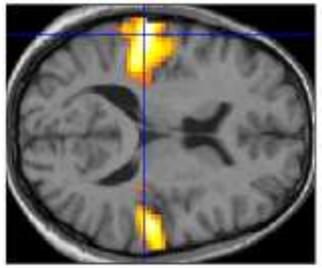
Segmentation

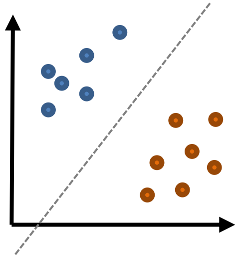


Mathematical Modeling



Hypothesis Testing

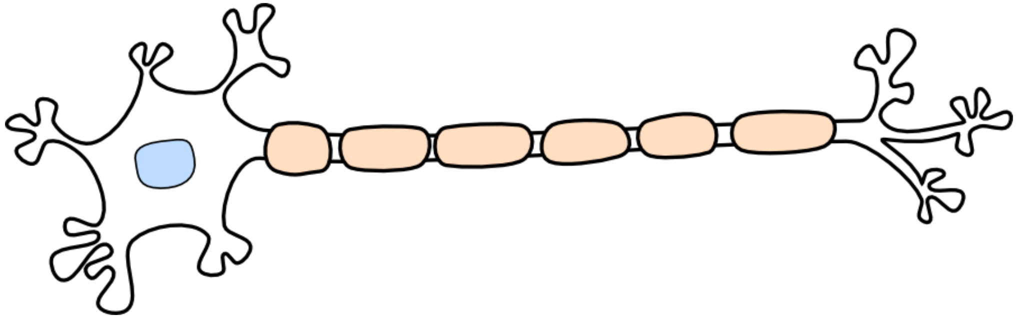


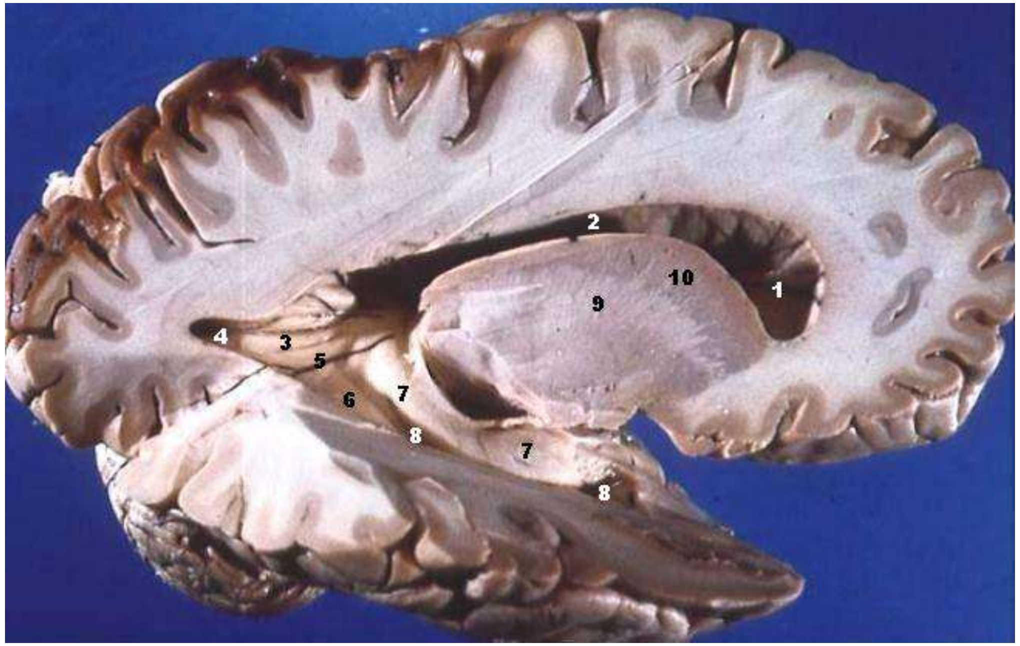


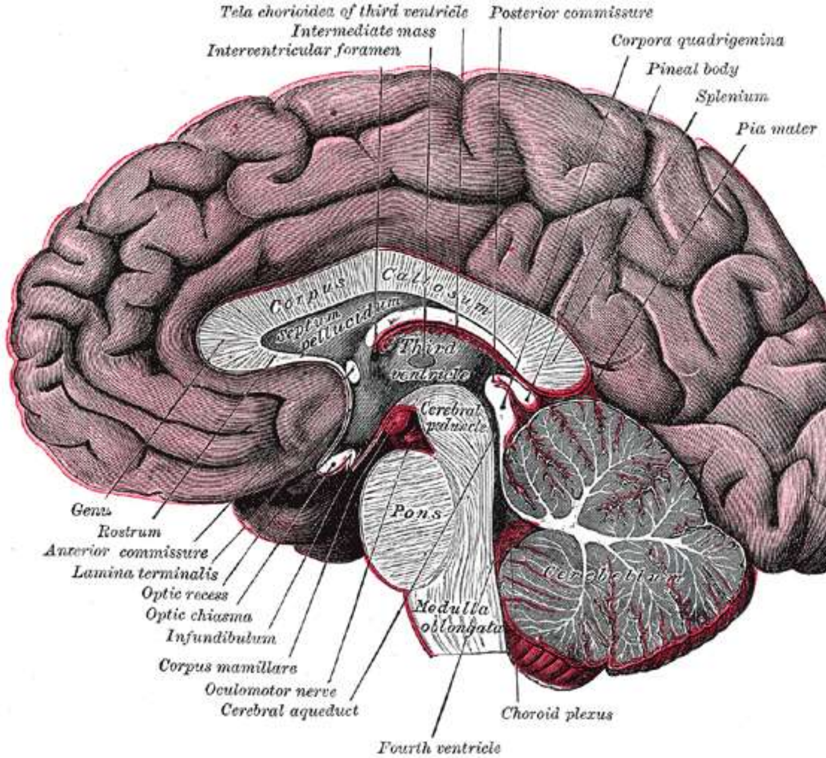
Machine Learning

Foundations of Neuroanatomy

- **Today**
  - Structure and functional units of the brain
  - From whole brain to cellular level

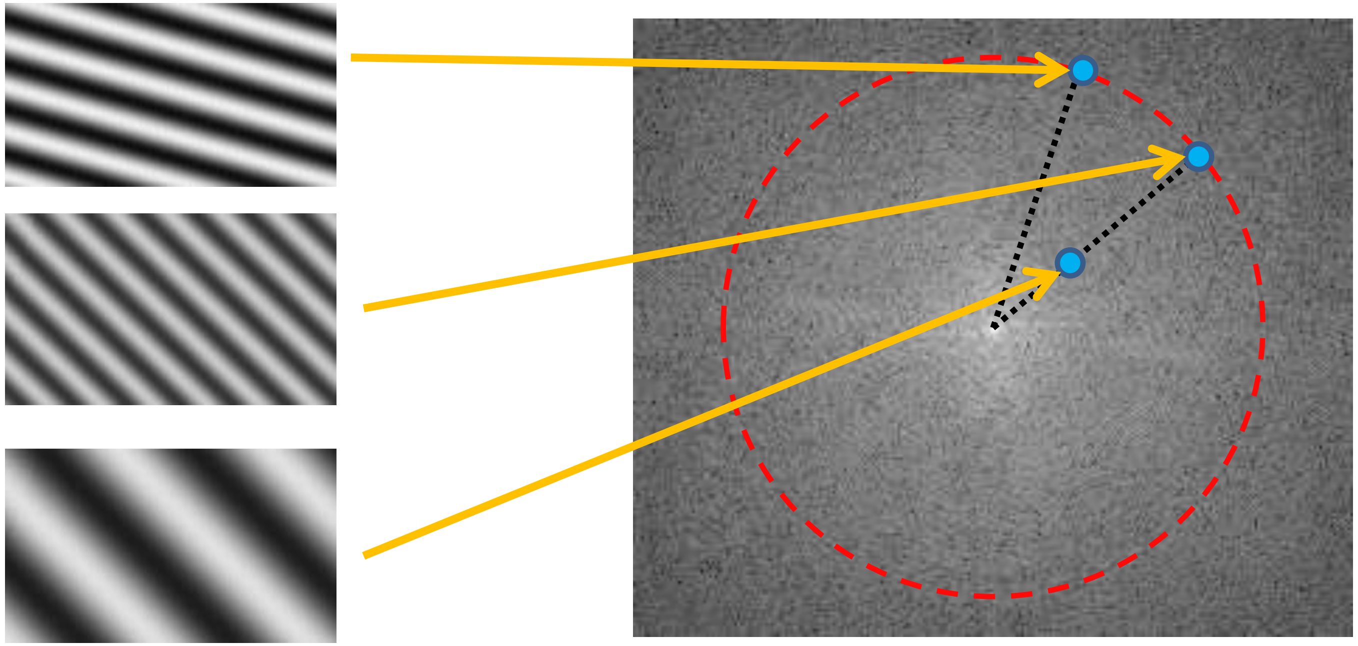


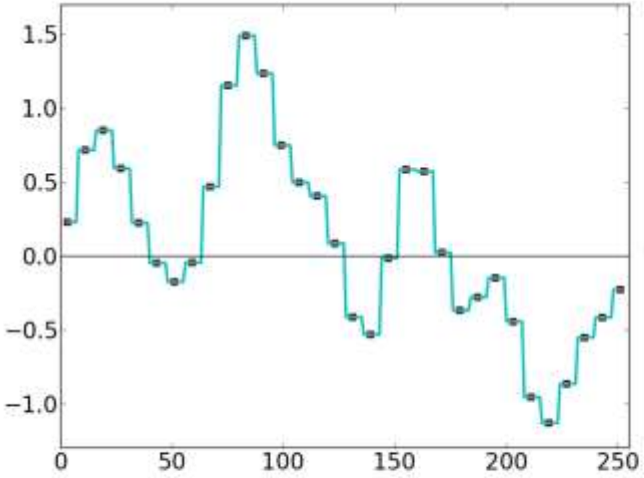


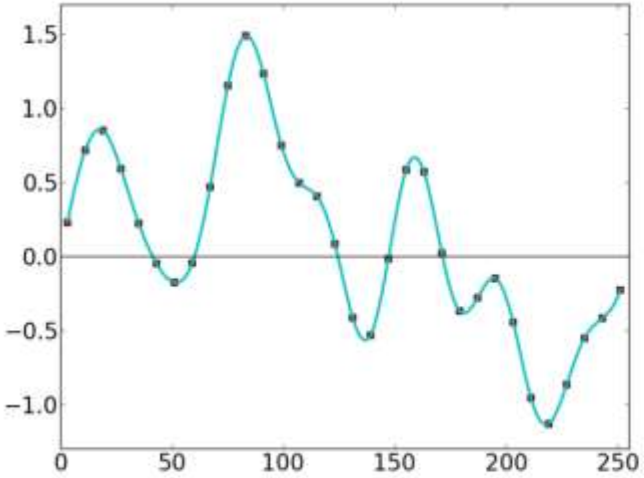


Fourier Transform / Signal Processing

- **Thursday and next week**
  - Important Fourier theorems and intuition
  - Sampling and reconstruction of (image) signals

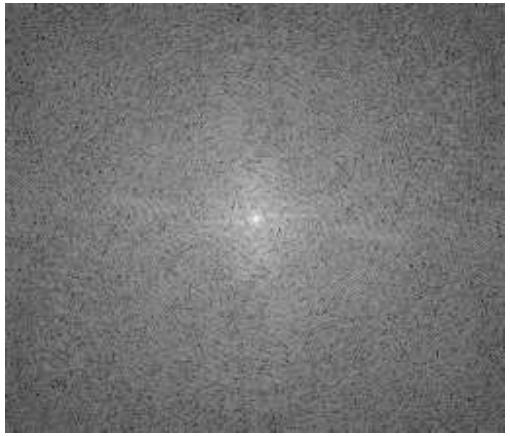






MR Acquisition and Reconstruction

- **Rest of October**
  - MR image formation and reconstruction
  - Different types of contrast
  - Artifacts



k-space

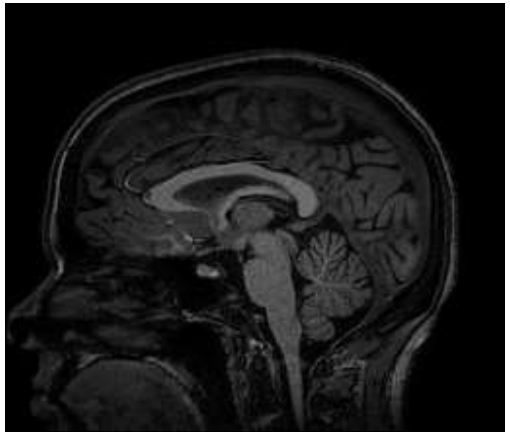
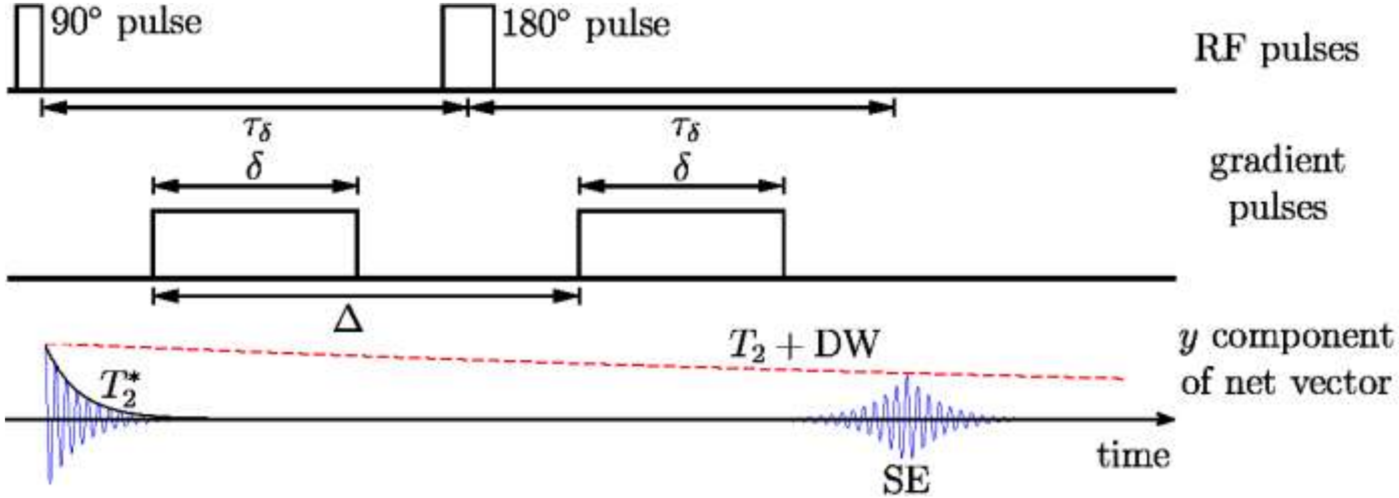
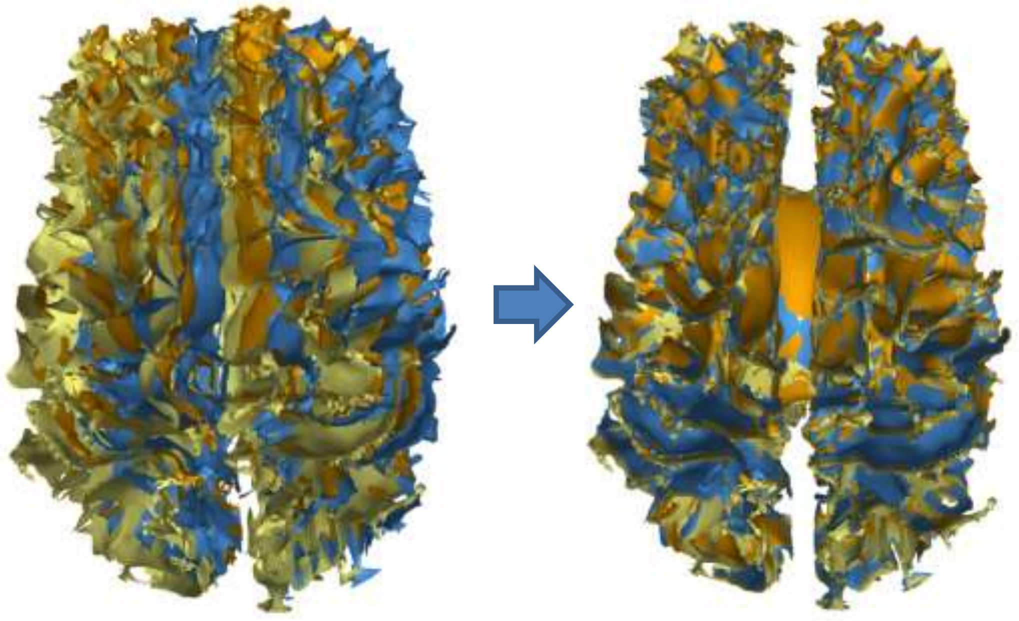


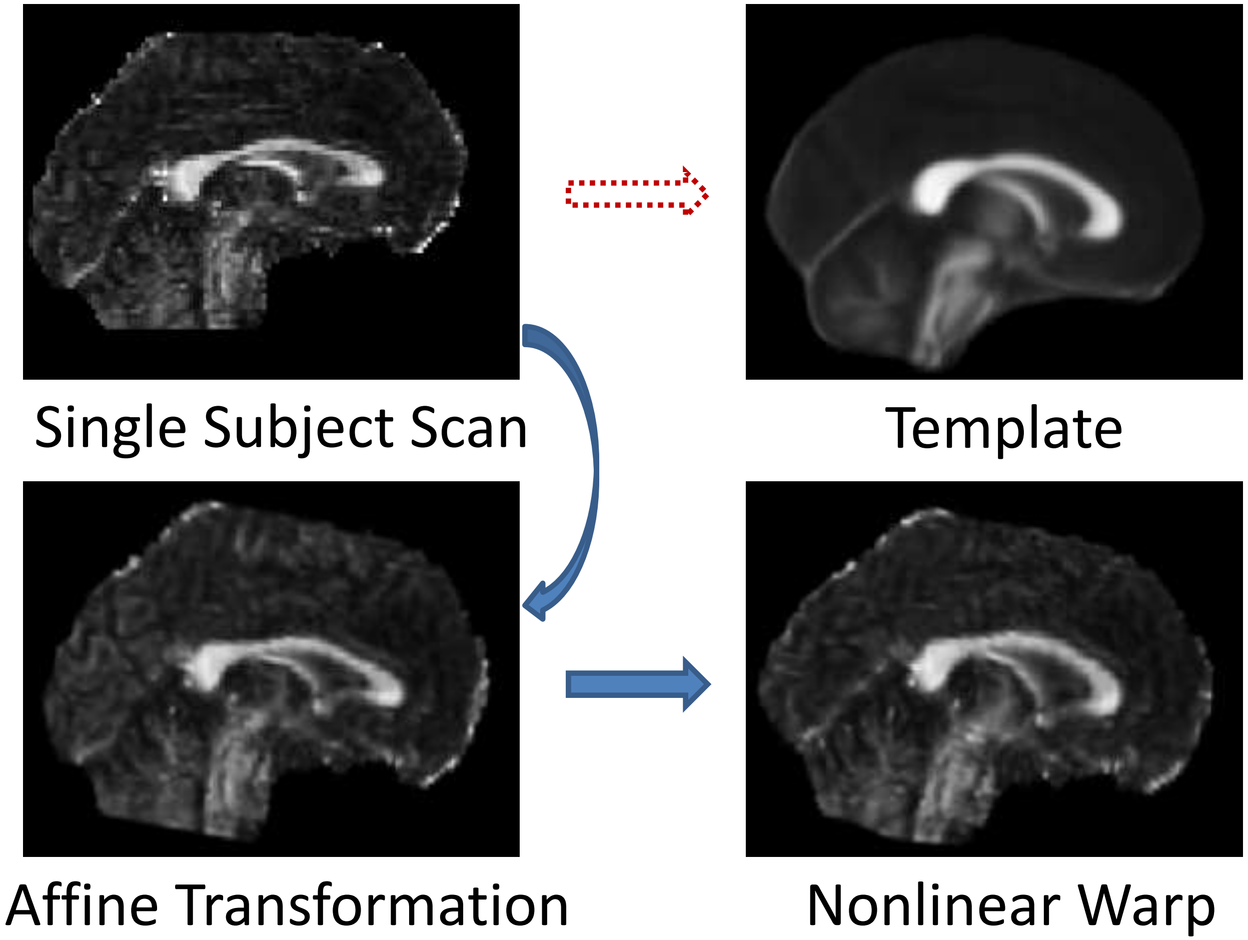
Image space



3D Image Registration

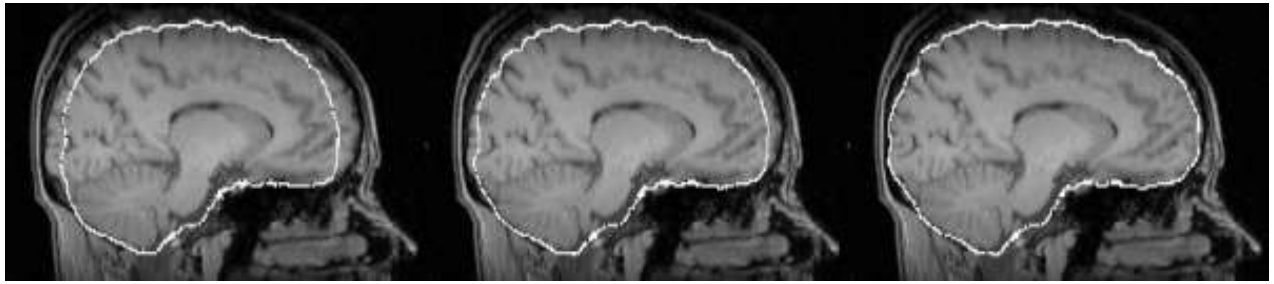
- **First half of November**
  - Cost functions and their optimization
  - Diffeomorphic registration
  - Brain atlases



