Stanford
MEDICINE

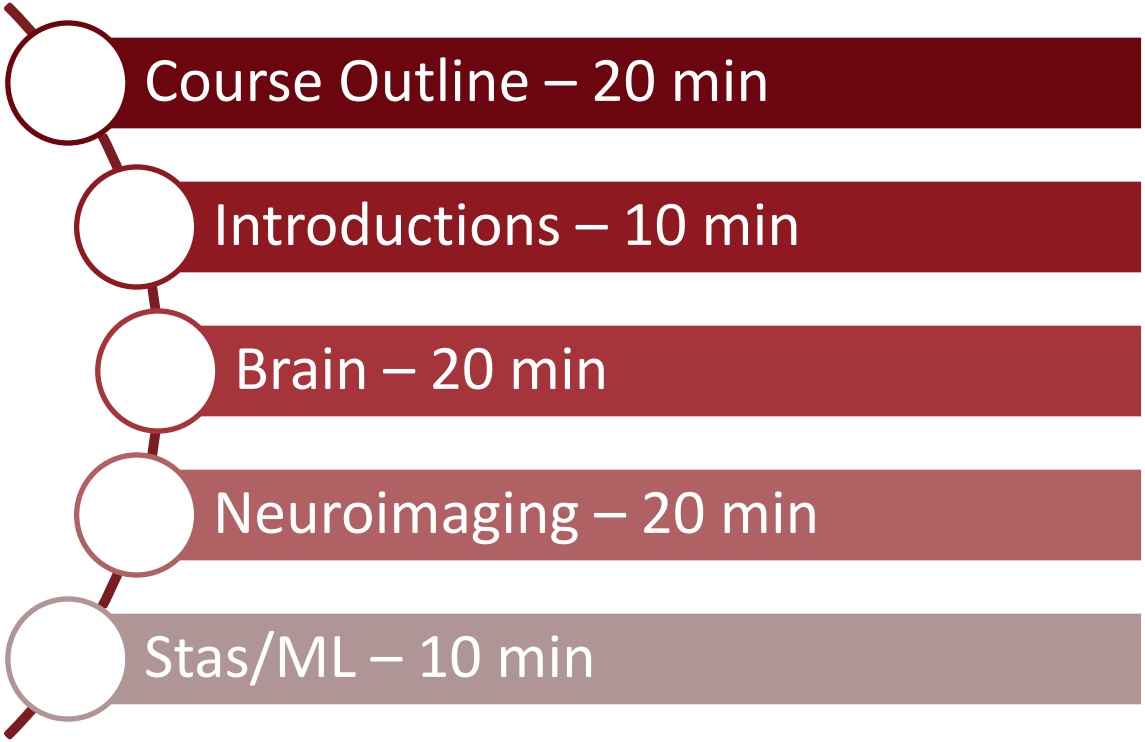
Department of Psychiatry
and Behavioral Sciences

Machine Learning for Neuroimaging

Autumn 2023
PSYC221/PSYC121/BIODS227

Session 1 – 9/26/2023

Today…


Course Outline – 20 min
Introductions – 10 min
Brain – 20 min
Neuroimaging – 20 min
Stas/ML – 10 min

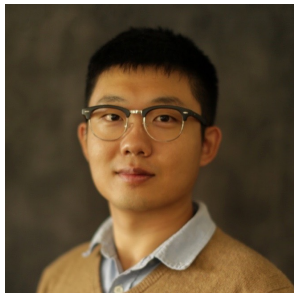
Instructors and Office Hours

Ehsan Adeli, Ph.D.,

Office hours:
Thursdays 2-3pm

Location:
Gates Building Rm 300 (or Zoom) – Please send me an email the day before

Qingyu Zhao, Ph.D.,



Office hours:
Tuesday 2-3pm

Location:
Zoom

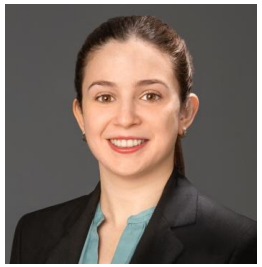
Kilian M Pohl, Ph.D.

Office hours:
Schedule only

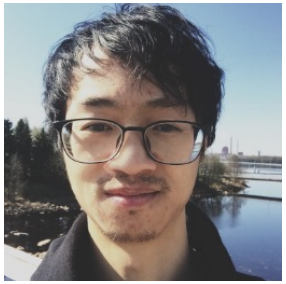
Location:
Zoom

Course Assistants

Camila Gonzalez, Ph.D.

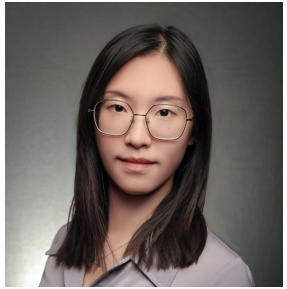


Wei Peng, Ph.D.



Magdalini Paschali, Ph.D.

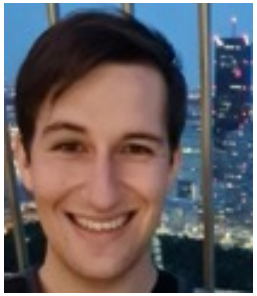
Jiahong Ouyang (EE)



Favour Nerrise (EE)

Yixin Wang (BioE)

Tomas Bosschieter (ICME)



Questions: Contact psyc221-aut2324-staff@lists.stanford.edu

Location

- Building 530 - Main Quad, Room 127
- Zoom (only accessible through Canvas).
  - Please do not share the Zoom links outside the class.
  - We **cannot** guarantee to record all sessions

- Course Website:
  - https://ml4n.stanford.edu/
- Canvas:
  - https://canvas.stanford.edu/courses/178562/

Grading

Assignments	10%
Attendance	5%
Mid-term (take-home exam**): Oct 26-28**	20%
Final Exam (take-home exam**): Dec 10-12**	30%
Project Proposal	10%
Project delivery and poster presentation	25%

3-Unit vs. 4-Unit Option

- All students are expected to attend every class session.
- The primary class content (3 units) will cover the fundamentals of machine learning, offer some limited hands-on training, and explore the application of ML to neuroimaging.
- Those opting for 4 units:
  - an extra hour of instruction weekly, diving deeper into core ML concepts, and receiving extended hands-on training.

