Method in Brain Research
1. Non-Invasive (Human)
   - Imaging
   - Computerized (Axial) Tomography (X-rays). Static pictures and high spatial resolution. Horizontal plane only. CT
  - Brain in action (e.g. movement of fingers)
  - Brain areas that function differently (e.g. depression)
  - Brain areas that ‘absorb’ a particular drug (e.g. L-Dopa in Parkinson’s)

- Functional MRI (fMRI). Modified MRI. Higher temporal resolution (~6-8 secs), low spatial resolution. (~5.25)
- Method from Bottom to Top: High to Low Spatial resolution
- Method from Top to Bottom: Low to High Temporal resolution

- 2-DG Autoradiogram 5.22
  - invasive: brain sliced after 2-DG absorption. Image obtained after ‘photographic-development’ like

- Diffusion Tensor Imaging 5.18
  - Use of MRI data to compute the movement of water molecules (along the axon). Efferent projections.

- Electrical: EEG
  - Electro Encephalon Gaphy. Recording surface electrical signals with ‘macro-electrodes’. High temporal resolution, low spatial resolution. Sleep studies, seizure detection.
  - Note: Electrical and imaging
    - Optical recordings (invasive): Open skull, imaging electrical activity. Used for research.
  - EEG Signals: Often used in Sleep Studies
Magnetic: MEG
- Transcranial Magnetic Stimulation: create a magnetic field to induce an electrical current (stimulation). Mostly superficial brain (cortex)
  - Stimulate in Motor Cortex -> Motor Evoked Potentials
  - Stimulate in Occipital Cortex -> phosphenes
- Variant: Repetitive TMS. Effects outlast the period of stimulation. Research tool.

Genetic
- In human: twin and adoption studies – Nature vs. Nurture
  - Monozygotic (identical twins): same chromosomes, genes.
  - Dizygotic (fraternal twins): Different chromosomes.
- Concordance for traits (e.g. schizophrenia, obesity, alcoholism), assess the influence of the environment.

2. Invasive (Most on Animal)
- In Vivo (alive) – Behaving
  - Ablation/Lesion: Mapping brain area to functions, and functions to behaviors.
    - Suction (mechanical), Radio Frequency (heat), Excitotoxic lesions (spare axons.)
    - Requires surgery. Small damage due to insertion of electrode. Use of ‘sham’ lesions for controls.
    - Variant: Reversible lesions (use of Specific chemicals, or cooling).
  - Cannula implantation (injecting a chemical substance). Target particular receptors in a specific brain area.
    - E.g. Injecting drug (block receptors)
  - Microdialysis: measuring the concentration of a specific chemical substance (e.g. neurotransmitter)
  - Optogenetic (relative new tech)
    - Inject a virus in a brain area. The virus carries genes that will produce light sensitive proteins.
      - ChR2: sensitive to blue, depolarizes the cell
      - NpHR: sensitive to yellow, hyperpolarize the cell
    - Implant an optical fiber that shines blue/yellow light with a laser.
    - Manipulate the activity of specific cell types in specific brain area.
      - High temporal resolution
      - High spatial resolution
      - Cell specific
• Single-unit recordings. Behavior: Conditioning, learning and memory (maze)
  • E.g. learning, memory, drug addiction, decision making, perception…
• In Vivo – Anesthetized
  • Stereotaxic surgery. Use of an atlas and skull landmarks (e.g. Bregma). Recording/Stimulation. Also done in human (local anesthesia). (Use skull landmarks to target a brain area) (5.5)
    • (Microdialysis.)
    • e.g. Study brain connectivity, single cell activity (intracellular, single unit), sleep.
• In Virto – Not alive [Study of brain tissue (extracted from the animal)]
  • Acute: Brain slices. Study of live single cell and small network properties. Calcium Imaging.
  • Culture: Study of live single cells, and intracellular mechanisms.
  • Histology (non-living tissue)
    • Staining
      • Fixative: Formaline.
      • Cut into slices (10-50 um), on a microtome.
      • Chemically treated (e.g. staining)
      • Mounted on slides.
      • Observed under a microscope.
        • Regular light
        • Fluorescent light
        • Electron microscope.
        • Scanning Electron Microscope (3D infos).
• Histology: Tracing (Anterograde, retrograde)
  • Example of the use of tracing:
    • General Question: what regions in the brain are involved in sexual behavior?
  • Anterograde: PHA-L (5.11, 5.12)
    • PHA-L
    • Staining: Immunocytochemistry (staining with an antibody
  • Retrograde and Anterograde Tracing
    • Retrograde Tracing: inject fluorogold in VMH, then see axons and terminals in PAG
    • Anterograde Tracing: inject PHA-L in VMH, then see cell bodies in medial amygdala
3. Non Invasive, Non Animal
• Computational Neuroscience/Neural Modeling
  • Using a computer to stimulate single neurons and synapses -> Computational Model.
  • Putting models together to build artificial neural networks
  • Stimulating neural activity
  • Brain-Machine Interface: Restore function through the use of a brain-controlled machine.