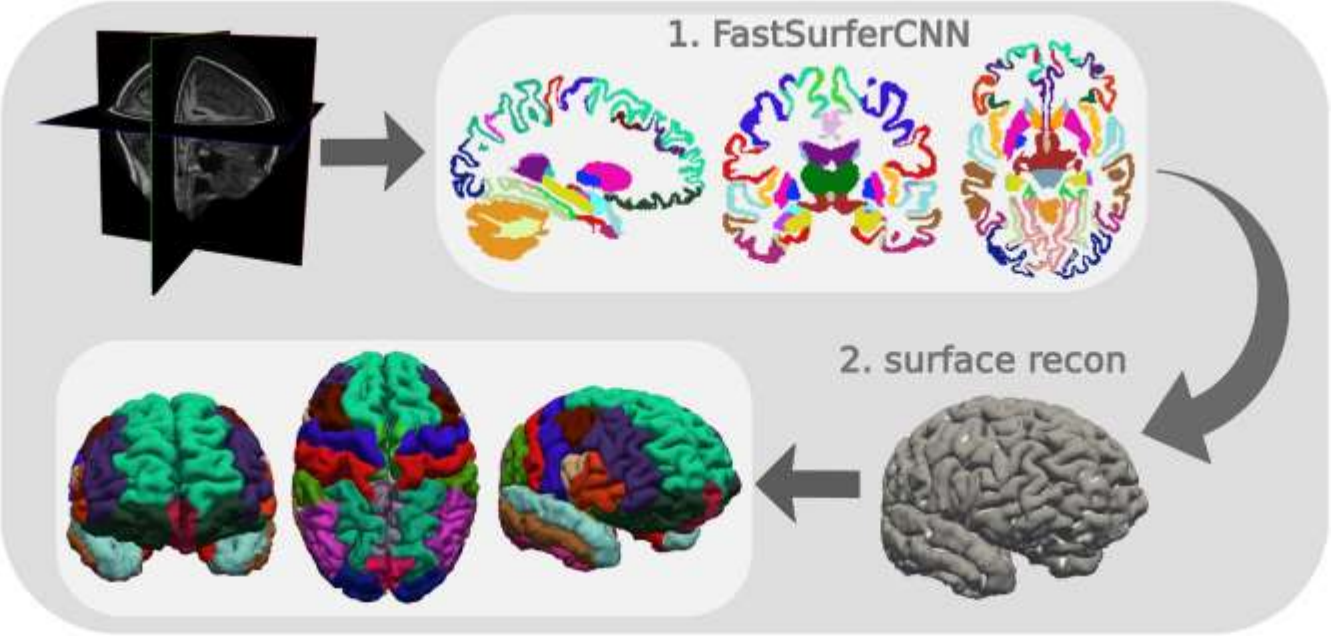


3D Image Segmentation

- **November / December**
  - Brain extraction
  - Tissue type segmentation
  - Cortical surface parcellation
  - Markov Random Fields
  - Deep Learning
  - Statistical inference in group studies



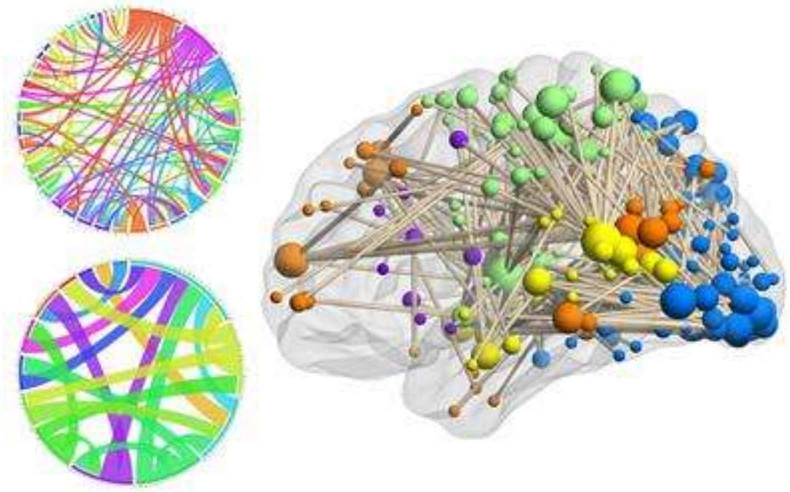
[Smith 2002]

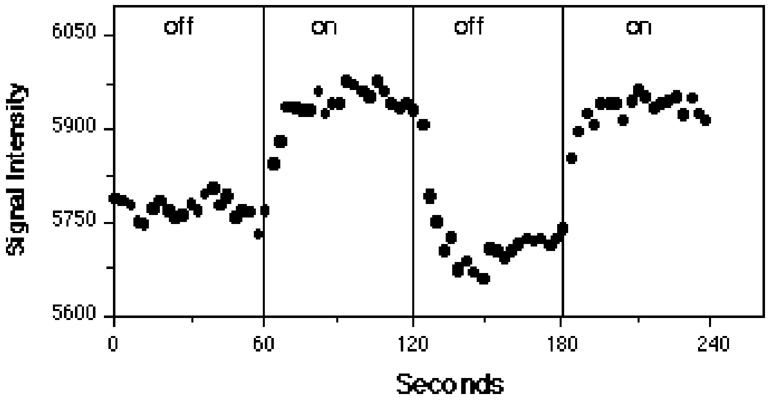


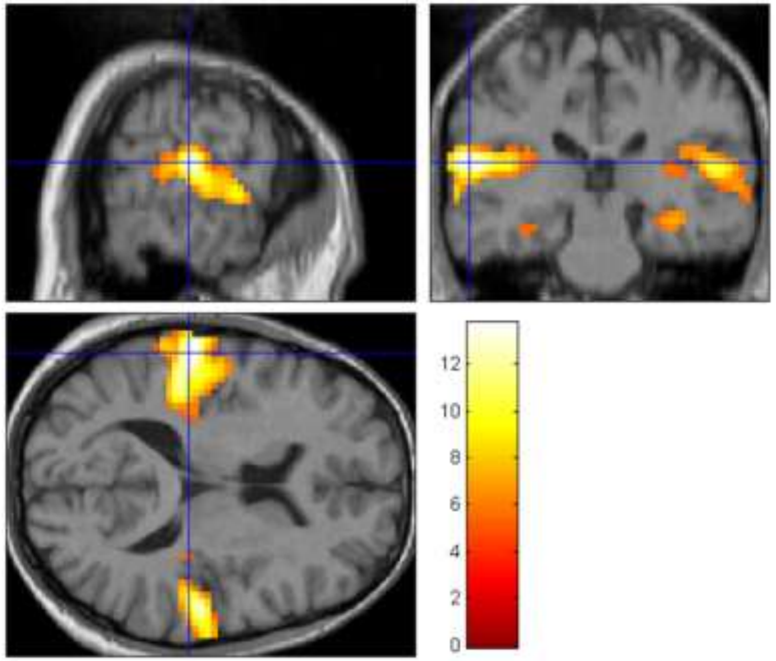
[Henschel et al. 2020]

Analysis of Functional MRI (fMRI)

- **December**
  - – BOLD mechanism
  - – Mathematical modeling
  - – Image processing pipeline
  - – Statistical inference
  - – Graph models

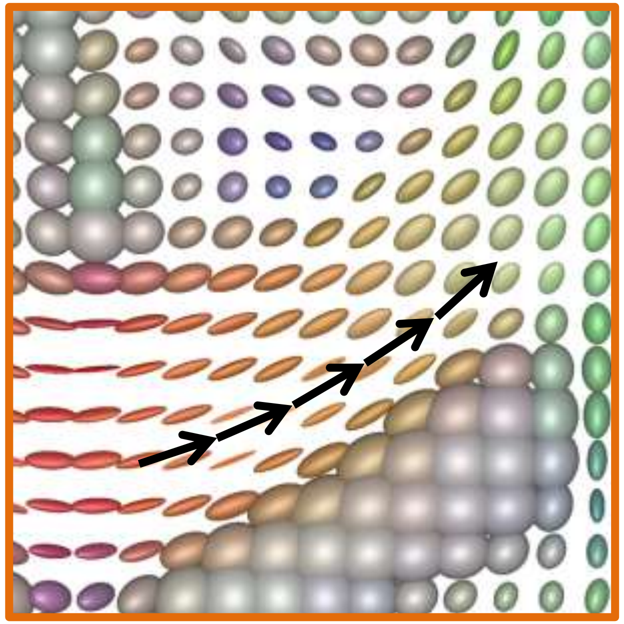


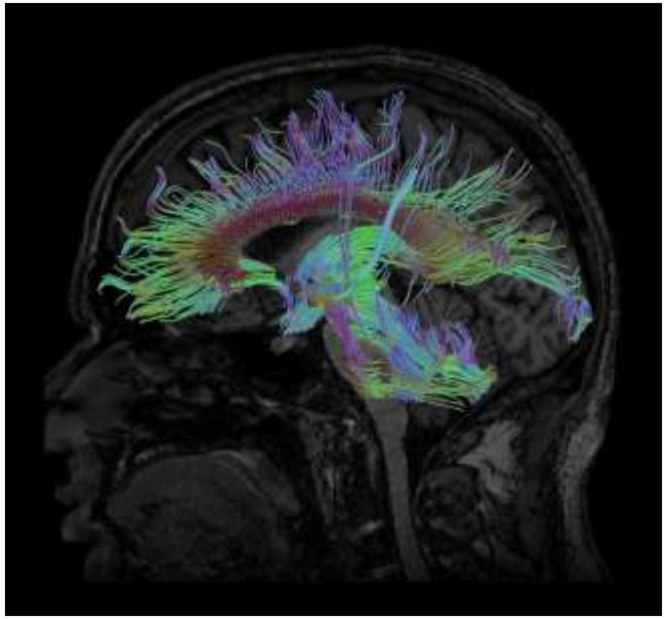




Analysis of Diffusion MRI (dMRI)

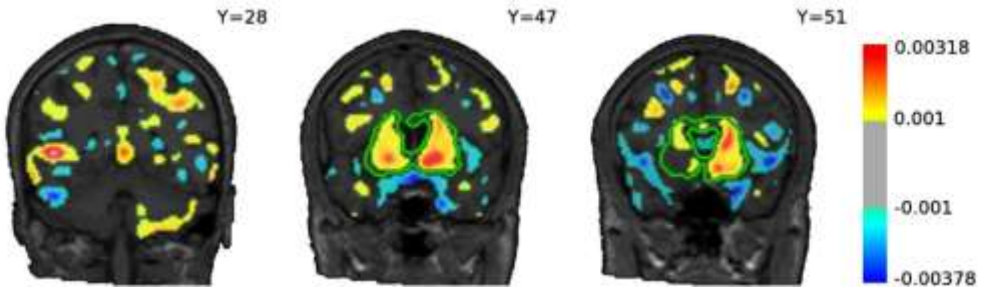
- **January**
  - Measuring water self-diffusion to break MRI resolution limit
  - Fiber tracking
  - Quantitative analysis



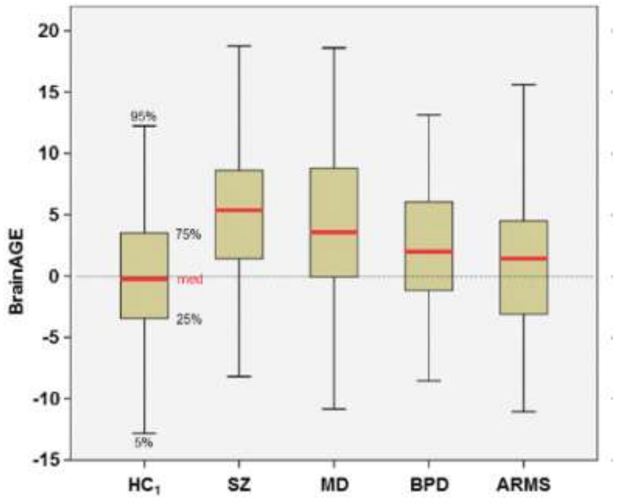


Supervised Classification and Regression

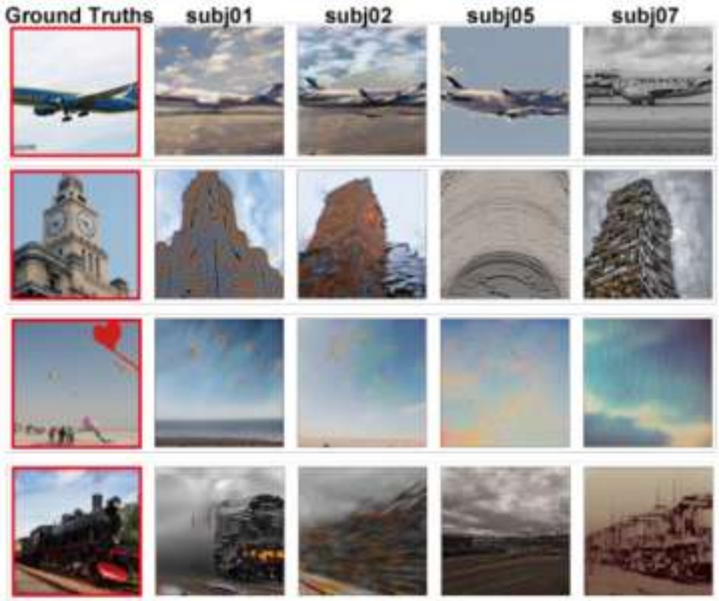
- **End of January**
  - Applications such as
    - Computer Aided Diagnosis
    - Estimating BrainAge
    - Reconstructing images a subject looked at in the scanner
    - Lie detection



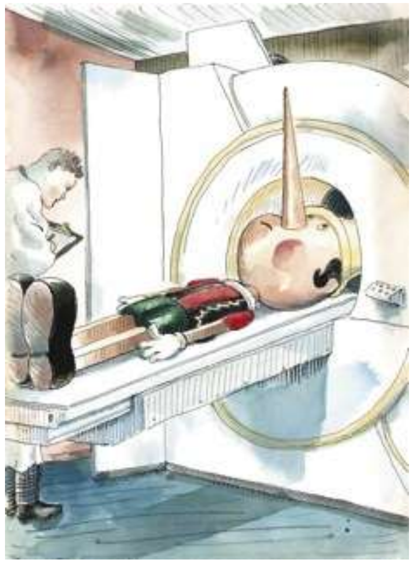
[Nieuwenhuis et al. 2012]



[Koutsouleris et al., 2013]



[Takagi/Nishimoto, 2023]



New Yorker, 2007

Visit a Scanner!

- I am planning a visit at Theodor Rüber‘s lab at Life&Brain (UKB campus), including their MR scanner, during the lecture slot on

February 2, 2026

Prerequisites

- Basic **mathematical background** (calculus, linear algebra)
- Some **programming background**
  - We will use Python, which is easy to learn even if you don't know it
- Helpful if you already know about **signal or image processing, machine learning,** and/or **statistics,** but not required
  - All important facts explained in this lecture

Learning Goals

- Learn about the **computer science methods** behind neuroimaging studies
  - Image processing, mathematical modeling, statistics, machine learning
- Ability to **solve small problems** in image analysis, to work in small teams and present your results
- **Understand** how neuroimaging results can (and cannot) be interpreted
- **Prepare** for a potential lab, seminar, MSc or even PhD thesis in the field

1.2 Organization

Lectures

- **Lectures** will take place
  - Mon 14:15-15:45 in HS 3 (Lecture Hall Building Campus Poppelsdorf)
  - Thu 14:15-15:45 in HS 3 (Lecture Hall Building Campus Poppelsdorf)
- As long as in-class participation remains sufficiently high, I am planning to make **lecture recordings** available
  - In case I should need to replace one or two live lectures with pre-recorded videos, this will be announced in advance.
- Slides, assignments, forum via **eCampus**
  - Please sign up there as an attendee

Exercises

- 6 Exercises (mixed theory / programming)
  - You will have at least one week to work on them
  - Discussion will replace a lecture slot. *Tentative* dates:
    - 2025: Mon Nov 10, Thu Nov 20, Thu Dec 4, Mon Dec 15
    - 2026: Thu Jan 15, Mon Jan 26
- Please work in teams of 2-3
- Requirement for being admitted to the exam:
  - At least **50% of overall points**
  - **Presenting at least one answer** in class

People

- **Lecture:**
  Prof. Dr. Thomas Schultz
  schultz@cs.uni-bonn.de

- **Exercises:**
  Annika Mikliss
  mikliss@cs.uni-bonn.de

Credit

- Based on exam at the end of the semester
  - If number of participants permits, it will be oral with flexible dates
- MSc students in **Computer Science / Cyber Security** at the University of Bonn will register via basis and receive **6 ECTS credits**
- The class is cross-listed for MSc students in **Media Informatics** or **HCIS** (RWTH Aachen) with **6 ECTS credits**
- Do we have any students from other programs?