Survey for extra class meeting time

- The scheduling of this additional hour will be determined based on the availability of the students enrolled for 4 units to ensure a mutually convenient time slot.

  - Thursdays 4-5:30 pm
  - Friday 3-4:30 pm

References

Textbooks (Not Required)

- Introduction to Neuroimaging Analysis
- Pattern Recognition and Machine Learning
- Elements of Statistical Learning
- Deep Learning from Scratch (Python)
- Machine Learning and Medical Imaging

Links at *https://web.stanford.edu/class/psyc221/#resource*

Programming?

- Python
- R / MATLAB (Optional)

Schedule and Syllabus

Week	Date	Lecturer	Topics	Materials and Assignments
Week 1	9/26 Tue	Ehsan Adeli Qingyu Zhao Kilian Pohl	**Course outline, What is the brain** • Course outline, introduction, course project • What is the brain and neuroimaging • Compile a list of definitions and connections to ML	
	9/28 Thu	Ehsan Adeli	**Intro to Multivariate Analysis**	
Week 2	10/3 Tue	Kilian Pohl	**Traditional MRI Processing**	
	10/5 Thu	Kyan Younes	**Brain Anatomy and Neuroimaging Basics**	**(Extra class for 4-unit students) Python Basics / Numpy / ScikitLearn [Hands on] (1.5 hours)**

Schedule and Syllabus

Week 3	10/10 Tue	Qingyu Zhao	**Intro to Statistical Analysis** - including intro to hypothesis testing	Homework 1 released
	10/12 Thu	Ehsan Adeli	**In-Depth Machine Learning** - Connection with Hypothesis Testing - Dimensionality reduction, Feature Selection	**(Extra class for 4-unit students) ML Supervised & Unsupervised Learning (1.5 hours)**
Week 4	10/17 Tue	Kilian Pohl	**ML-based MR Preprocessing** - EM for image inhomogenety - PCA for noise - ICA network "	Homework 2 released
	10/19 Thu	Camila Gonzalez	**Hands on Statistics & ML (Python)** - application to MRI"	**(Extra class for 4-unit students) ML Q/A (1 hour)**

Schedule and Syllabus

Week 5	10/24 Tue	Kilian Pohl	**Brain Structural Analysis**	Homework 1 due
	10/26 Thu		**Midterm exam** **Project proposal presentation**	
Week 6	10/31 Tue	Kilian Pohl	**Longitudinal Analysis**	Homework 2 due
	11/2 Thu	Ehsan Adeli	**Confounders and Metadata**	**(Extra class for 4-unit students)** **MRI Generative Models (1 hour)**

Schedule and Syllabus

Week 7	11/7 Tue		**Democracy Day, No classes**	
	11/9 Thu	Kilian Pohl	**Connectome Based Modeling I**	**(Extra class for 4-unit students) ML/Python Libraries for Connectome Analysis (1 hour)**
Week 8	11/14 Tue	Russ Poldruck	**Largescale Neuroimage Analysis & OpenNeuro**	Homework 3 released
	11/16 Thu	Qingyu Zhao	**Connectome Based Modeling II**	
Week 9	Thanksgiving		**No Classes**	

Schedule and Syllabus

Week 10	11/28 Tue	Ehsan Adeli	**Generative AI and Applications to Neuroscience**	
	11/30 Thu	TBD	**Models for Clinical Neuroimaging**	Homework 3 due **(Extra class) Projects Q/A (1 hour)**
Week 11	12/5 Tue		**Project presentation**	
	12/7 Thu		**Project presentation**	
Week 12	12/12 Tue		**Final exam**	

Projects

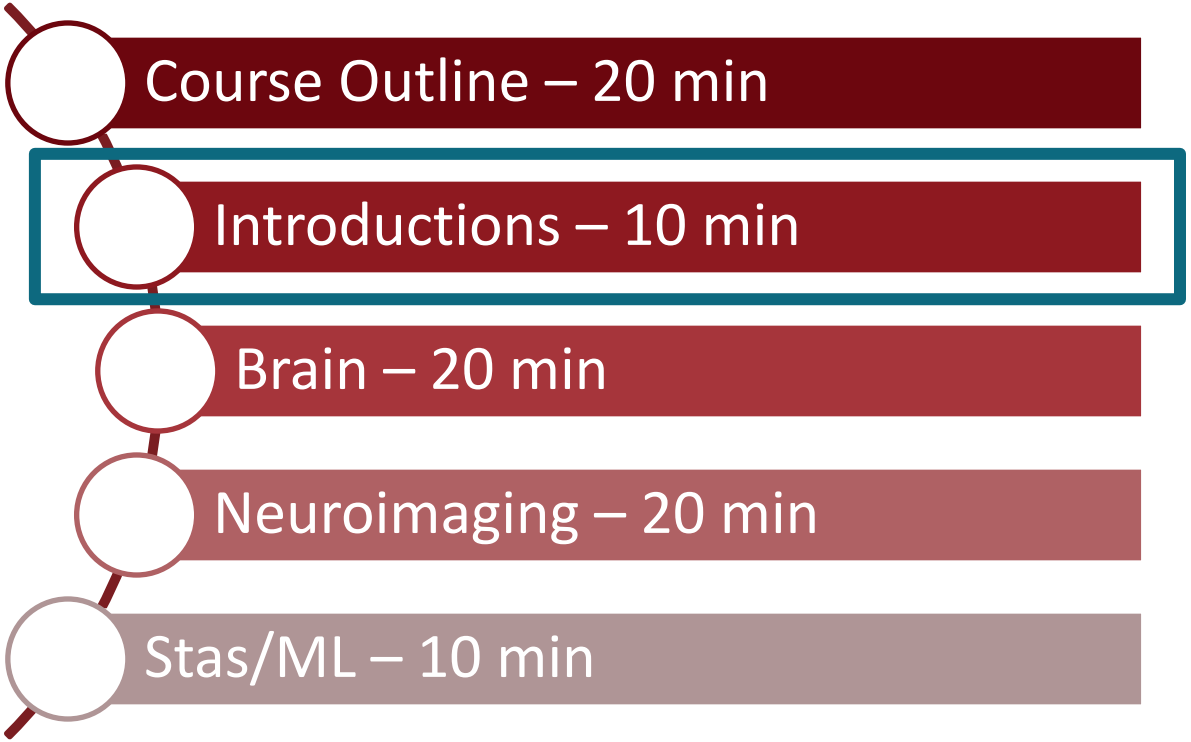
- Human Connectome Project (HCP)
- Alzheimer's Disease Neuroimaging Initiative: ADNI
- Parkinson's Progression Markers Initiative (PPMI)
- ABIDE - International Neuroimaging Data-sharing Initiative
- OASIS Brains - Open Access Series of Imaging Studies
- Multimodal Brain Tumor Segmentation Challenge 2020 (BraTS)