Advertisement: Lecture by Prof. Stöcker

- Our lecture includes a short introduction to MR physics
  - At a level that is appropriate for computer scientists
- Lecture by Prof. Tony Stöcker for MSc Physics goes into much more detail:
  - Physics in Medicine: Physics of Magnetic Resonance Imaging
  - Tue 10-12h, Thu 16-18h, SR I (Nußallee 14-16)
  - Find more details on basis

1.3 Foundations of Neuroanatomy

The Human Brain in Numbers

Avg Volume:
1300 cm^3

Avg Mass:
1.5 kg

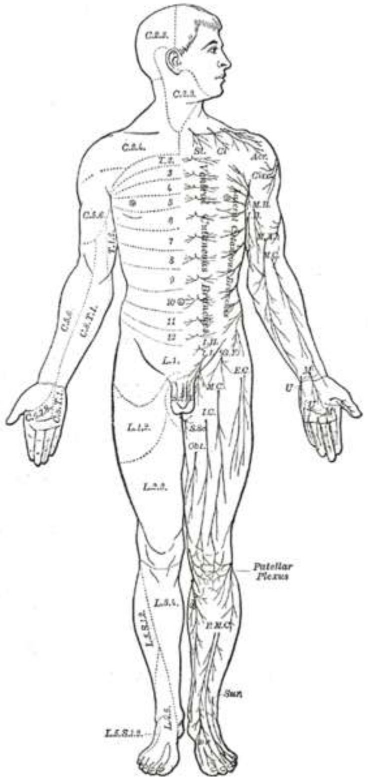
Uses **up to 20%** of the body's energy supply

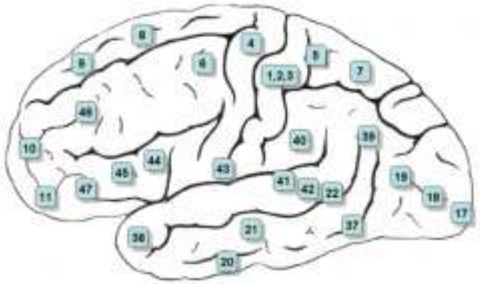
120 billion neurons, making **≈10^{14} connections**

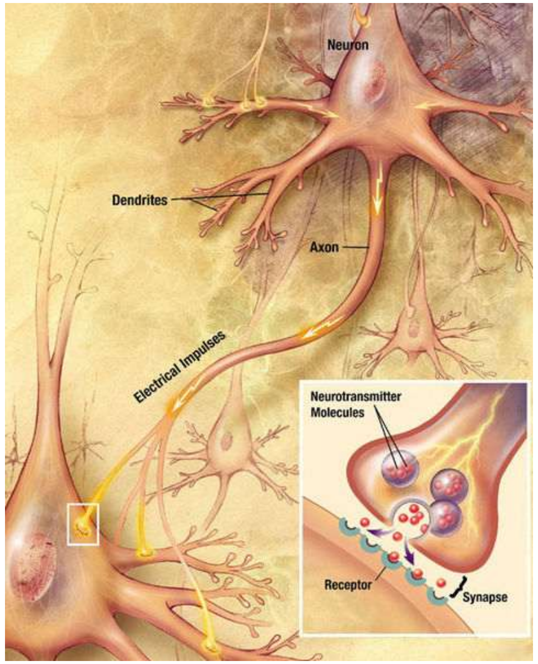
Image Source: Patrick R. Lynch @ wikimedia commons

A Top-Down Approach

We will start by looking at the nervous system as a whole and work our way down to its individual cells







The Nervous System

The nervous system has two main parts:

- **Central Nervous System** (CNS)
  - Brain
  - Spinal cord
- **Peripheral Nervous System** (PNS)
  - Sensory (afferent) and motor (efferent) neurons

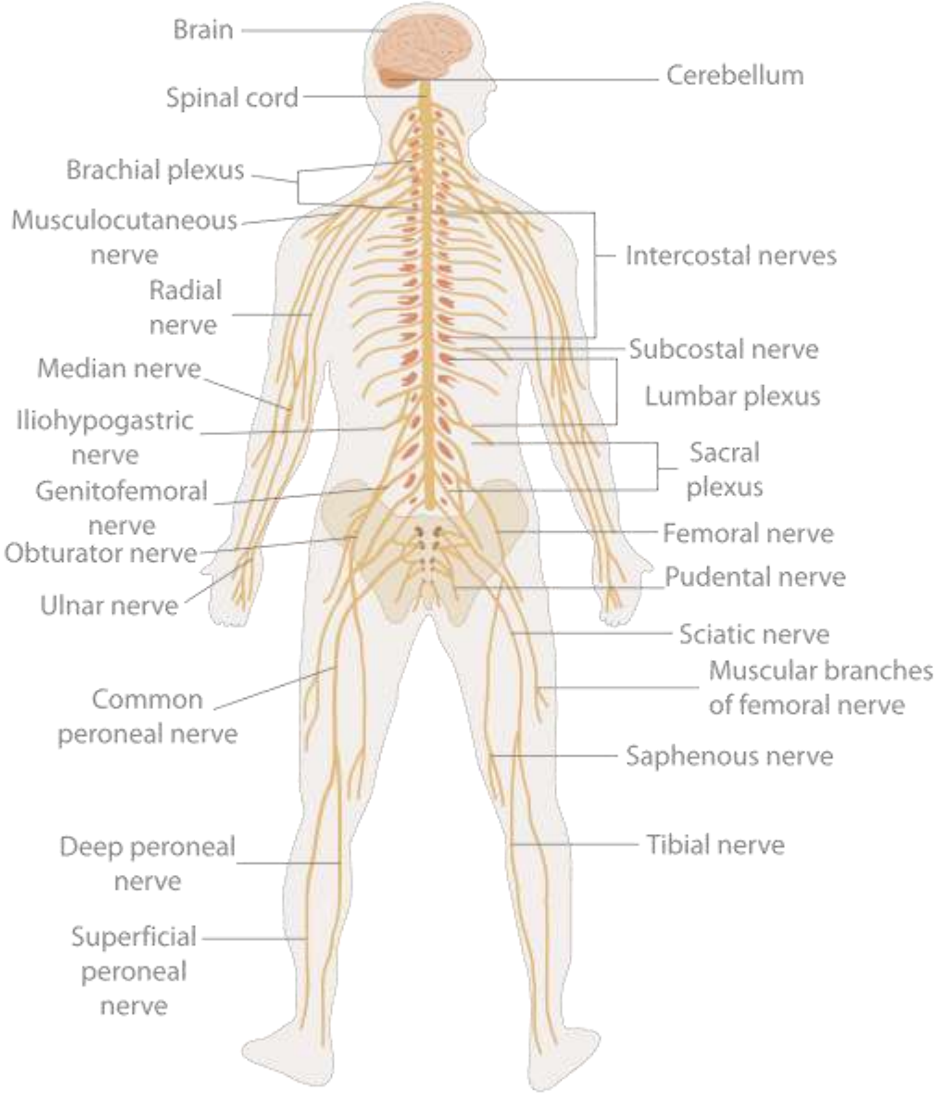


Image Source: theEmirr @ wikimedia commons

PNS: Somatic vs. Autonomic System

- **Somatic nervous system** (soma=body) innervates skin, muscles, and joints. It is responsible for transmitting their sensory stimuli and for their voluntary control.
- **Autonomic nervous system** receives information about the body’s internal state. It innervates glands (Drüsen), viscera (innere Organe) and blood vessels, without voluntary control.

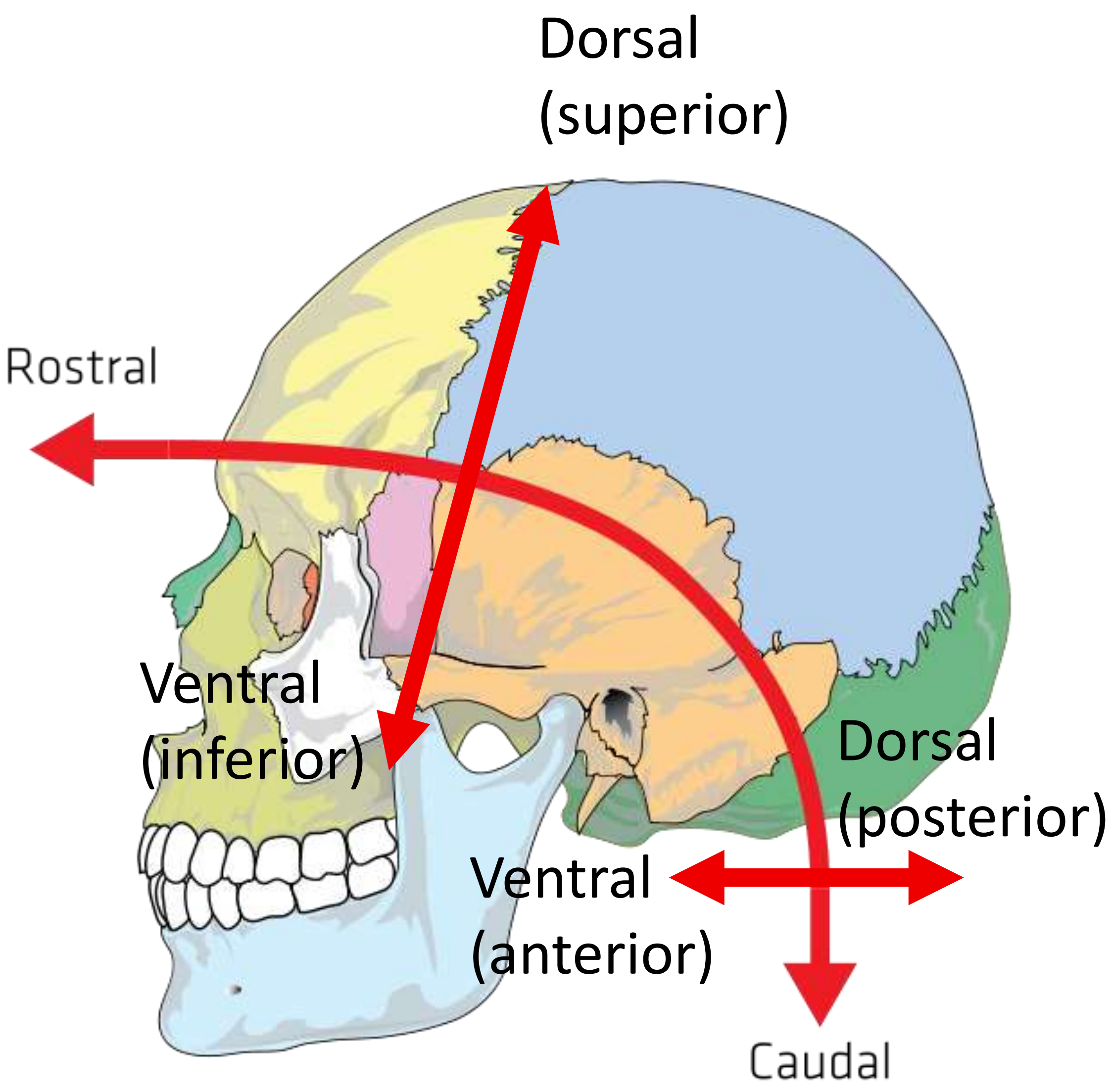
Axes

Anatomical axes in the head:

- left / right
- rostral / caudal
- dorsal / ventral

More common in 3D imaging:

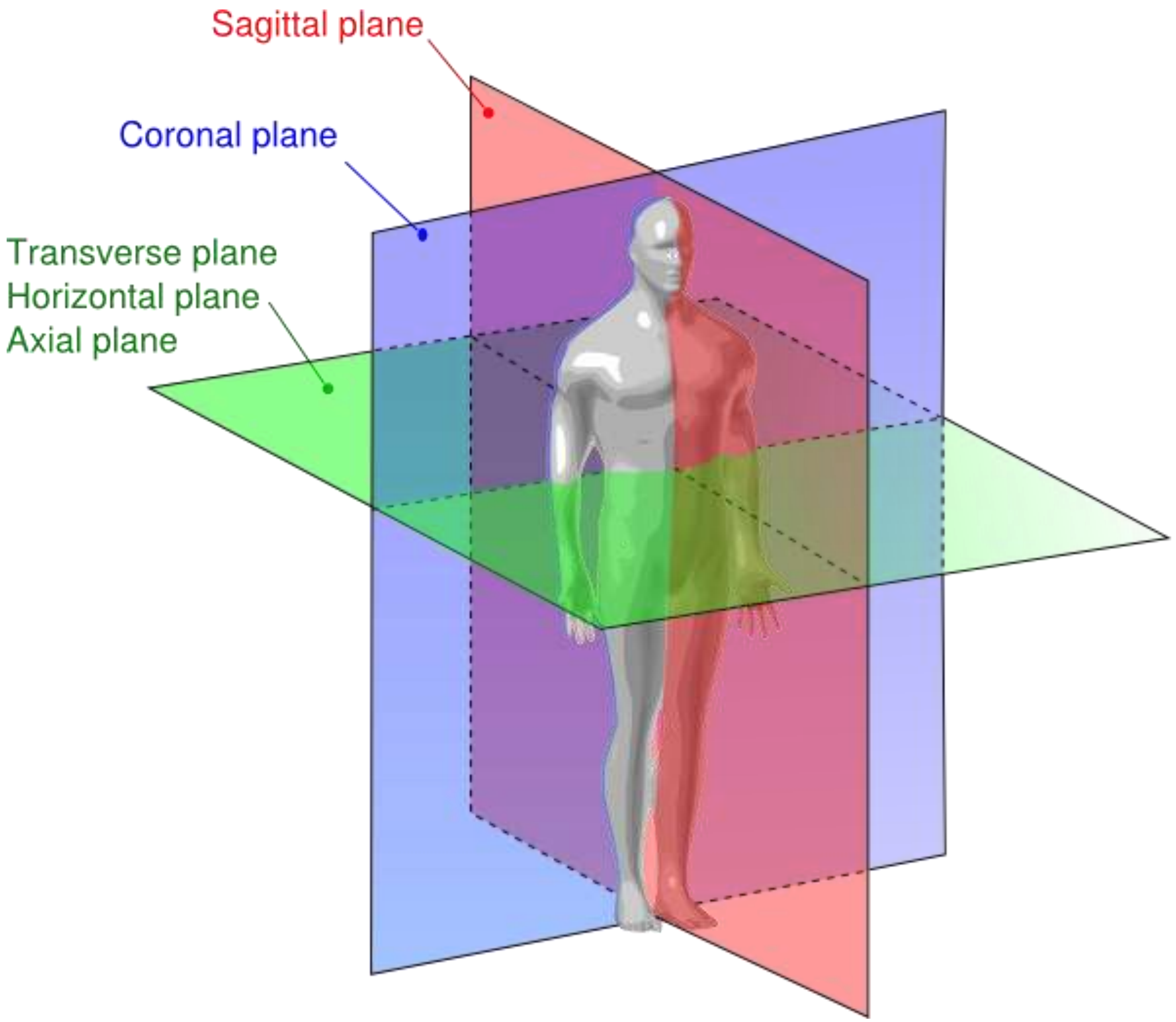
- anterior / posterior
- superior / inferior



Planes

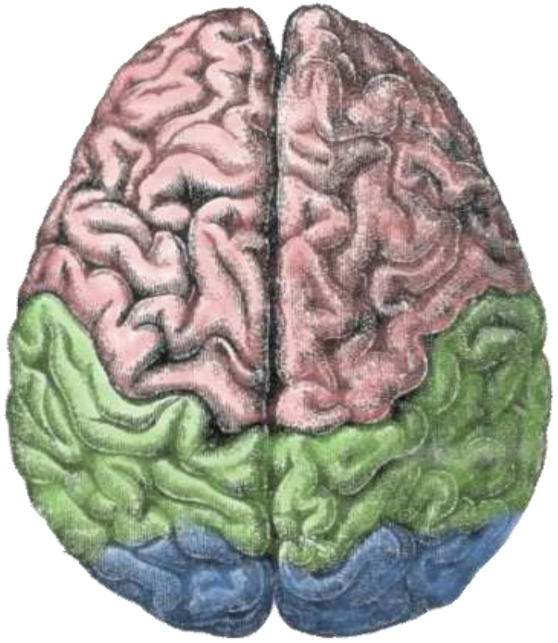
In MR imaging, the body planes commonly coincide with the following coordinate axes:

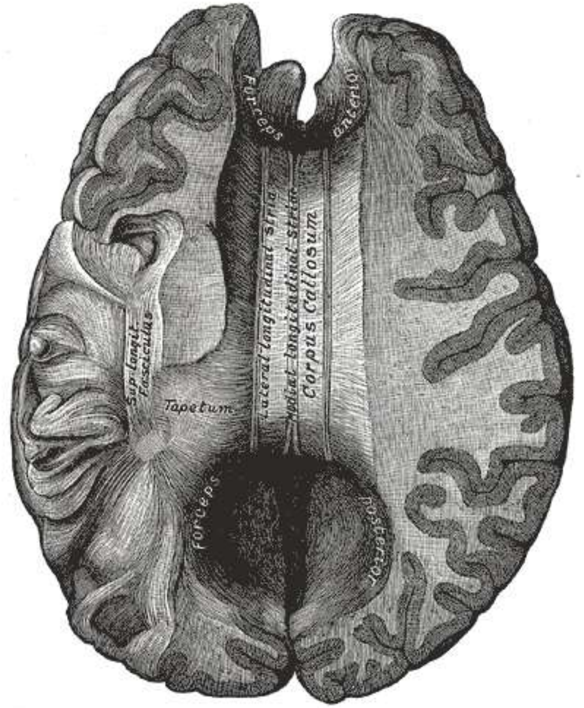
- Sagittal: yz
- Coronal: xz
- Axial: xy



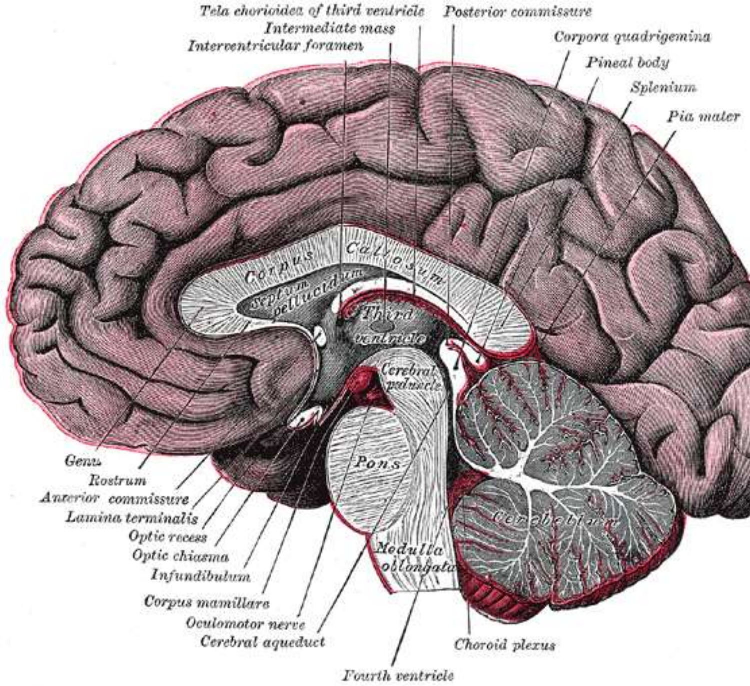
Hemispheres

The longitudinal fissure subdivides the brain into left and right hemisphere, connected by the corpus callosum





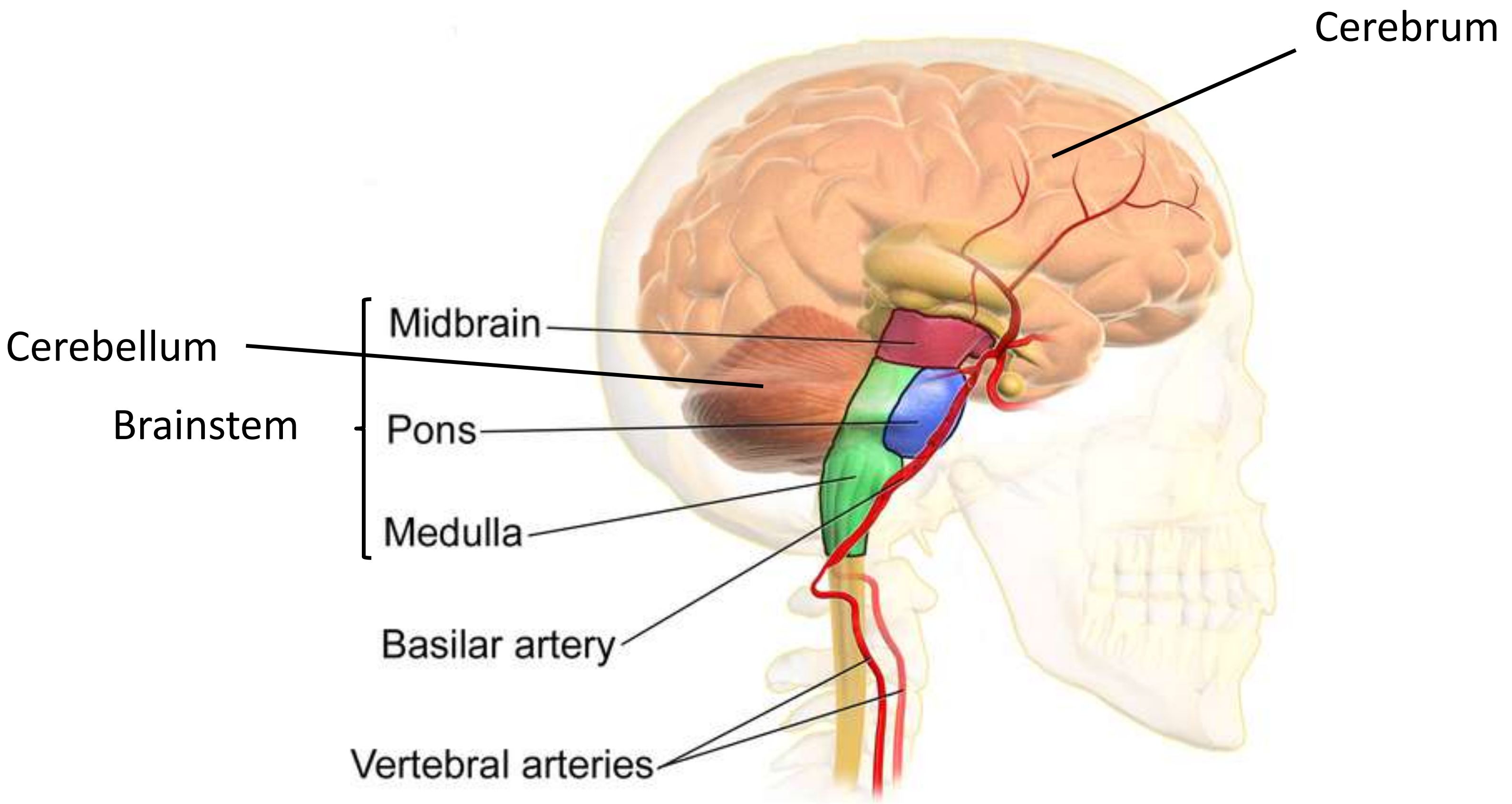
Horizontal view



Mid-sagittal view

Macroscopic Structure of the Brain

A macroscopic subdivision of the brain is made based on evolutionary development:

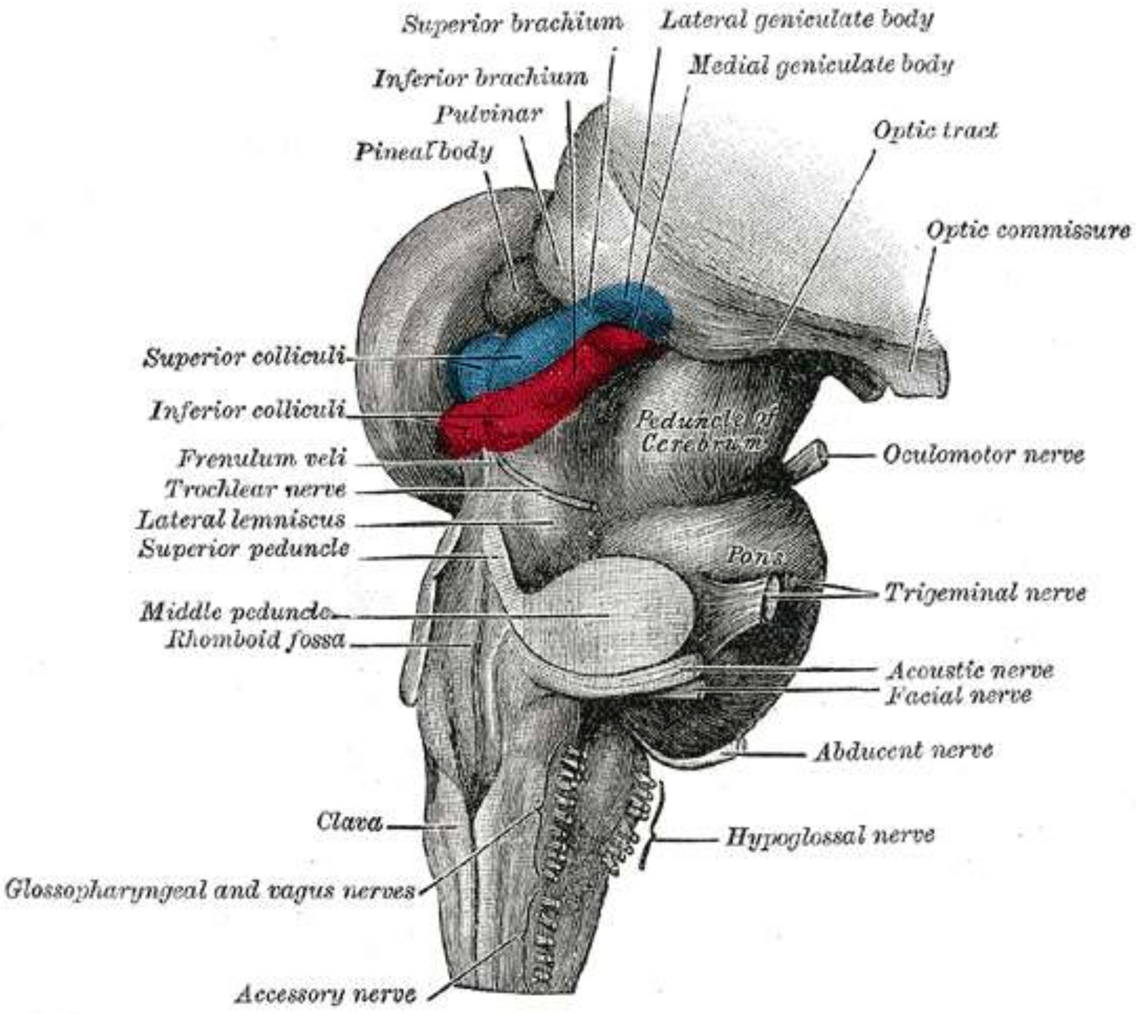


Adapted from: Bruce Blaus @ wikimedia commons

The Brainstem

Oldest part of the brain

- Connects the brain to the rest of the body
  - Continuation of the spinal cord
  - Cranial nerves leave or enter (e.g., face/neck)
- Key role for control of respiration, blood pressure, heart rate
- Damage almost always life threatening



The Cerebellum

- Roughly 10% of the brain volume, but contains half of the neurons in the CNS
- Regulates motion by integrating information from motion and sensory systems
  - Posture, balance, coordination
- Also contributes to non-motor language skills, decision making, and emotion

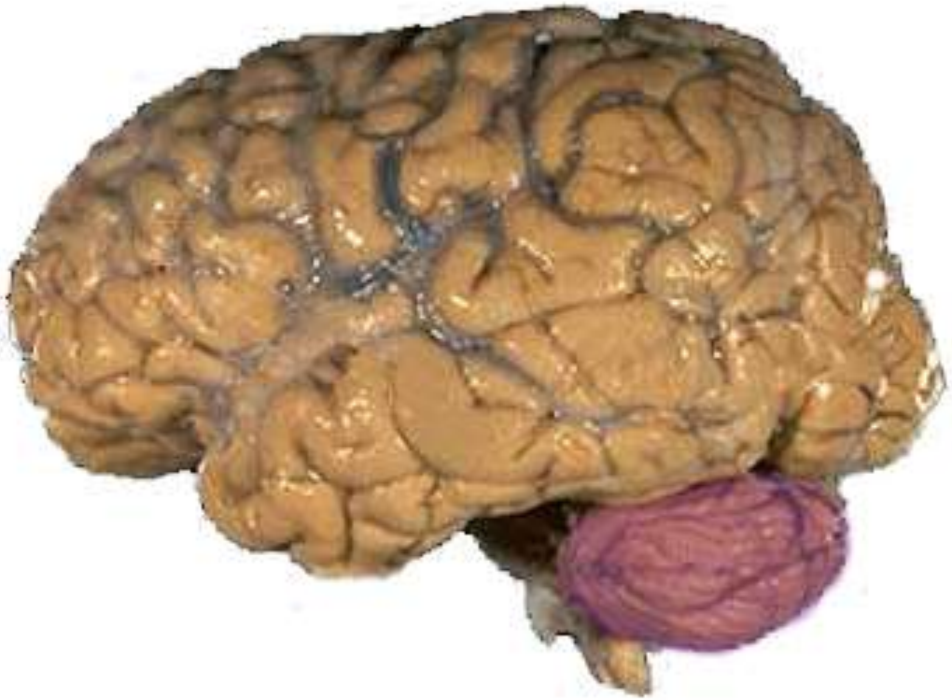


Image Source: NIH

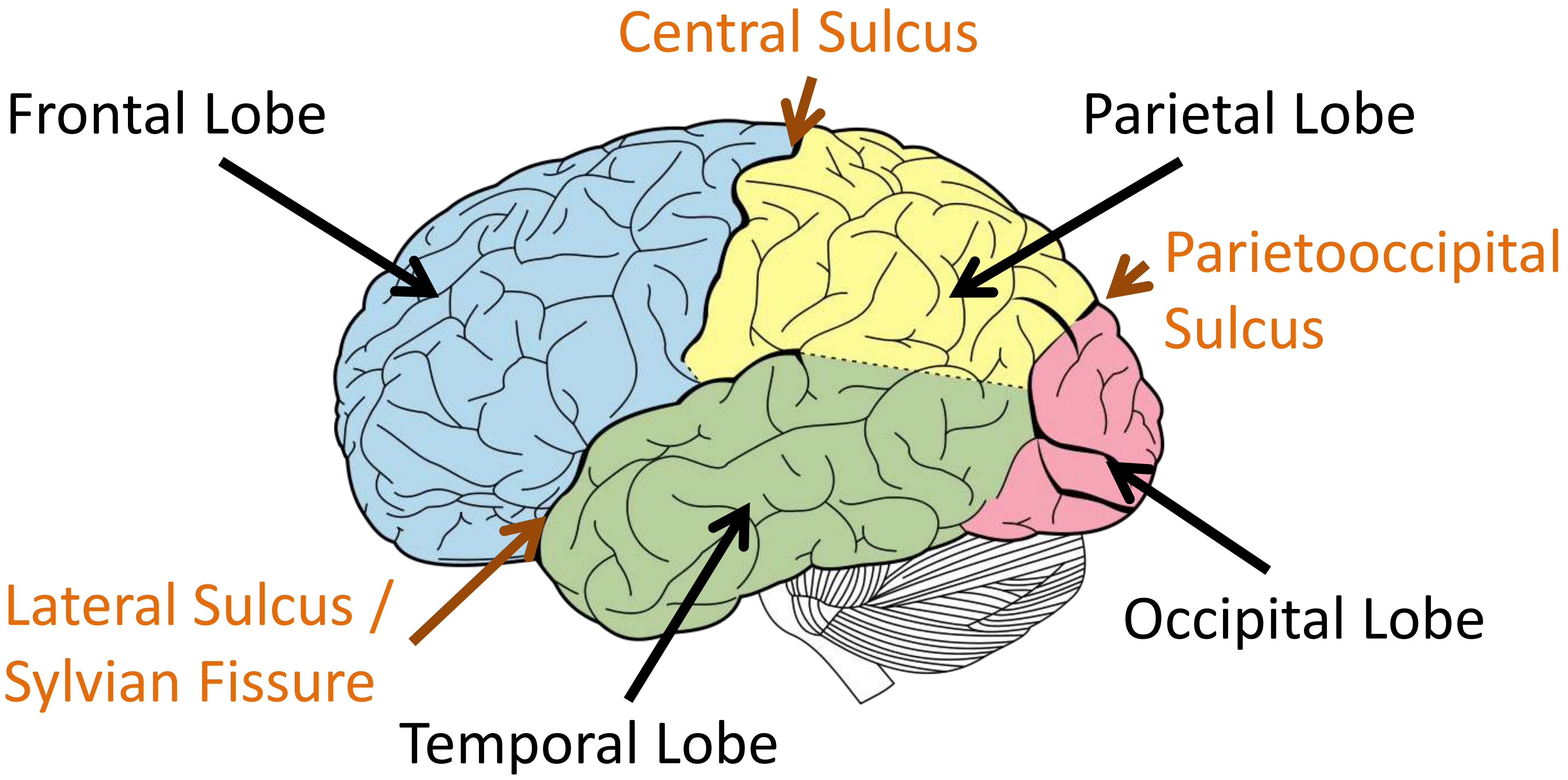
The Cerebrum

- High-level functions such as memory, attention, perceptual awareness, thought, language, and consciousness
- Consists of:
  - – Cerebral Cortex
  - – Hippocampal Formation
  - – Amygdala
  - – Basal Ganglia

Image Source: Body Parts 3D

Lobes of the Cerebrum

Based on macroscopic landmarks, the cerebrum is further subdivided into four lobes

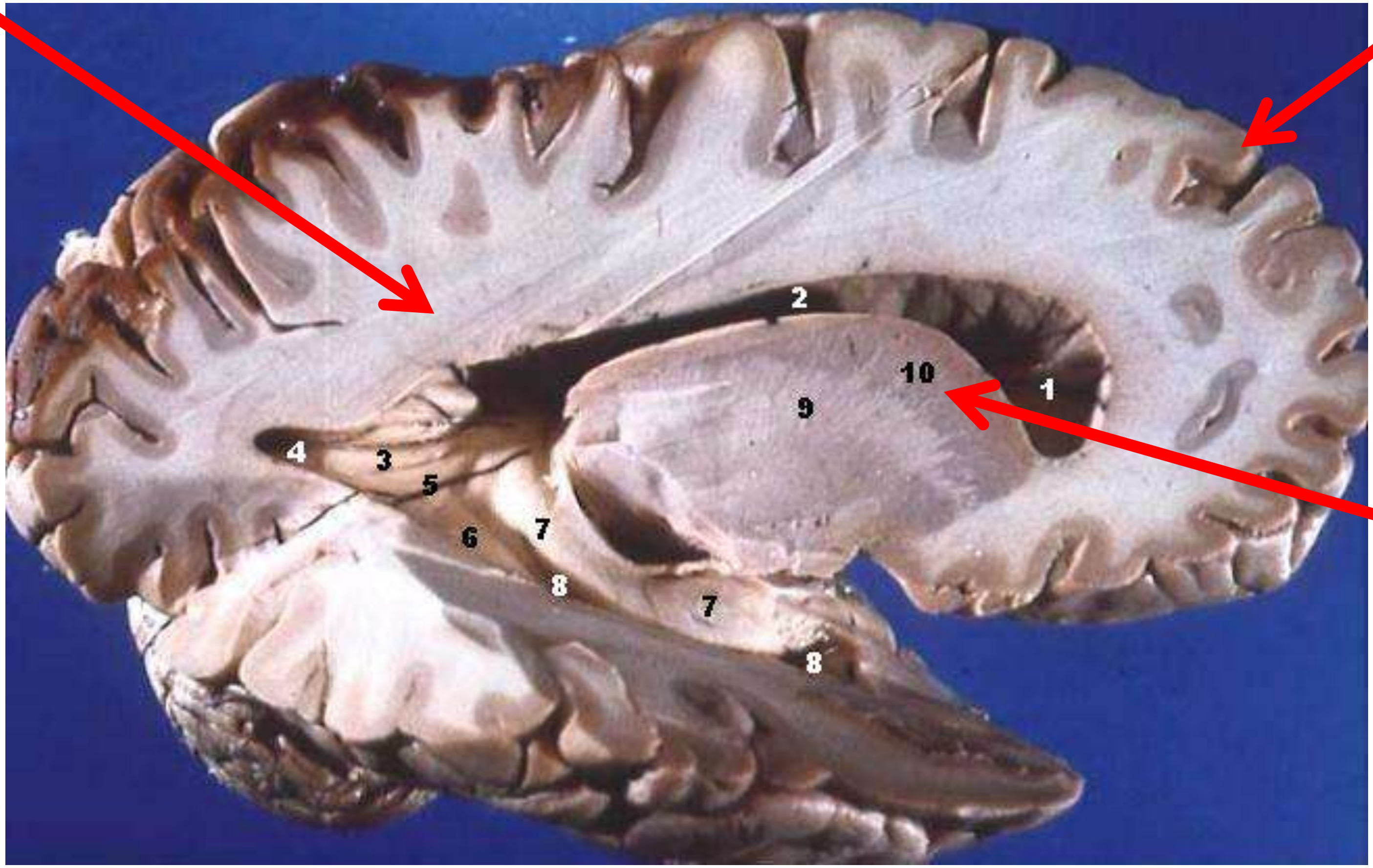


Gray Matter vs. White Matter

- In brain dissections, some parts appear gray, others look white

White Matter

Cortical Gray Matter

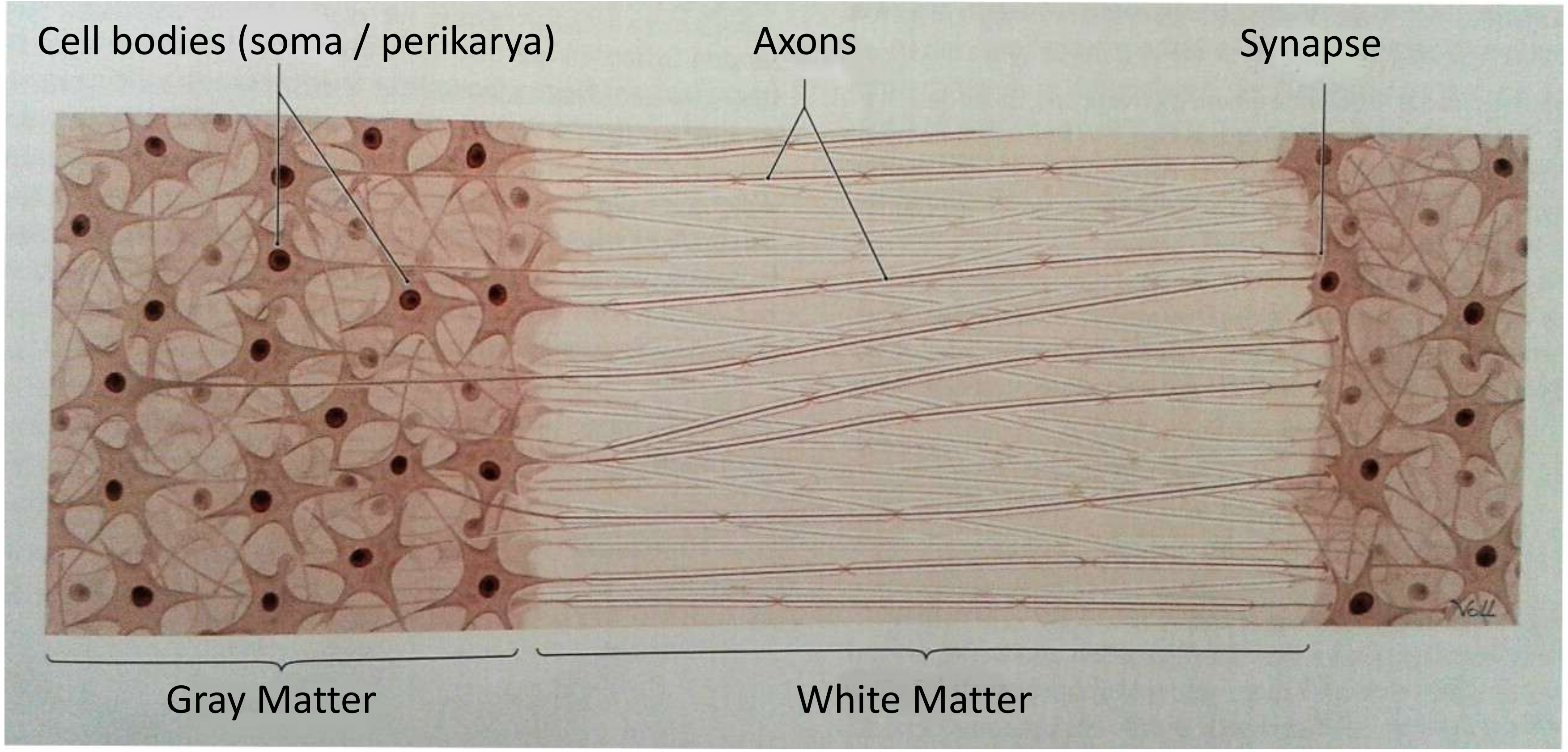


Deep Gray Matter

Image Source: John A. Beal @ wikimedia commons

Gray vs. White: Histology

- Gray matter mainly consists of the cell bodies
- White matter mainly consists of axons