- Explore ideas
  - We have a list of public datasets listed on the website
  - Based on your interests and research goals, form teams, and select a topic of choice (implementation, research, entrepreneurship, … all are welcome)
  - Related Conference:
    - MICCAI, MIDL
    - NeurIPS
    - MLforHC
    - SfN
- Find your teammates (Canvas)
- Surveys for matching teammates will be sent out

Projects Survey

- By the end of week 3
- Through Canvas (you will receive email notifications)

Today…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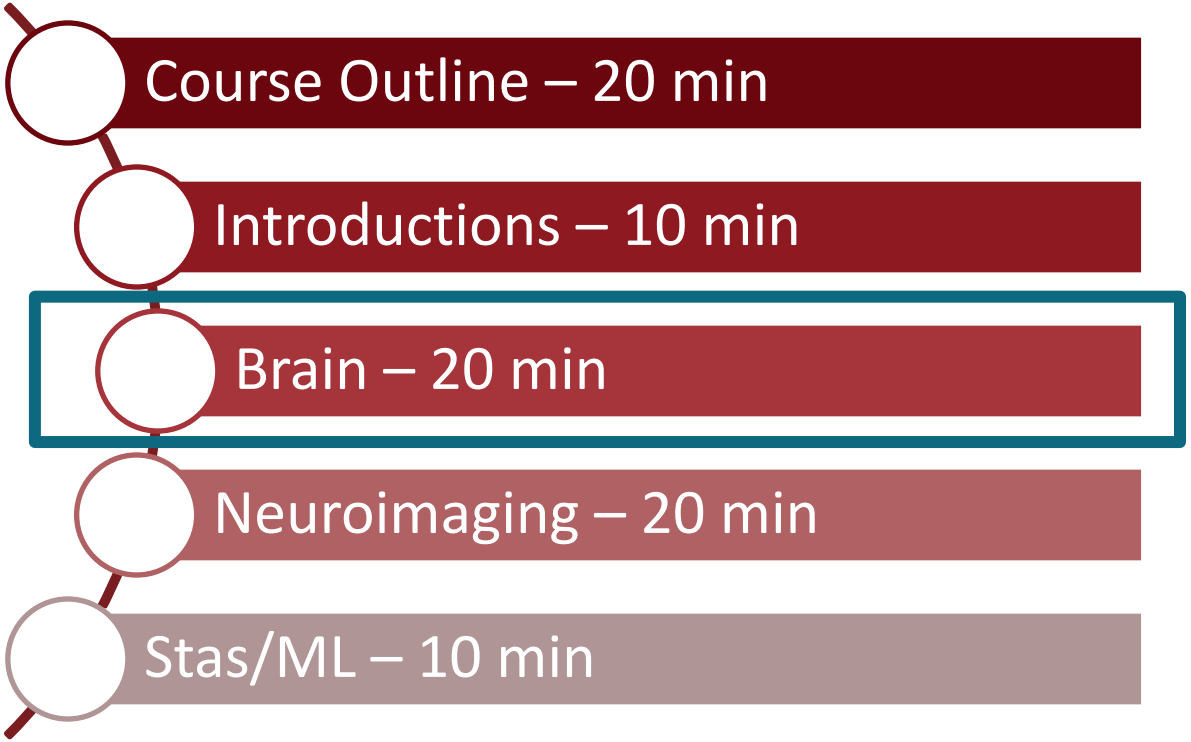
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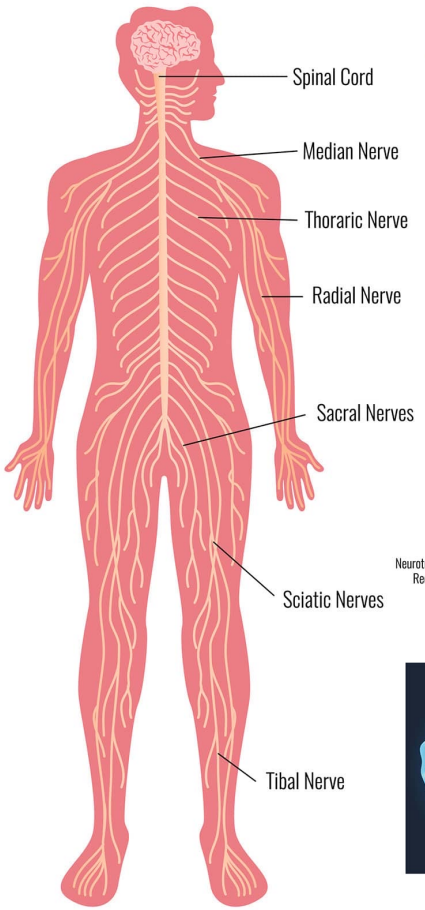
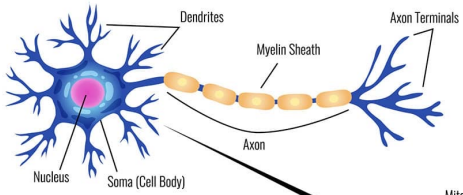
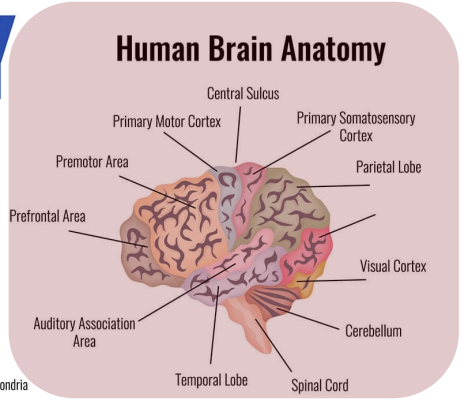
The Human Brain