Adapted from: Schünke, Lernatlas der Anatomie

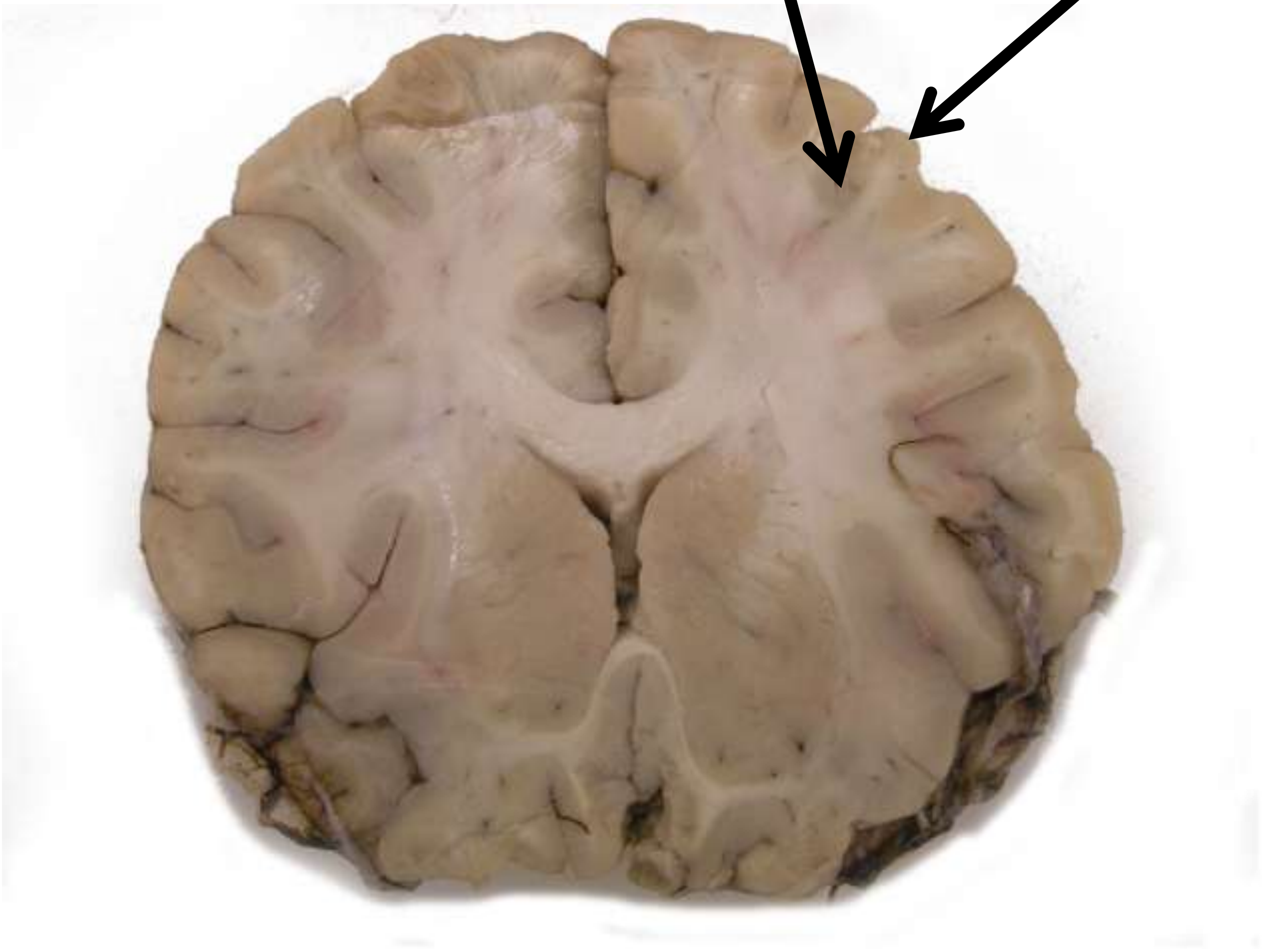
The Cerebral Cortex

- Cortex = gray matter at the outermost part of the cerebrum
- Highly folded
  - – Gyri (elevations)
  - – Sulci (grooves)
- Thickness: 2-4 mm
- Area: 2500 cm^2

  ≈4 A4 sheets

Sulcus

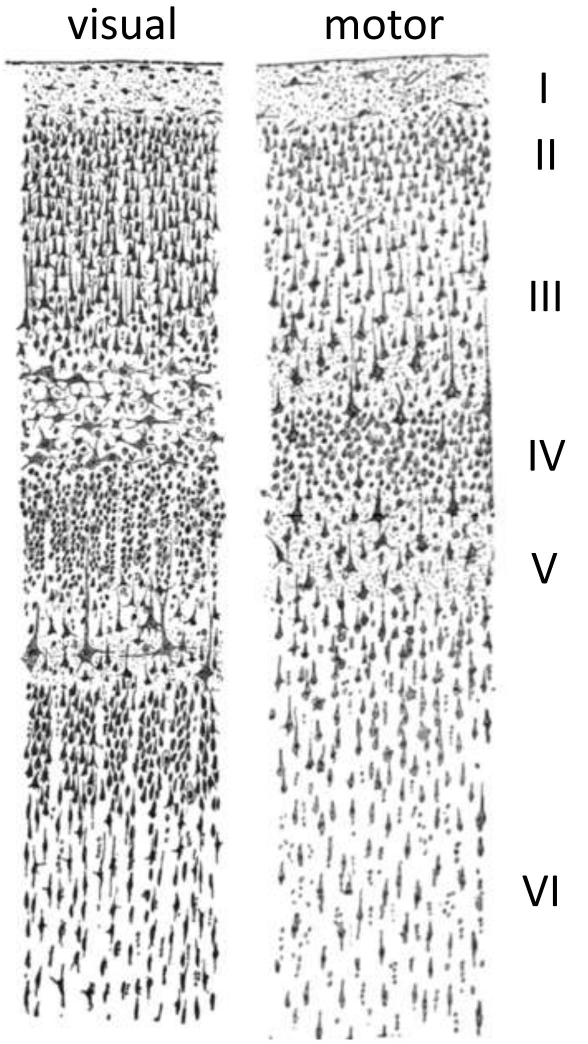
Gyrus



[Rajalakshmi L Nair et al., 2006]

Structure of the Cortex

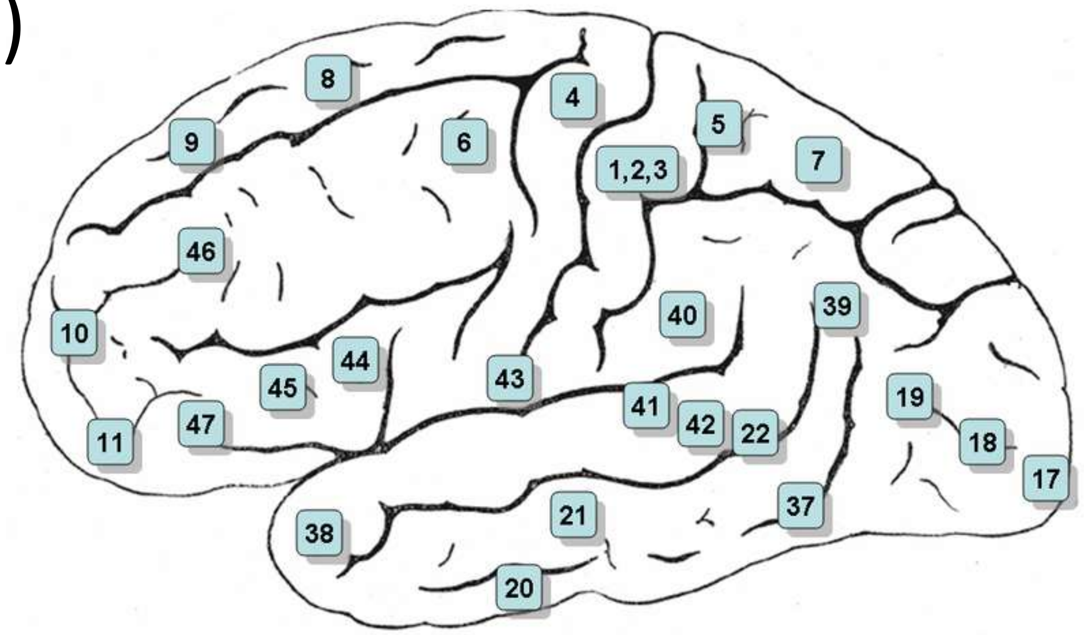
- Horizontal layers:
  - In 95% of the cortex (neocortex/ Isocortex), at least six layers
    - Differ in visual appearance and connectivity (e.g., input / output, brain region)
  - In remaining 5% (allocortex), less than six layers
- Vertical columns:
  - Based on overlapping input
  - Diameter: 200-800 µm



Drawing by Santiago Ramon y Cajal, 1899

Brodmann's Areas

- **Korbinian Brodmann** (1868-1918) subdivided the cortex into more than 50 distinct areas, based on the neuronal layering



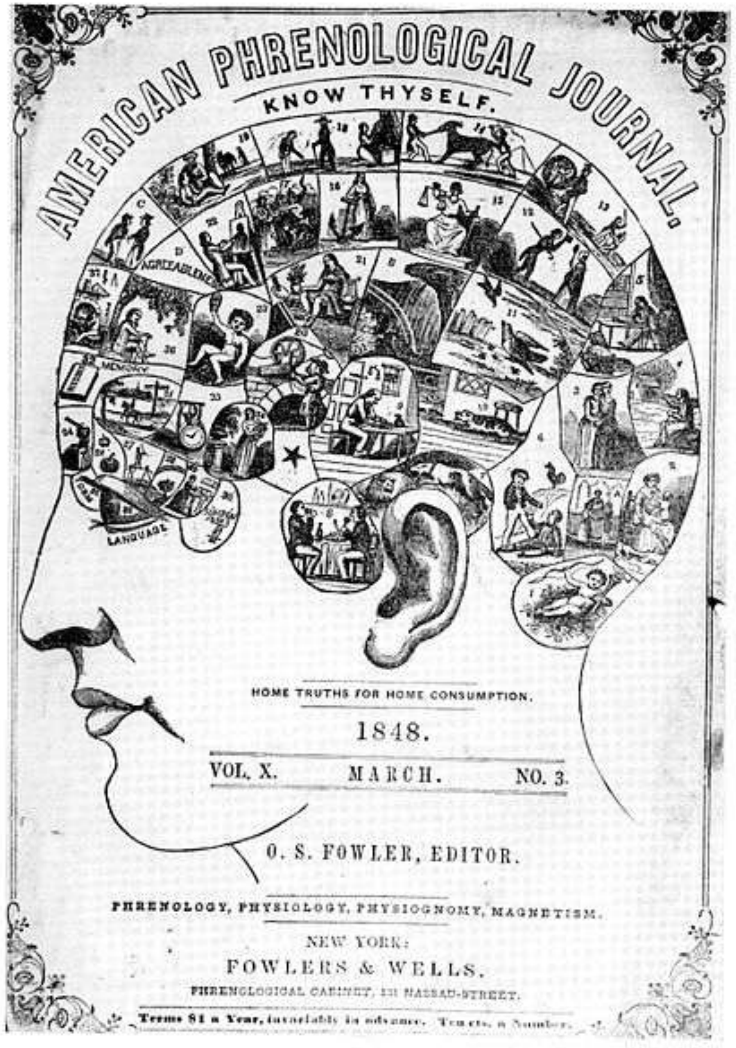
- Discussed and refined over time, still in use
- Many areas have been found to correspond to functional units

Functional Localization and Integration

- Different parts of the brain specialize in different functions. This can be seen from:
  - **Connectivity:** Visual cortex receives input from eyes, motor cortex connects to the muscles etc.
  - **Damage** to local regions affects certain functions, but leaves others intact
  - **Imaging methods** that will be discussed in this lecture visualize which regions are “activated”
- **But:** The brain is highly connected, and complex functional networks that involve many regions are required for most non-trivial perception or behavior

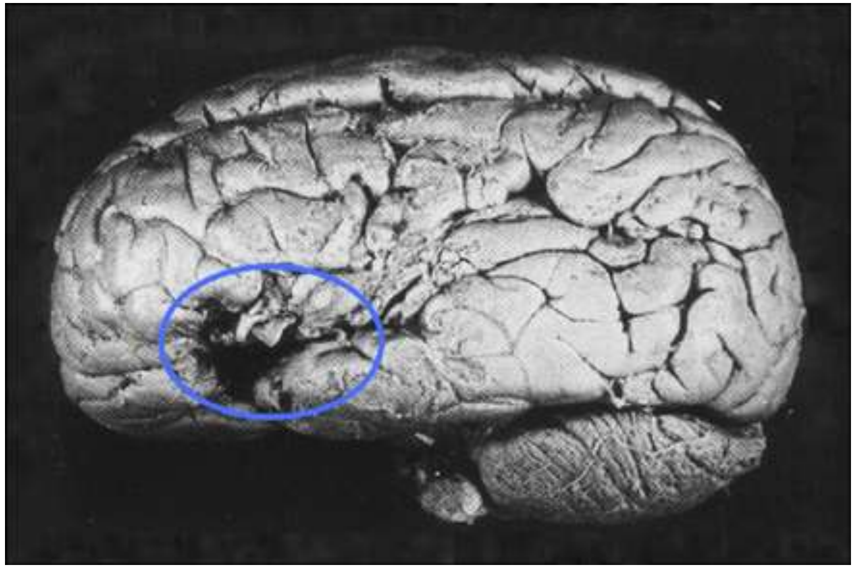
Historical Note: Phrenology

- **Phrenology** ("knowledge of the mind") is a pseudoscience developed by Franz Joseph Gall in 1796 and widely popular in the early 19th century
- Tried to correlate mental ability and traits of character with **cranial shape**, which was thought to reflect over- or underdeveloped brain regions
- Lost credibility in 1840s and induced great skepticism about **functional localization** in general



Historical Note: Paul Broca and David Ferrier

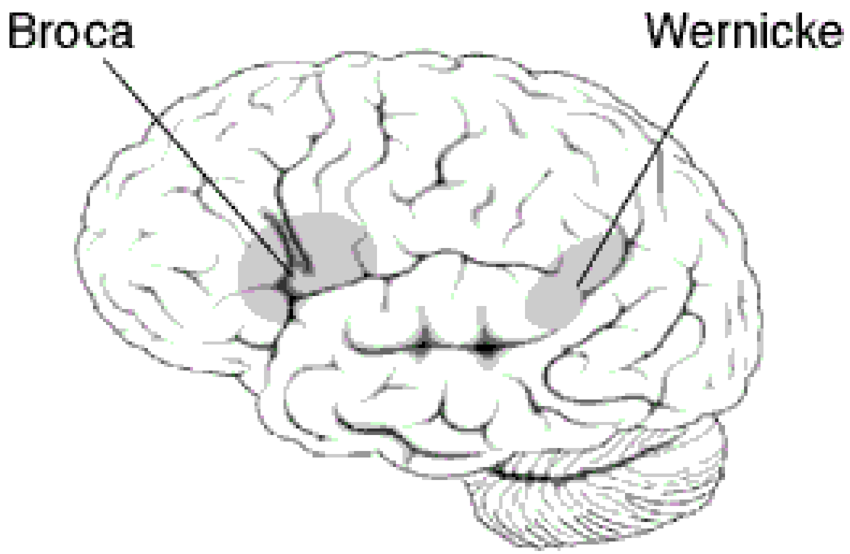
Two scientists were instrumental in restoring confidence in functional localization:



- **1861:** Paul Broca dissects the brain of a patient ("Monsieur Tan") with a specific and limited loss of speech production and a clearly circumscribed lesion
- **1881:** Working with macaque monkeys and dogs, David Ferrier demonstrates that specific behavior can be evoked by stimulation and destroyed by surgical lesions

Broca's and Wernicke's Areas

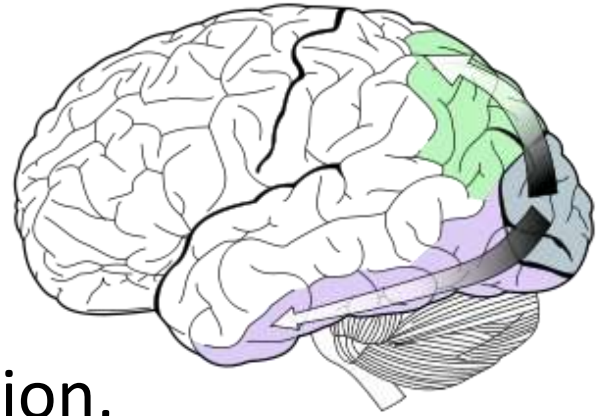
Two language-specific areas in the left hemisphere:



- **Broca's area** (Brodmann 44/45)
  - Important for producing speech
  - Injury leads to slow and halted speech
- **Wernicke's area** (Brodmann 22)
  - Important for understanding speech
  - Injury can lead to meaningless "word salad"
- Homotopic areas in right hemisphere relevant for emotional content of speech

Visual Cortex

- Primary visual cortex in Brodmann area 17
- Contralateral response:
  – Right hemisphere receives input from left visual field
- Higher-level processing:
  – Dorsal stream (“where”, fast, guides behavior)
  – Ventral stream (“what”, slower, conscious perception, recognition, memory)



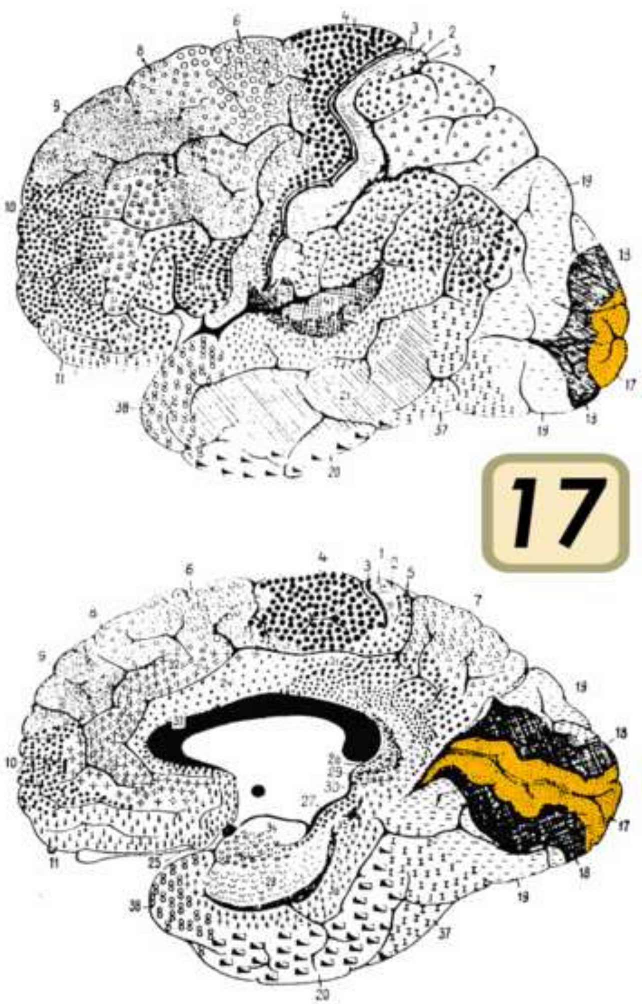


Image Source: Selket @ wikimedia commons

Auditory Cortex

- Primary auditory cortex in Brodmann areas 41 and 42
- Strictly contralateral response in some mammals (e.g., rats), but not in humans; might be due to development of language
- Dorsal “where” and ventral “what” path similar to visual system

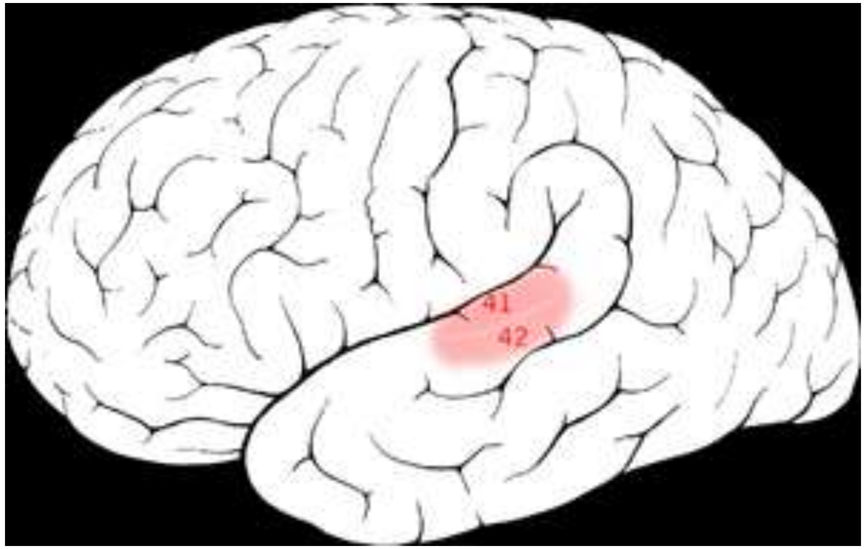


Image Source: Dryke @ wikimedia commons

Somatic Motor and Sensory Cortex

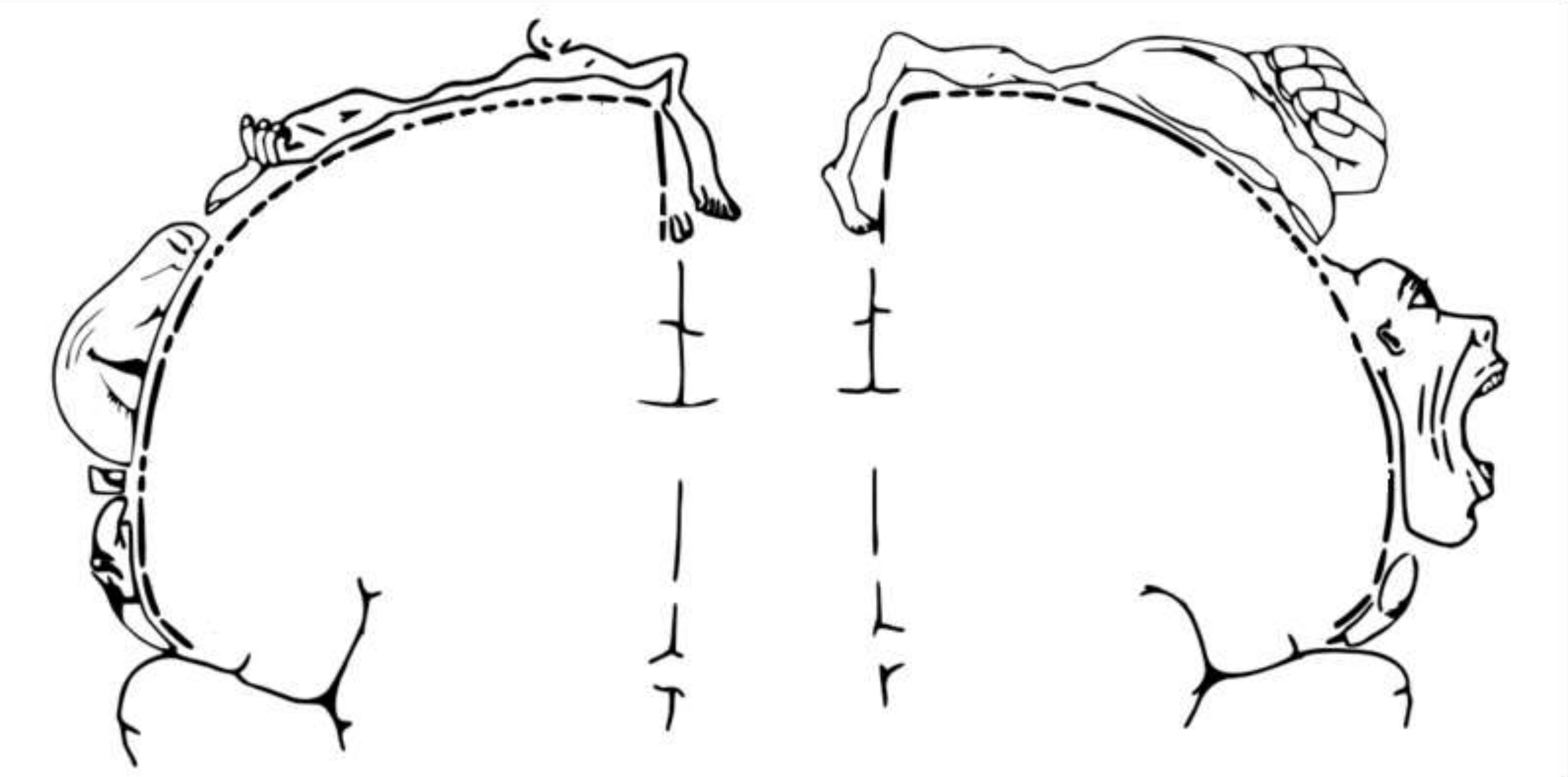
- Primary **somatosensory cortex** (sense of touch, pain, and limb position) is in the postcentral gyrus (Brodmann 1/2/3)

- Primary **motor cortex** is in the precentral gyrus (Brodmann 4)

Image Source: Was a bee @ wikimedia commons

The Homunculus

Different parts of the body are represented at different locations along the somatosensory or motor cortex



Somatosensory Cortex Motorcortex

The Interrupted Homunculus

- Based on functional MRI, [Gordon et al. 2023] propose that
  – the homunculus is interrupted by a somato-cognitive action network (SCAN)
  – motor effector regions have a concentric organization

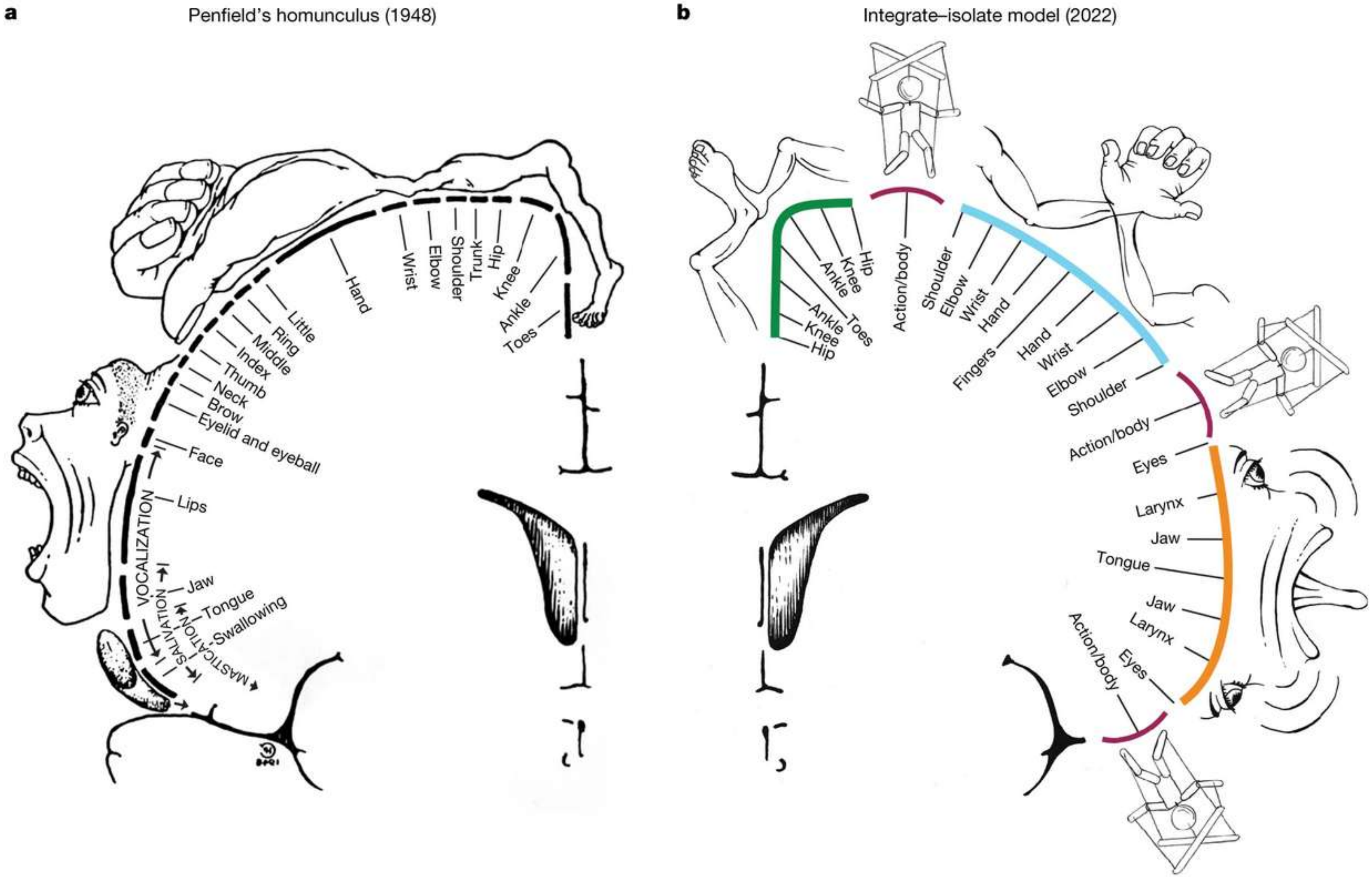


Image from [Gordon et al., Nature 2023]

The Thalamus

- Deep gray matter structure
- Two halves, connected in the thalamic adhesion
- Consists of many small nuclei
  - Defined by separating laminae (myelinated axons) or cell architecture
- Serves as a relay for sensory input
  - Exception: Olfaction (sense of smell)
  - Also involved in some motor pathways
- Diffuse projections regulate cortical activity

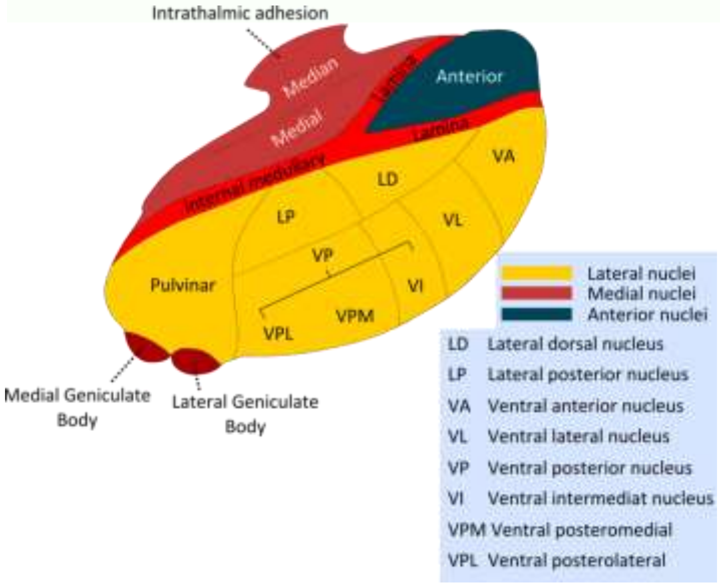
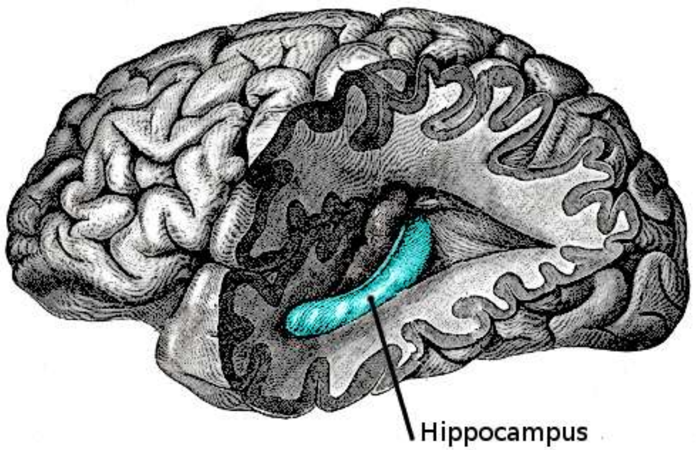
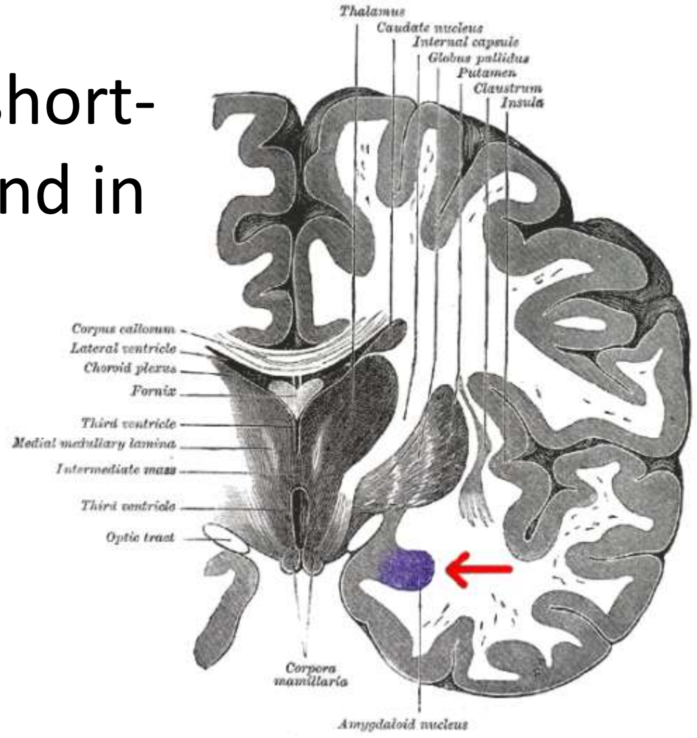


Image Sources: Life Science Databases / madhero88

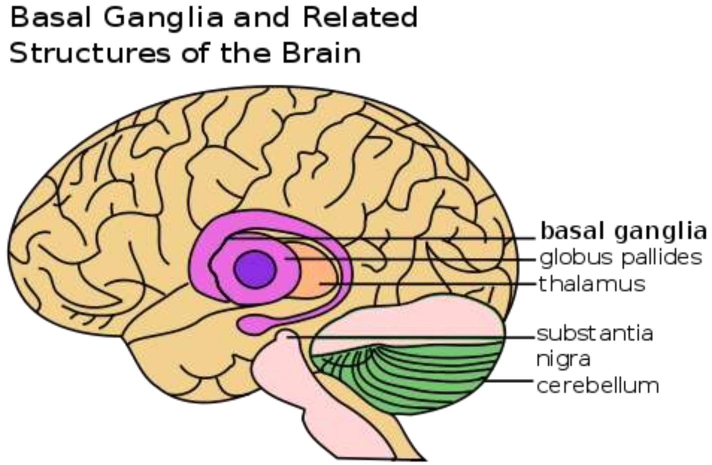
Hippocampus, Amygdala, Basal Ganglia



- Hippocampus
  - Plays a role in consolidating short-term to long-term memory and in spatial navigation



- Amygdala
  - Plays a role in memory and emotions



- Basal Ganglia
  - Group of strongly connected nuclei
  - Role in procedural learning, forming of habits, action selection

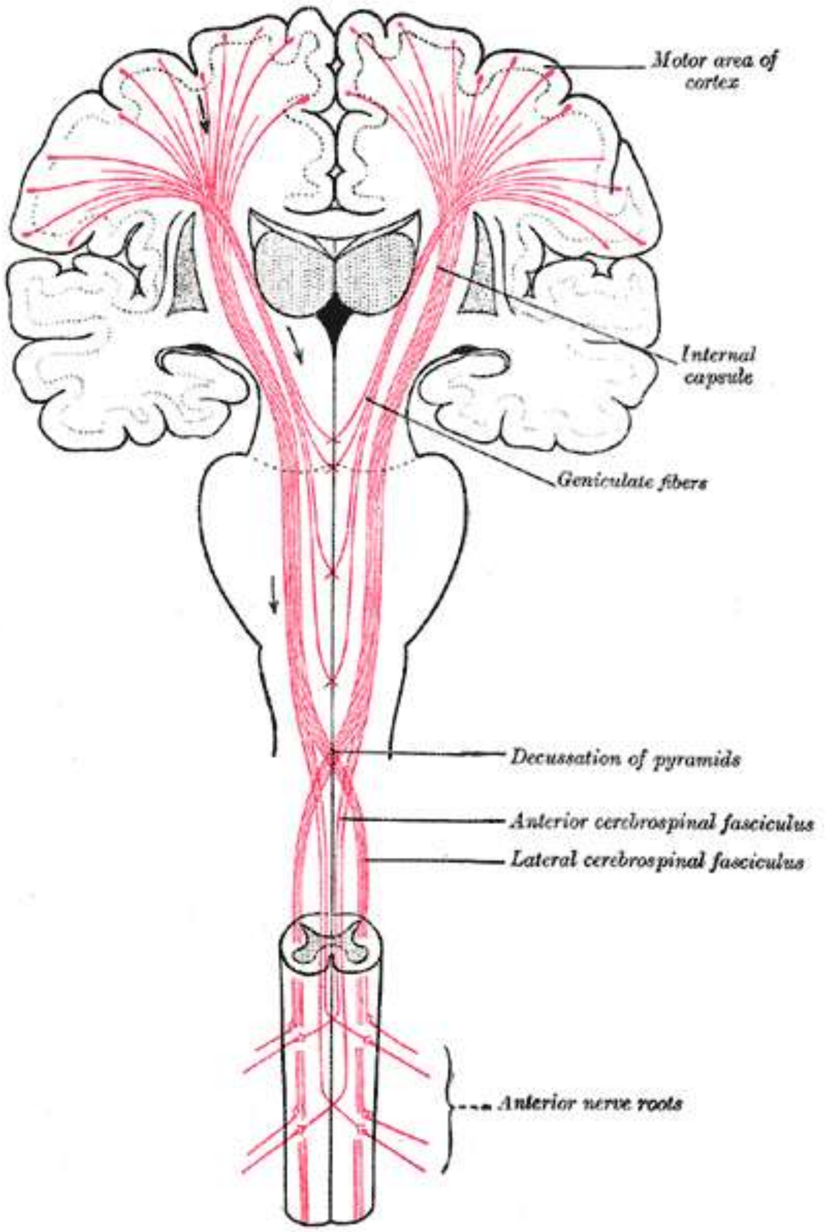
White Matter Architecture

- White matter consists of elongated axons that transmit information between different parts of the brain
- Axons are organized in **fiber bundles**
  - **Association Fibers:** Within the same hemisphere
    - Short: Connecting adjacent gyri (“U-fibers”)
    - Long: Connecting more distant parts
  - **Commissural Fibers:** Connect the hemispheres
  - **Projection Fibers:** Connect cortex with lower parts of the brain or the spinal cord

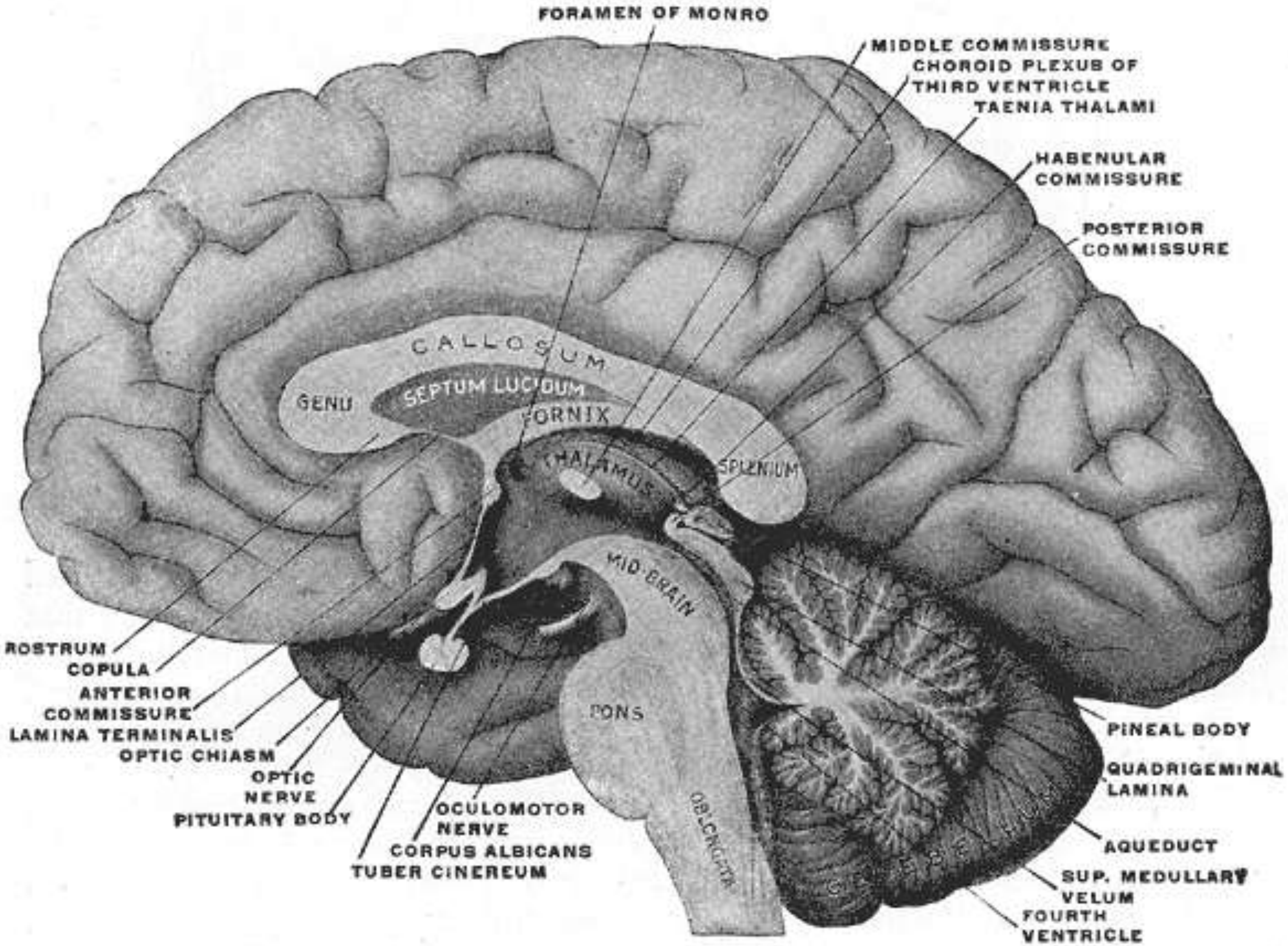
Projection Fibers

- **Efferent:** Motor tract
  - – Corticospinal fibers
  - – Geniculate fibers
  - – Corticopontine fibers