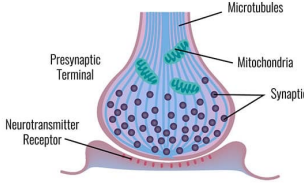
- One of the largest organs, but also the least understood organ
- CNS = brain + spinal cord
- ~3 pounds (2% of body weight)
- Center for all thought processes, decision making, emotion, memory, behavior control …
- Each part of the brain controls different body functions
- An old estimate of 100 billion neurons, 100 trillion neural connections, giving rise to a complex neural network

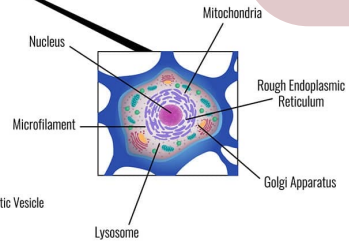
NEUROLOGY

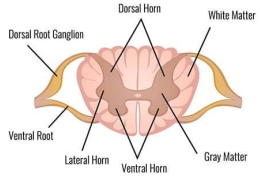


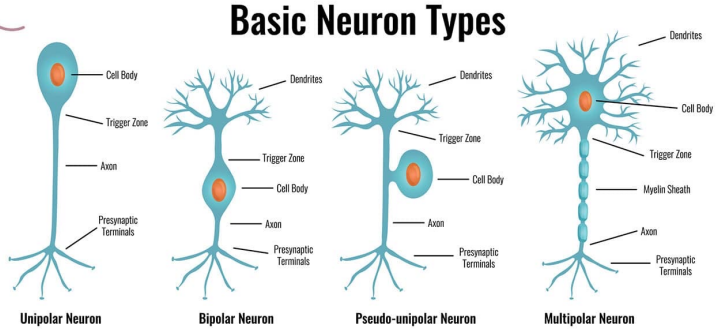






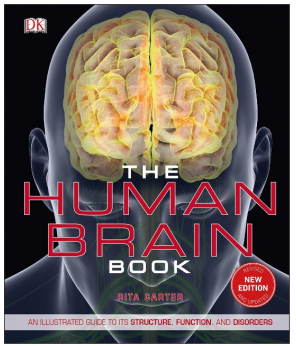






← PSYC 121 / PSYC 221

NEPR 205:
Neurosciences Anatomy Core



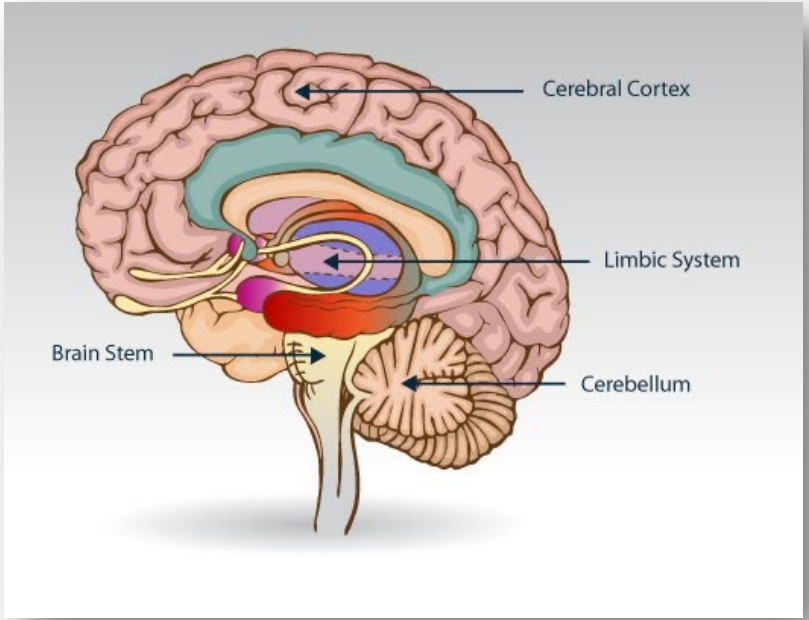
By Rita Carter

Stanford MEDICINE | Department of Psychiatry and Behavioral Sciences

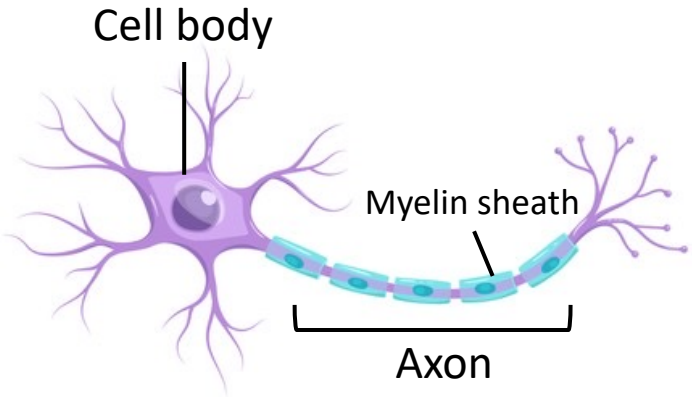
Basic Anatomy

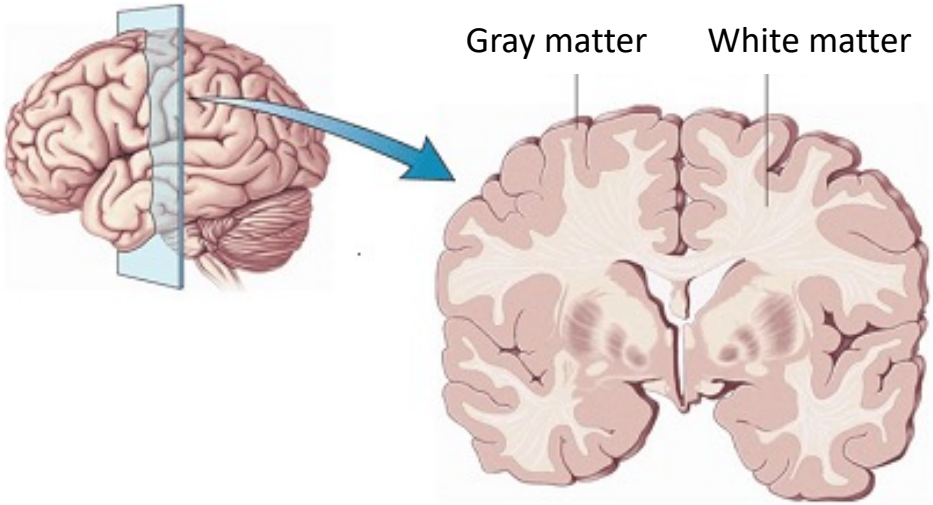
4 Main Parts:

- **Cerebrum**: reasoning, decision making, visual, auditory, somatosensory, olfactory …
- **Cerebellum** (little brain): motor learning, posture, balance, fine movement …
- **Brain Stem**: breathing, consciousness, blood pressure, heartbeat, sleep …
- **Limbic System**: emotion, memory …



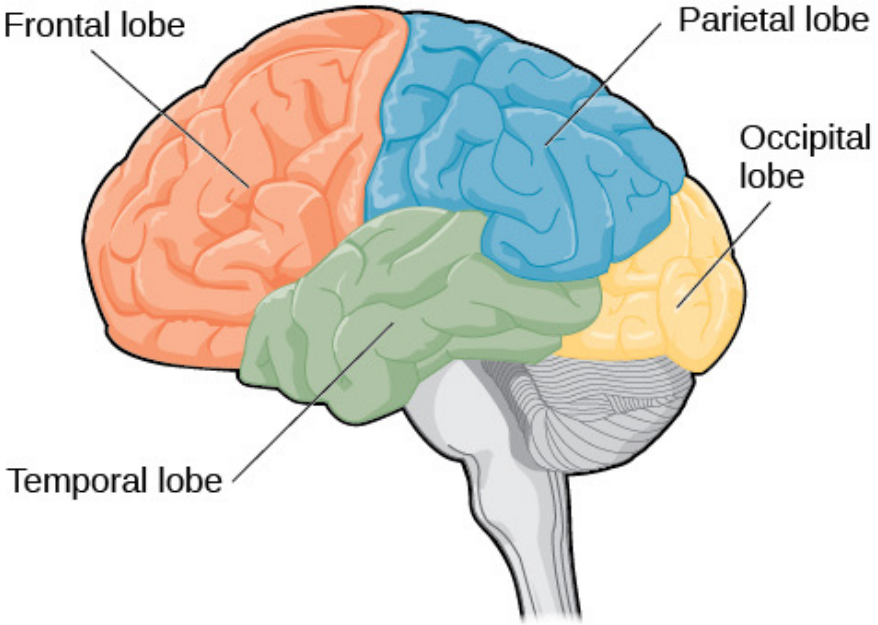
Gray and White Matter





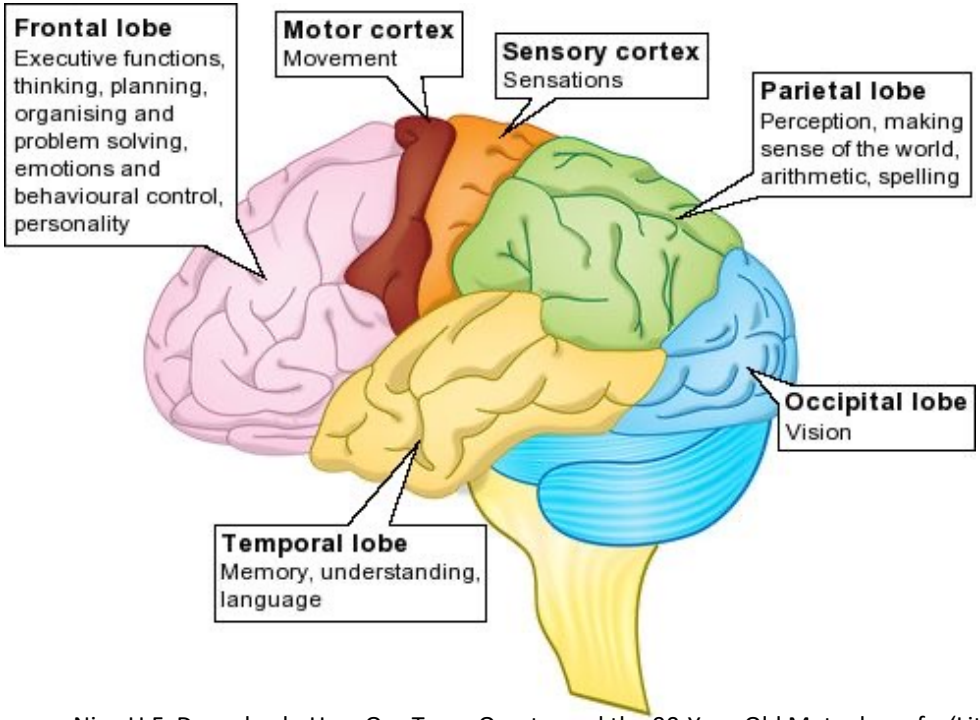
- Axons have a myelin sheath to help signal travel along axons
- Myelin sheath looks “white”, cell body looks “gray”
- More gray matter on the cortex (outside) and more white matter on the inside
- White matter passes signal between different gray matter regions across cortex