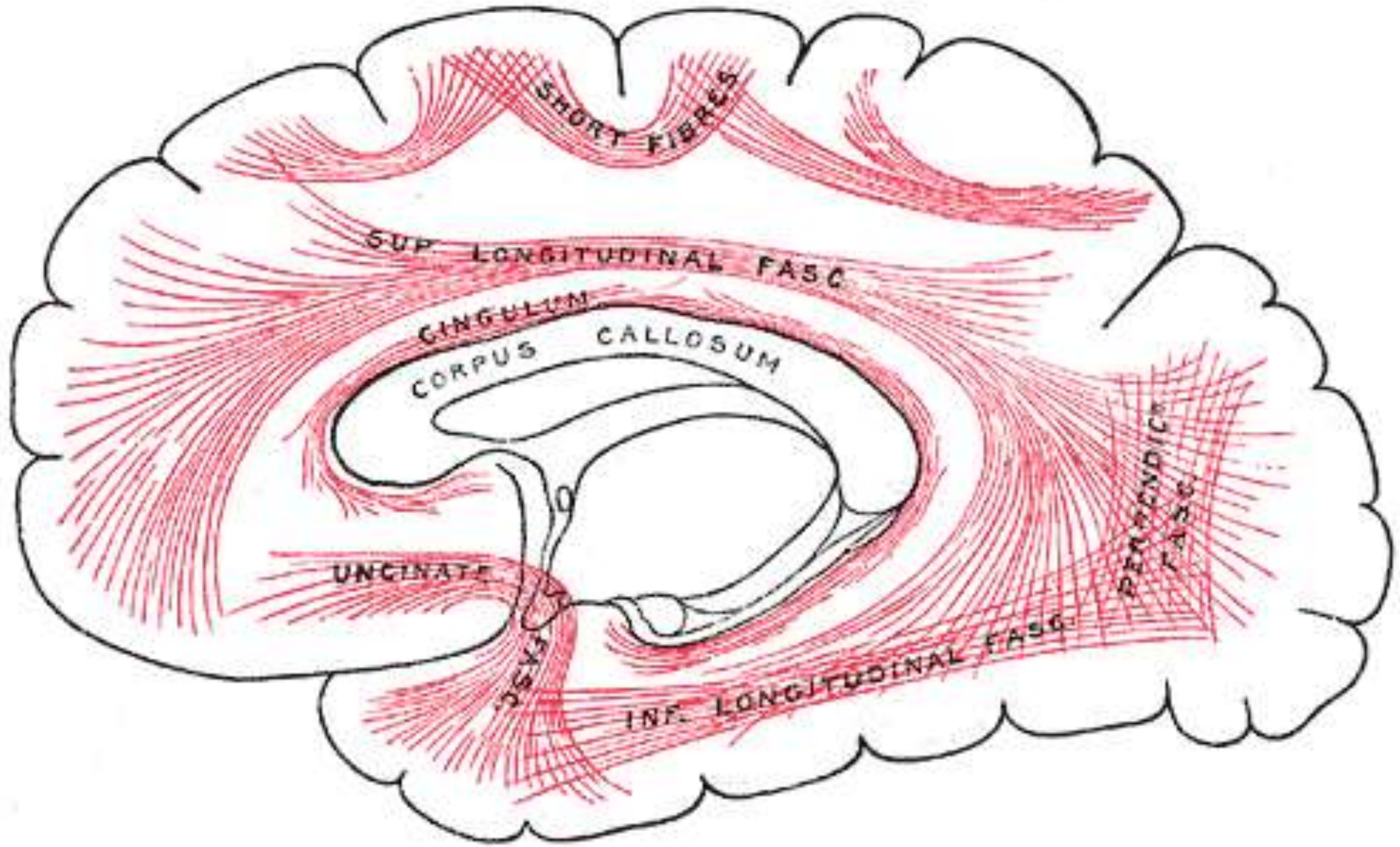
- **Afferent:**
  - – Optic and acoustic tracts
  - – Superior cerebellar peduncle
  - – Thalamocortical tracts



Commissural Fibers

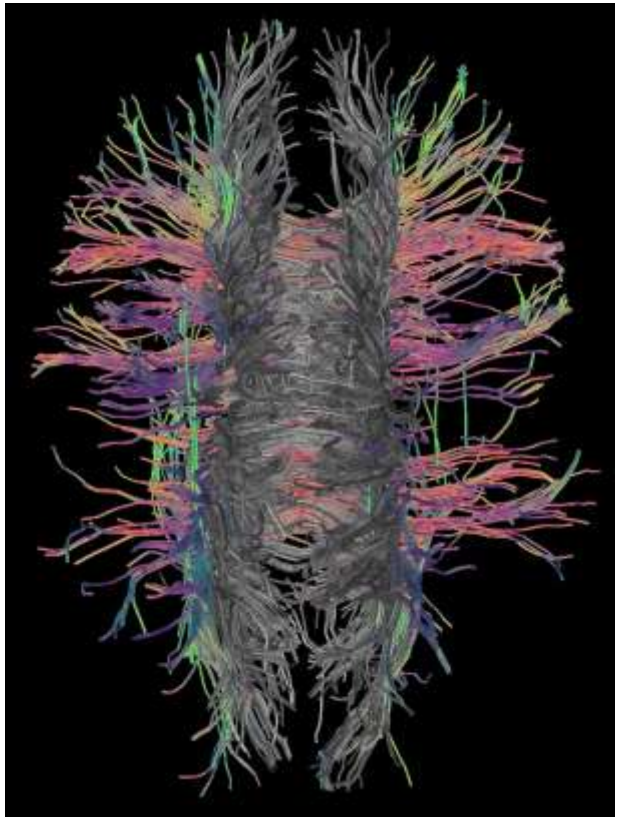


Association Fibers



Studying the Connectome

- Connectome = complete map of the connections in the human brain
- Even larger-scale than Genome (3×10^9 base pairs vs. $\approx 10^{14}$ synapses)
- NIH Human Connectome Project
  - 1,200 healthy adults
  - Specific follow-up projects



[Schultz/Seidel 2008]

- Rhineland Study (DZNE): Prospective study on healthy ageing, plans to follow up on more than 20,000 participants for decades

The Ventricular System

- Ventricles = system of cavities, filled with cerebrospinal fluid
- Continuous with central canal of spinal cord

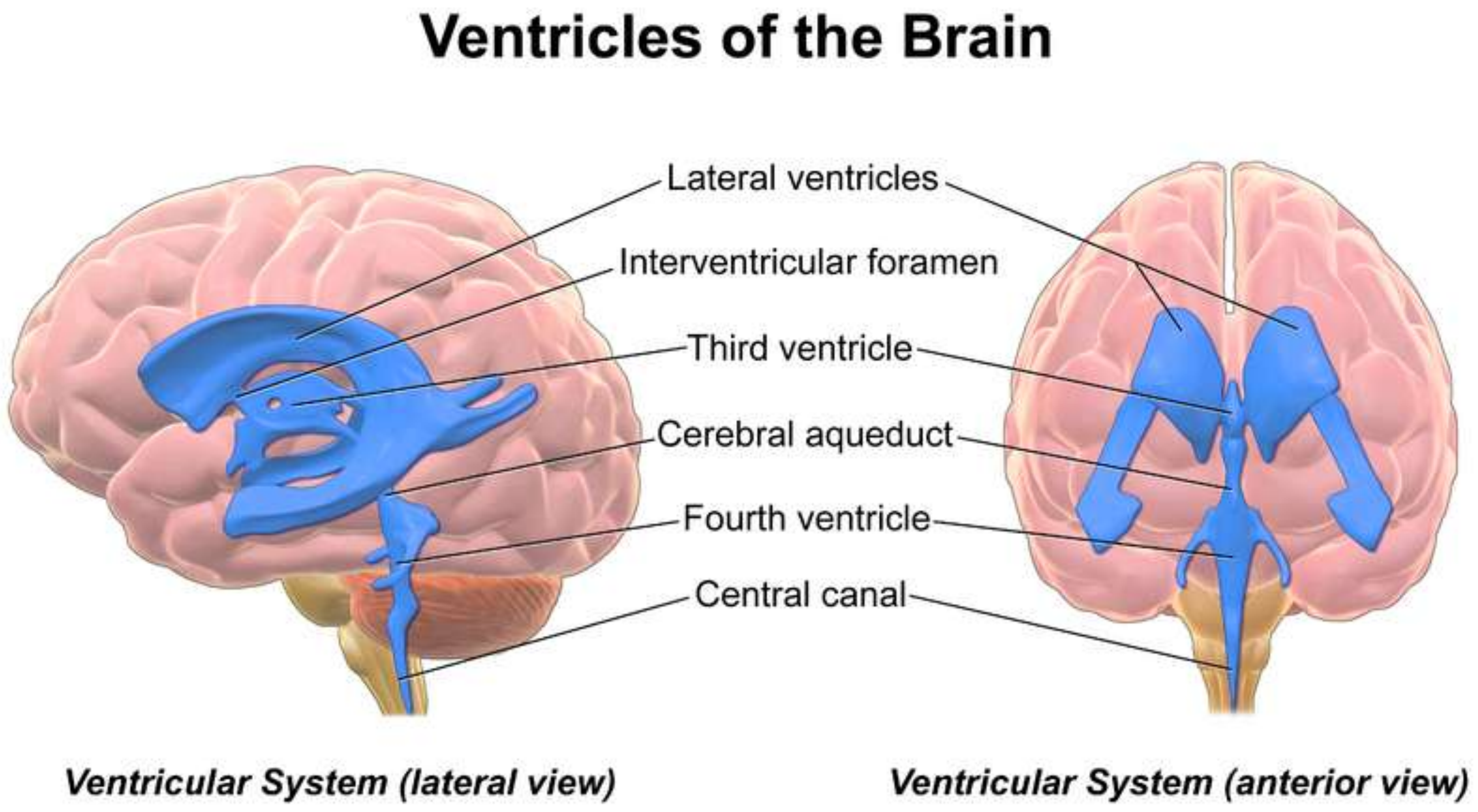
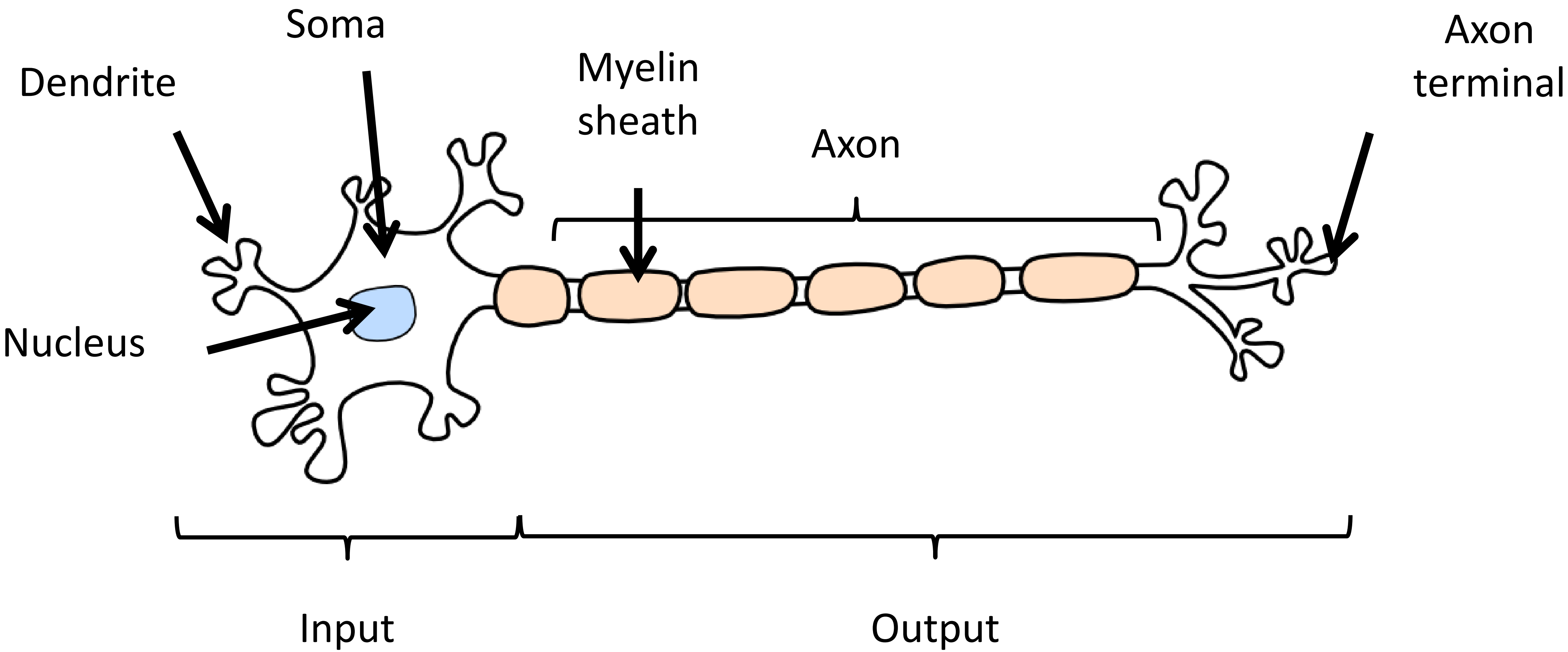


Image Source: Bruce Blaus @ wikimedia commons

Cells in the Nervous System

- **Neurons**
  - Receive, integrate, transmit information
  - Operate through electrical impulses
  - Communicate through chemical signals
- **Glia Cells**
  - Support neurons
    - structurally and by providing nutrients
    - Eliminate pathogens or dead cells, maintain homeostasis
  - Form insulating myelin sheaths
  - Ratio of glia cells to neurons varies across the brain

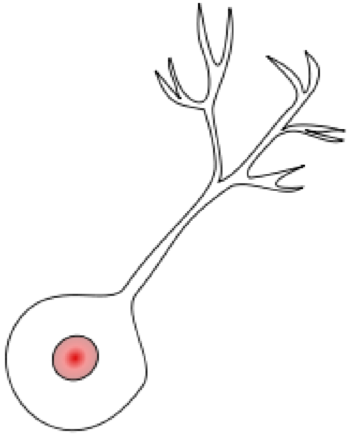
Basic Structure of a Neuron



Polarity

Unipolar: Axon, but no dendrite; least common in the human NS

1



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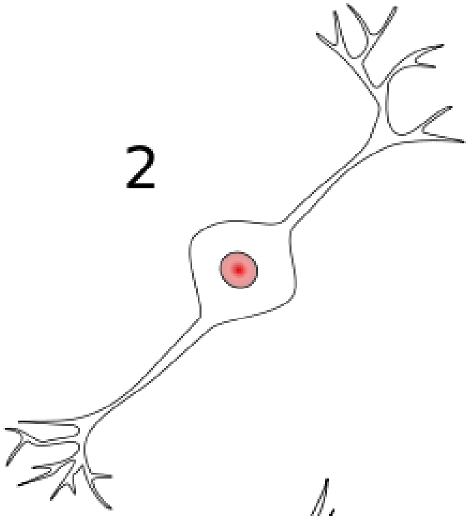
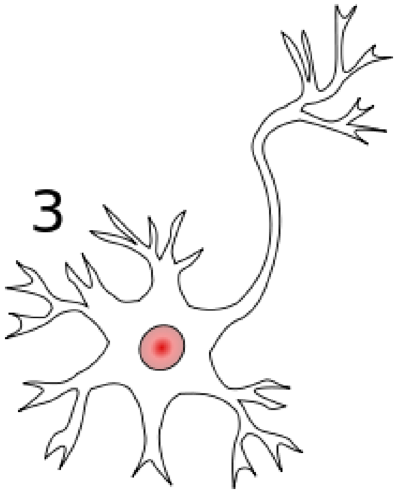


Bipolar: Axon and Dendrite; many sensory neurons

Multipolar: Single axon, multiple dendrites; inter-neurons or pro-jection neurons

3



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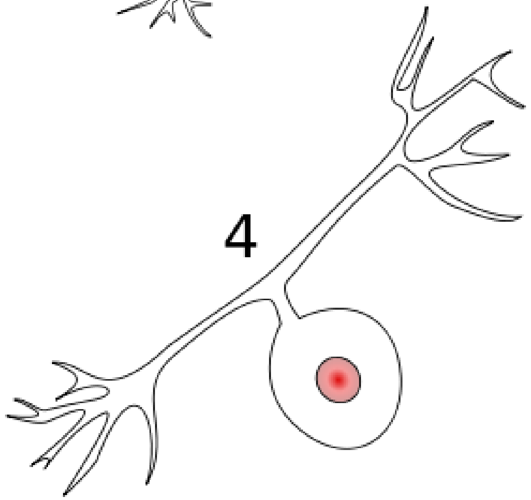


Pseudounipolar: Occur in peripheral sensory system; act as a bipolar neuron

Special Types of Neurons

- **Sensory Neuron**
  - Activated by sensory input
    - Sound, light, heat, physical contact
  - The retina consists of brain tissue and is considered part of the central nervous system
- **Motorneuron (effector)**
  - Ends at a muscle and causes it to contract
  - Single neuron can innervate multiple muscle fibers (forming a motor unit)
- Reflex: Coupling of sensory to motorneurons at the level of the spinal cord

Function of the Neuron

- The basic function of a neuron is a spatiotemporal integration of its inputs, and a binary ("all-or-nothing") action potential as an output
- Based on electrically charged ions within and outside the cell
  - At the baseline, the semipermeable cell membrane leads to an unequal distribution of ions, and to a negative potential (-70mV) of intracellular compared to extracellular space

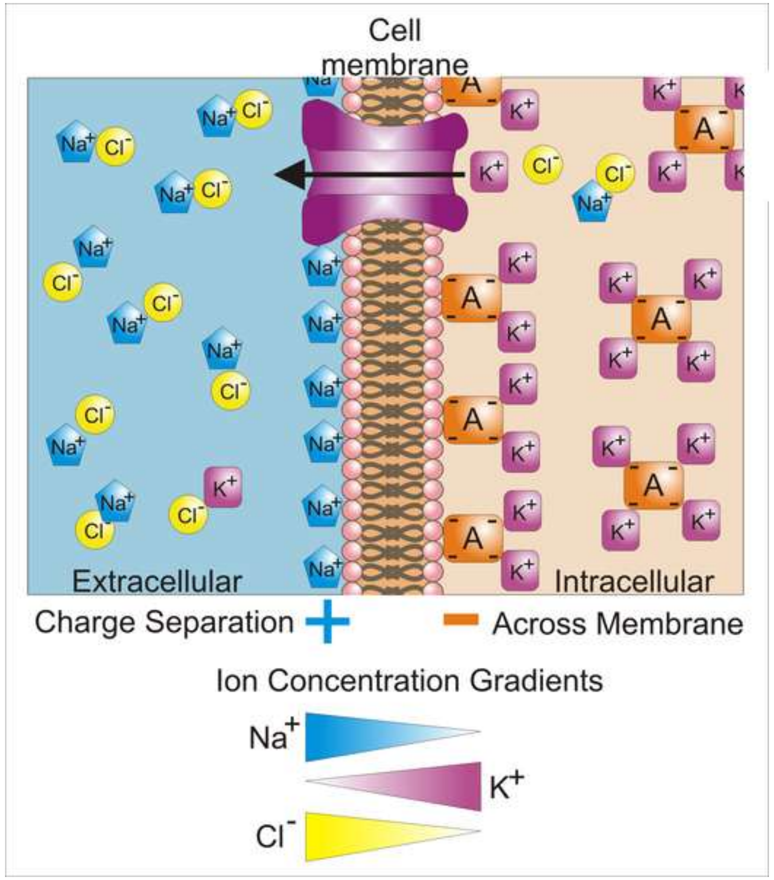


Image Source: Synaptitude @ wikimedia

Action Potential

- Incoming activations can depolarize the membrane
  - At -55mV, voltage-gated ion channels open, and sodium flows into the cell, leading the membrane potential to quickly rise to +40mV