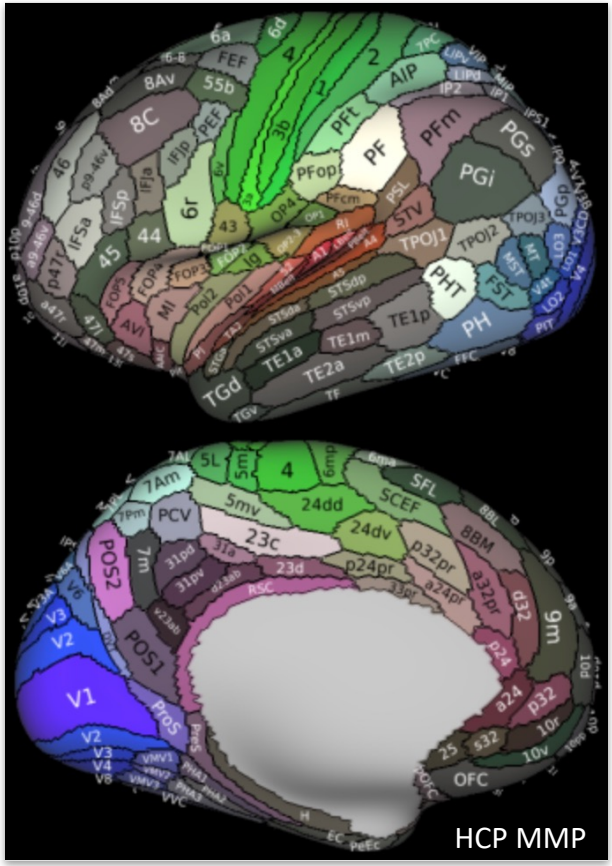
Cerebrum



- **Frontal lobe**: executive control, reasoning, decision making, emotion and behavioral control;
- **Parietal lobe**: perception, visuo-spatial processing, movement
- **Temporal lobe**: auditory processing, language
- **Occipital lobe**: visual processing

Finer and finer Parcellations

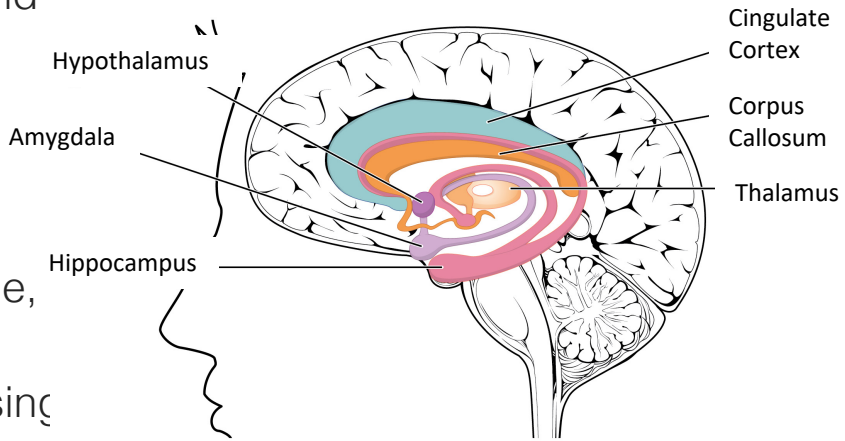




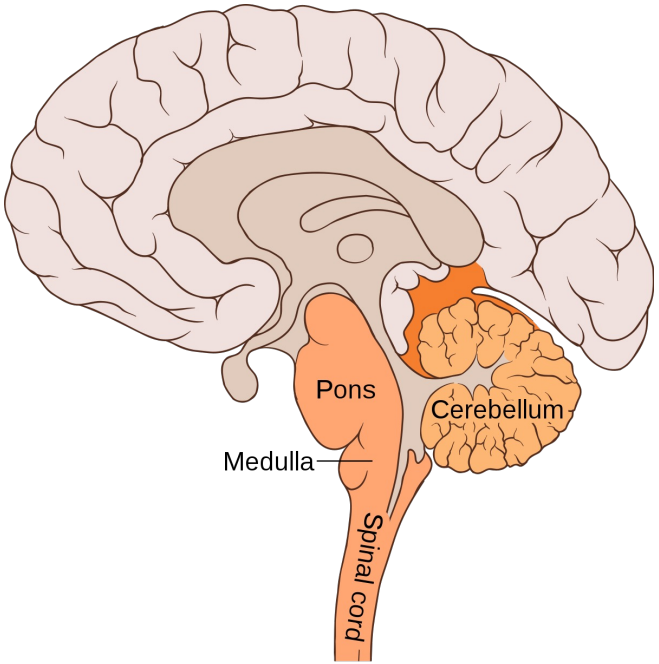
Nico U.F. Dosenbach, How Our Team Overturned the 90-Year-Old Metaphor of a 'Little Man' in the Brain Who Controls Movement, 2023

Limbic System

- **Thalamus**: a relay station of all incoming motor and sensory information
- **Hippocampus**: memory, navigation
- **Amygdala**: emotional responses (fear, anxiety, aggression)
- **Hypothalamus**: body temperature, hunger, fatigue, sleep, and circadian rhythms …
- **Cingulate cortex**: emotion formation and processing learning, memory …



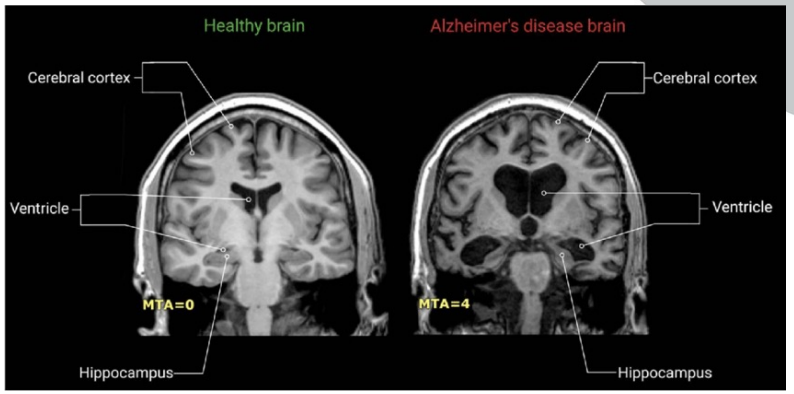
Cerebellum and Brain Stem

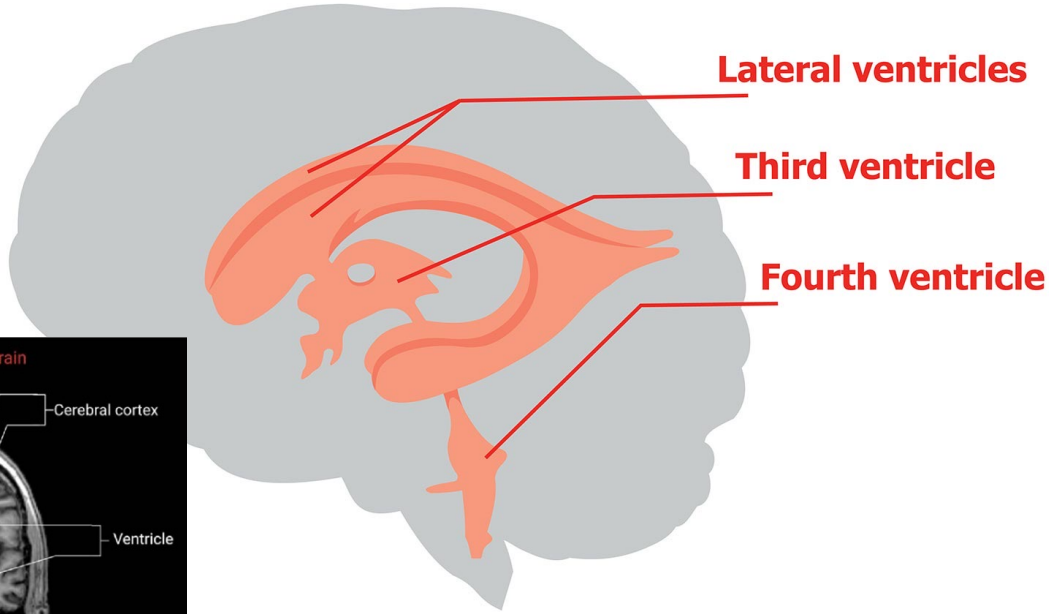


- **Cerebellum**: 2nd largest portion of the brain (10% weight, 50% neurons); Posture, balance, cognition and learning
- **Pons**: unconscious processes, sleep, breathing, respiration, swallowing, eye-ball movements …
- **Medulla oblongata**: connecting brain to spinal cord

Ventricles of the brain

- “Cavities” in the brain
- 4 ventricles in total
- Filled with CSF





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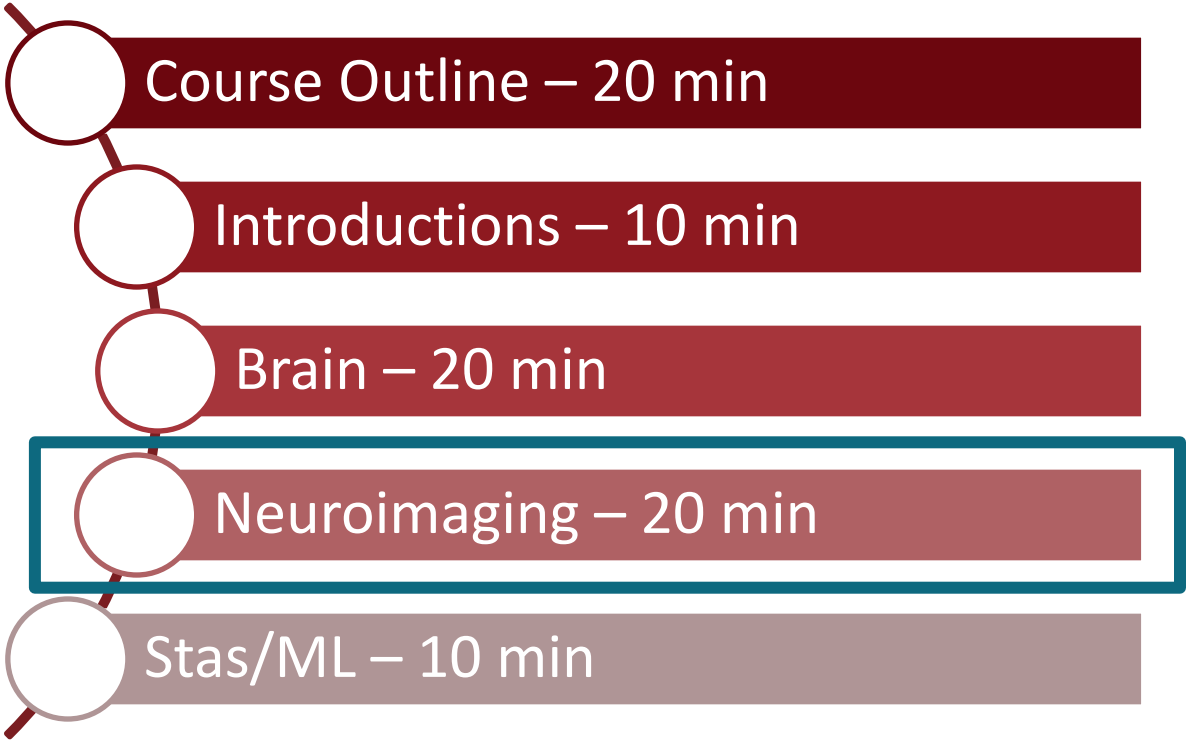
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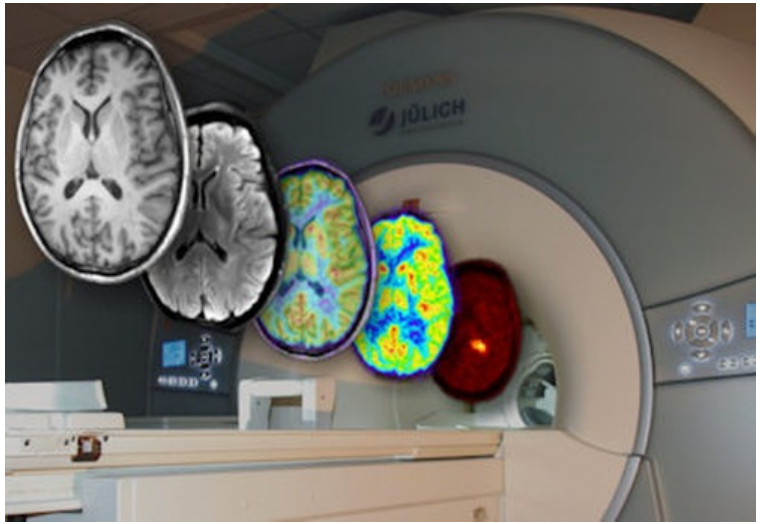
What is neuroimaging?

Process of producing images that capture structure and function of the nervous system (which include the brain).



How to measure brain anatomy and function ?