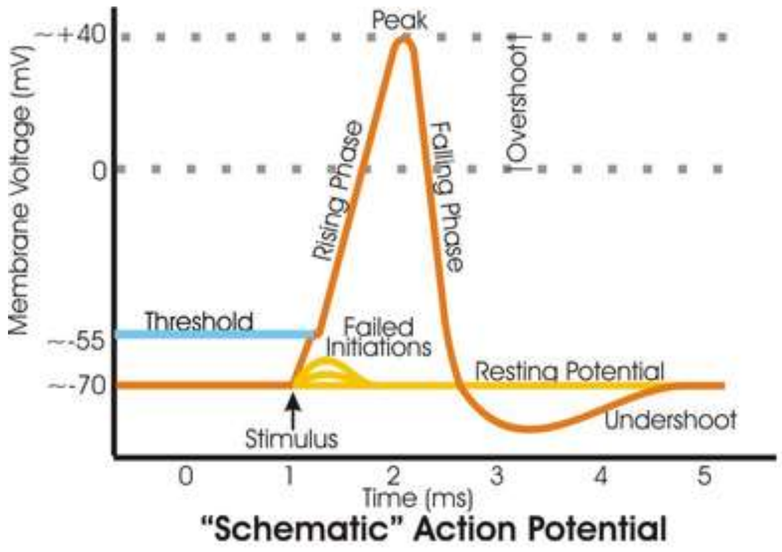


Image Source: Synaptitude @ wikimedia

  - Increased potential causes sodium channels to close again and potassium channels to open, leading to a rapid decrease and hyperpolarization
  - It takes time for potassium channels to close and sodium channels to become active again, leading to a refractory period in which no further action potentials can take place

Action Potential Propagation

- Action potentials originate at the axon hillock and travel along the axon
  - Refractory period prevents retrograde propagation

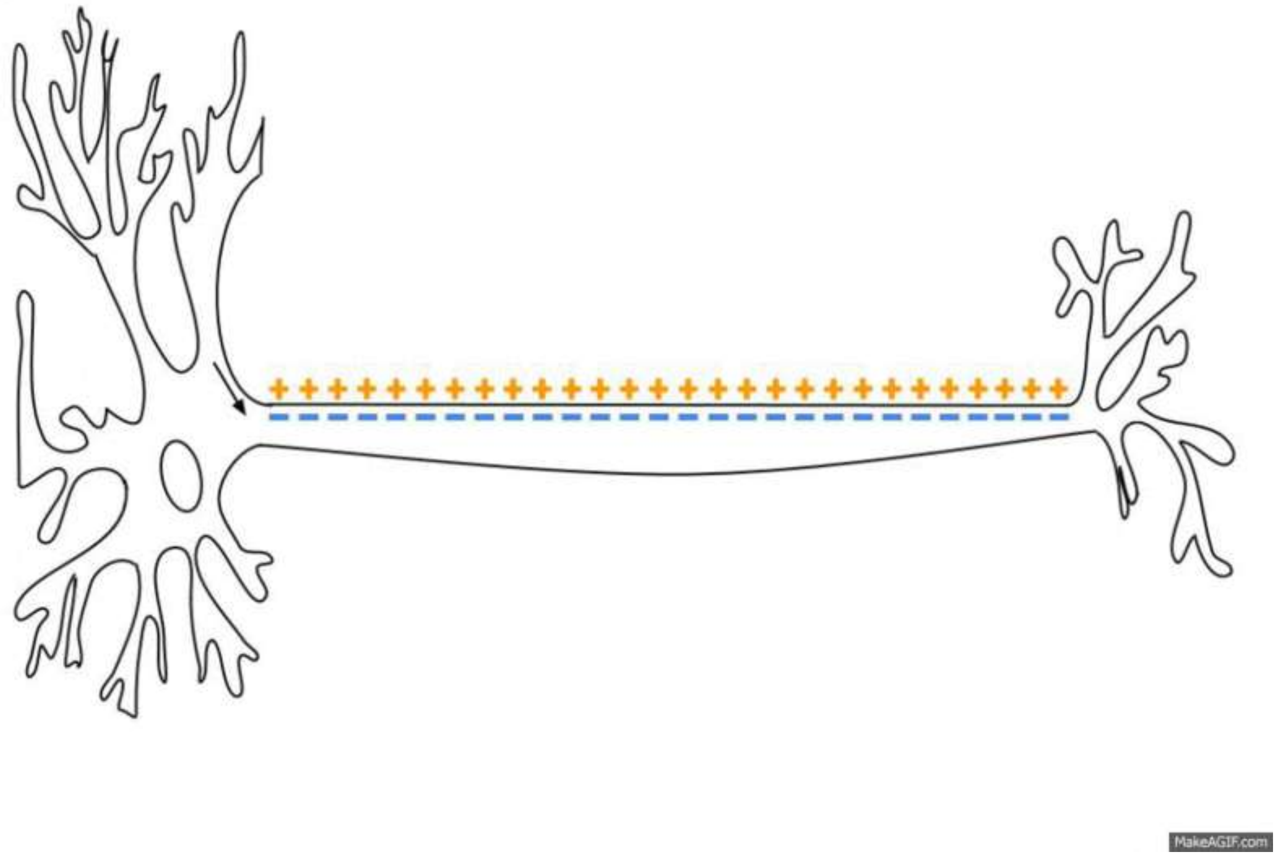
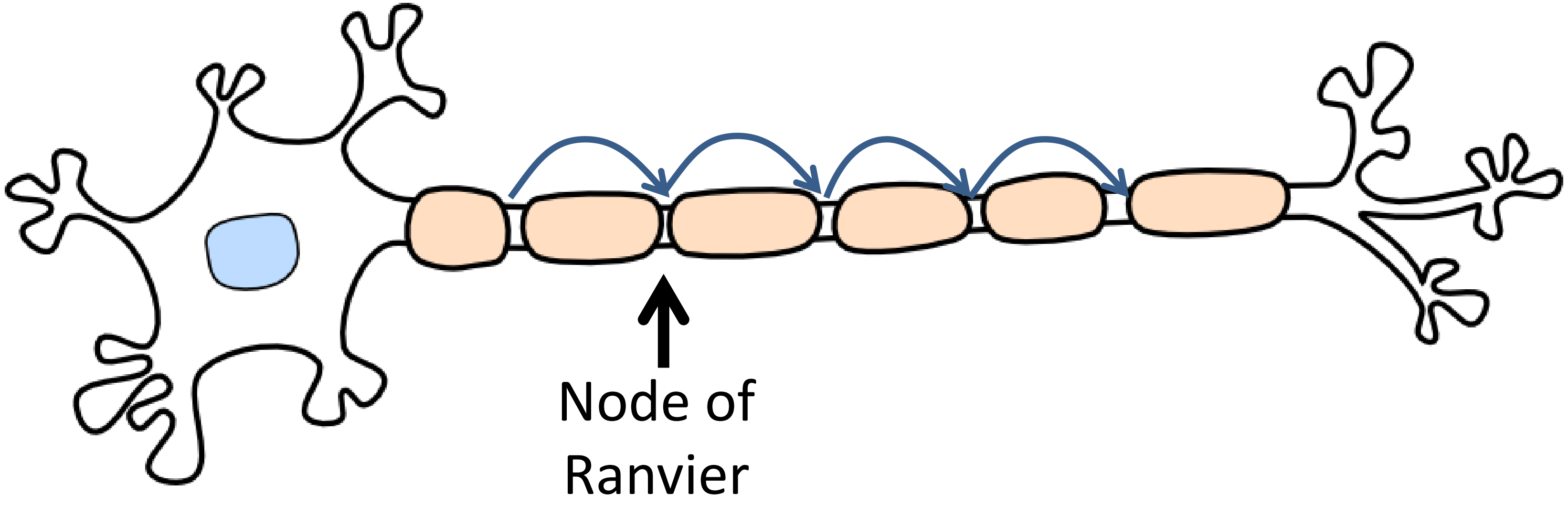


Image Source: Lauren Taylor

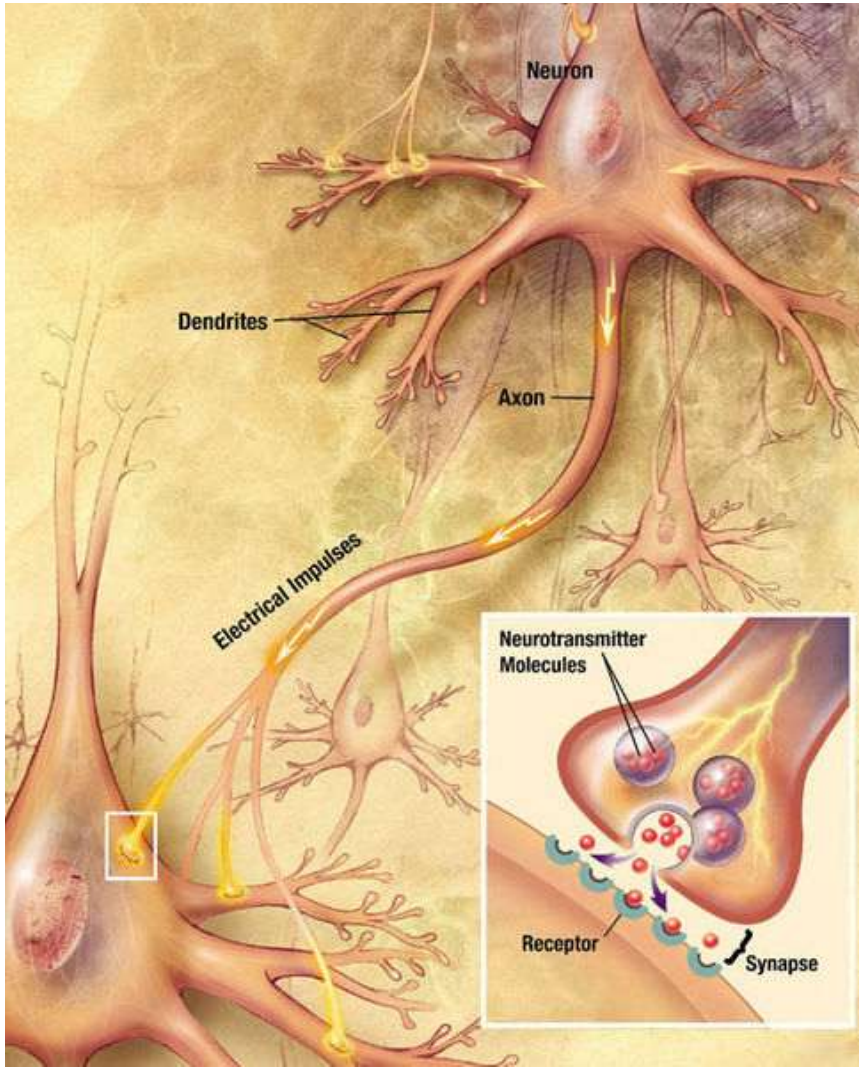
Myelination

- **Myelin** acts as electrical insulation, leading to **saltatory conduction**
  - "Hopping" from one node of Ranvier to the next
  - Accelerates conduction by a factor of ≈10
  - Provided by Schwann cells (PNS), oligodendrocytes (CNS)
  - Generated during brain maturation, destroyed by some types of neurodegenerate disease (e.g., Multiple Sclerosis)



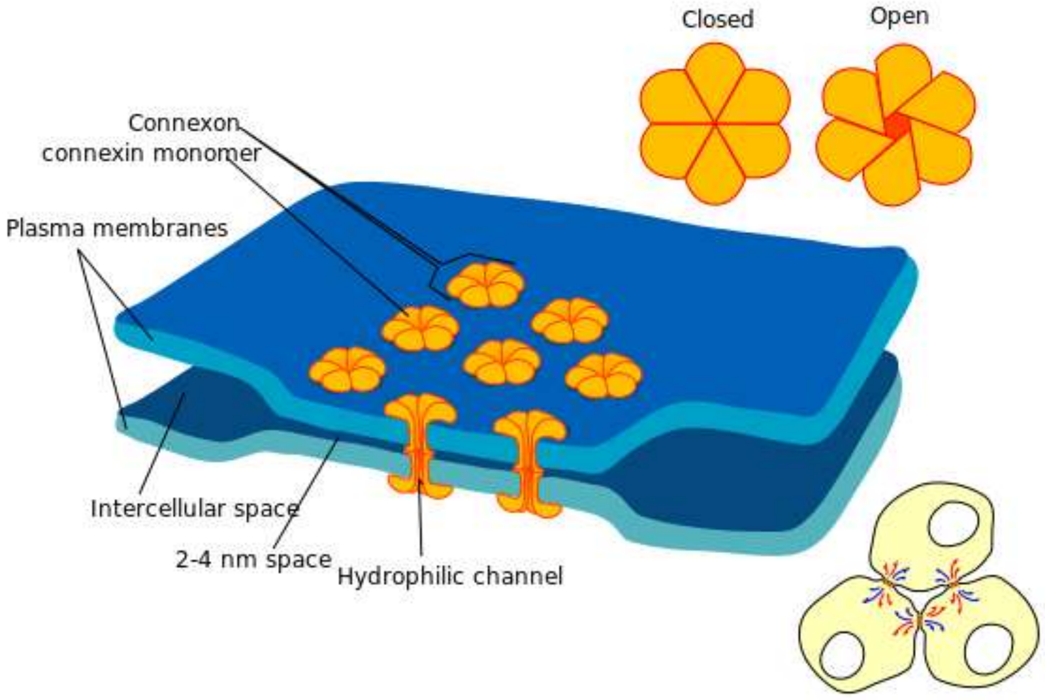
Synapses

- Axons communicate across a short distance of extracellular space, the *synaptic clef*
  - A synapse is formed by the axon terminal of the pre-synaptic (transmitting) neuron and the dendrite of the post-synaptic (receiving) one
  - Communication across synapses is mostly by release of a chemical (neurotransmitter) whose release is triggered by a pre-synaptic action potential



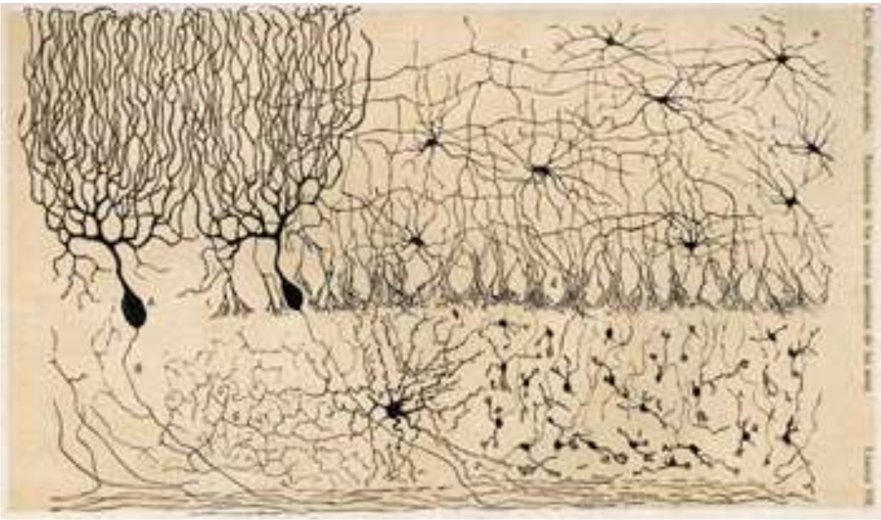
Gap Junctions

- In the retina, some neurons are connected directly, through **gap junctions**
- Differences from chemical synapses:
  - – Faster transmission
  - – Always excitatory
  - – Can work in either direction
  - – ≈10x smaller gap



Historical Note: Discovering the Neuron

- Historically, the brain was thought of as a *syncytium,* an assembly of cells that are in close and direct connection
- In 1839, **Schwann** and **Schleiden** first publish the idea that the central nervous system consists of distinct cells
- Stains developed by **Camillo Golgi** and **Santiago Ramon y Cajal** confirm this theory. They share the Nobel prize for physiology or medicine (1906)
- The term “neuron” is coined in 1891 by **Heinrich Wilhelm Waldeyer**



The Connectome at Cellular Level

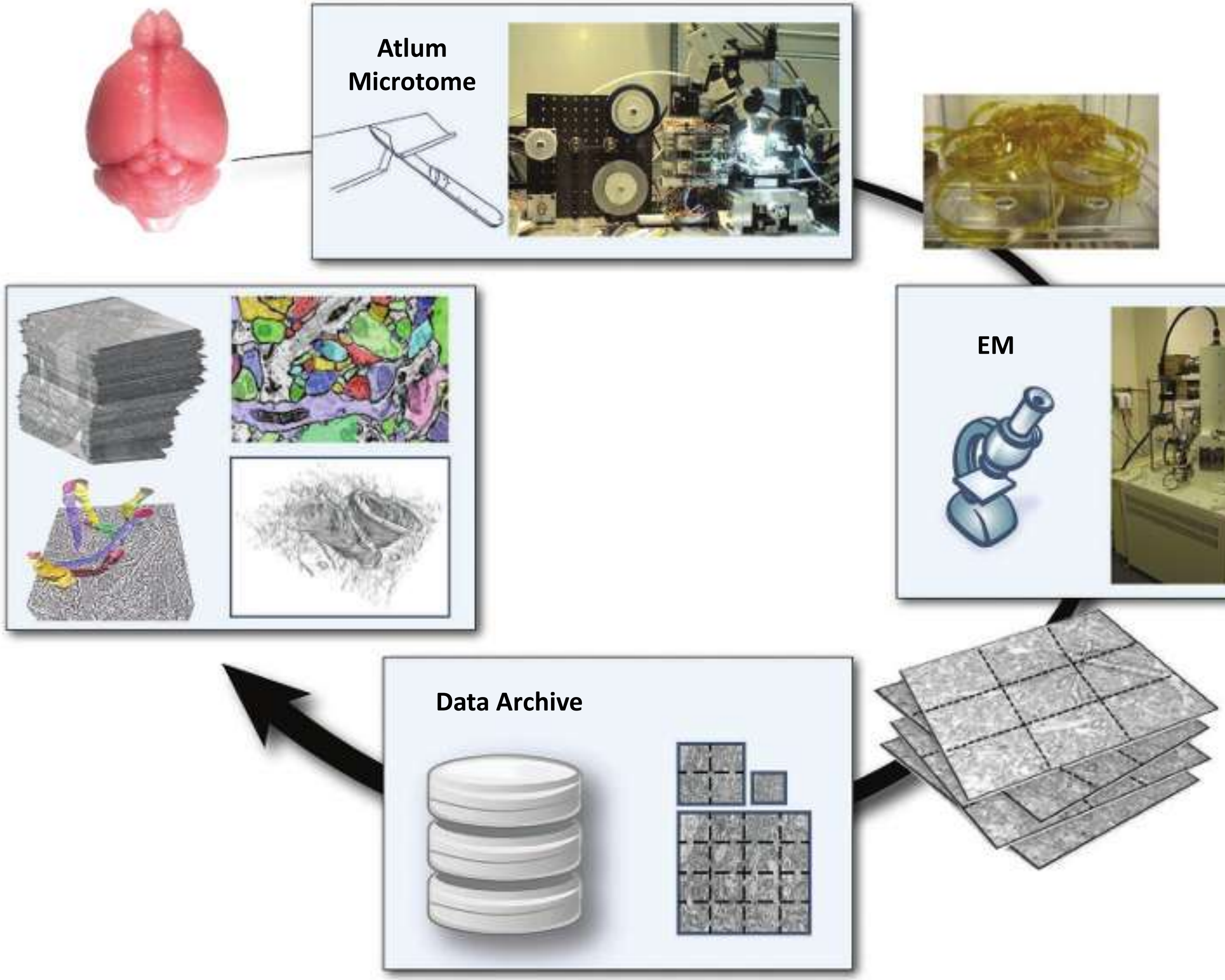


Image from [Beyer et al. 2013]

Summary: Neuroanatomy

You should now understand:

- The basic structure of the **nervous system**
  - Central vs. peripheral
- The basic structure of the **brain**
  - Macrostructure, e.g., brainstem vs. cerebellum vs. cerebrum, cortical lobes
  - Basic function of some parts of the brain
  - Gray matter vs. white matter
  - Structure of the cortex
- Morphology and function of **individual neurons**

Further Reading

- John H. Martin: *Neuroanatomy Text and Atlas.* 4th edition, McGraw Hill, 2012
- Stanley Finger: *Minds behind the brain. A history of the pioneers and their discoveries.* Oxford University Press, 2000

References

- Suzana Herculano-Houze: *The Human Brain in Numbers: A Linearly Scaled-up Primate Brain.* Front Hum Neurosci. 2009 3:31
- Joseph T. Devlin et al: *Functional Asymmetry for Auditory Processing in Human Primary Auditory Cortex.* The Journal of Neuroscience 2003 23(37):11516–11522