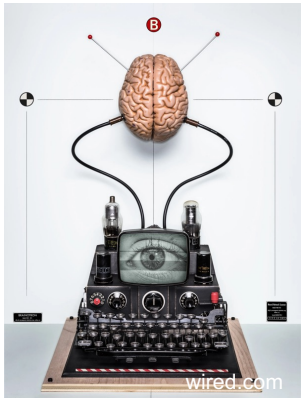
Cut open & measure

Invasive

Record movement & response

No anatomy and only indirect function

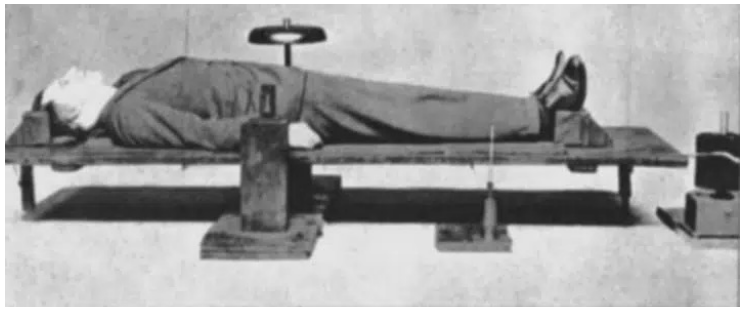
Build tool



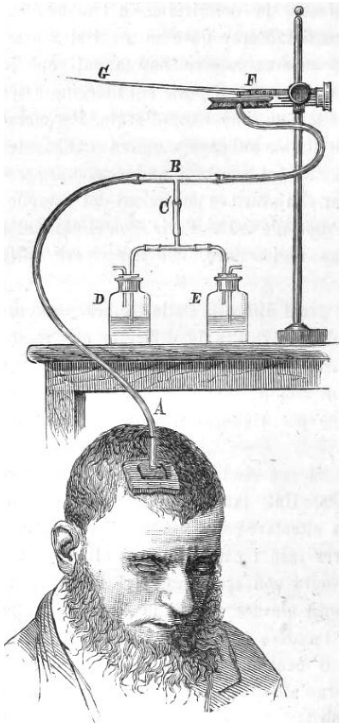
How should it look like ?

1st Neuroimaging Technique (1880)

- Non-invasively measure the redistribution of blood during emotional and intellectual activity
- Forerunner of the more refined techniques of fMRI and PET

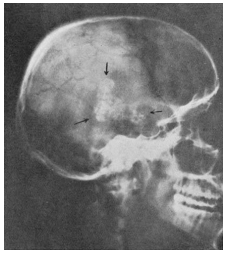


Human Circulation Balance

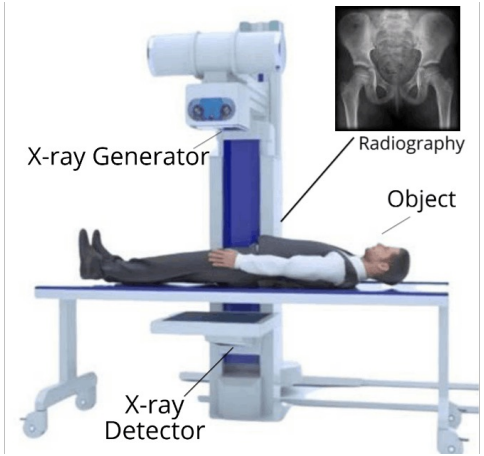


X-Ray (1895)

- Measures high-speed electrons (generated via electro-magnetic radiation of short wavelength) striking a solid target – initial used for diagnosis of cerebral infarctions and tumors



MC Sosman, 1927



https://www.vedantu.com/evs/how-do-x-rays-work

Read: Leeds & Kiefer, Evolution of Diagnostic Neuroradiology from 1904 to 1999, Radiology 2000; 217:309 –318

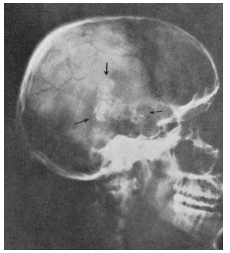
X-Ray (1895)

- Measures high-speed electrons (generated via electro-magnetic radiation of short wavelength) striking a solid target – initial used for diagnosis of cerebral infarctions and tumors

- Pneumoencephalography (a.k.a. "air study“, commonly used until 70s) replaces cerebrospinal fluid (CSF) with air before X-ray is taken so that brain structures show up

- Computed tomography (CT, starts in 70s) acquires multiple X-rays taken from different angles to produce 3D images.

Read: Leeds & Kiefer, Evolution of Diagnostic Neuroradiology from 1904 to 1999, Radiology 2000; 217:309 –318



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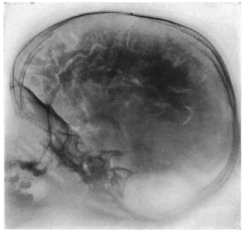
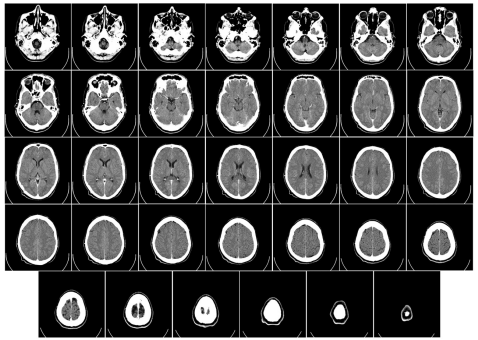


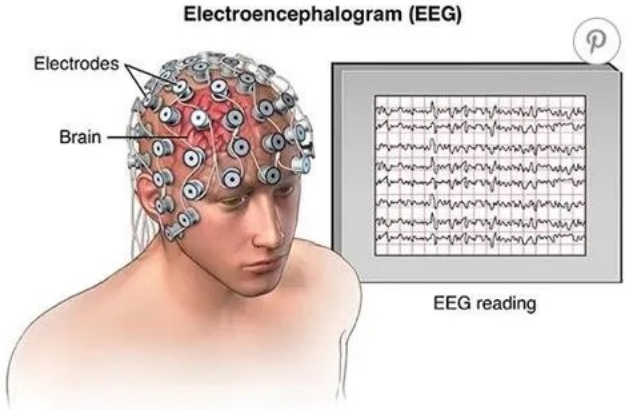
Pneumoencephalography



Computer Tomography

Electroencephalography (EEG, 1912)

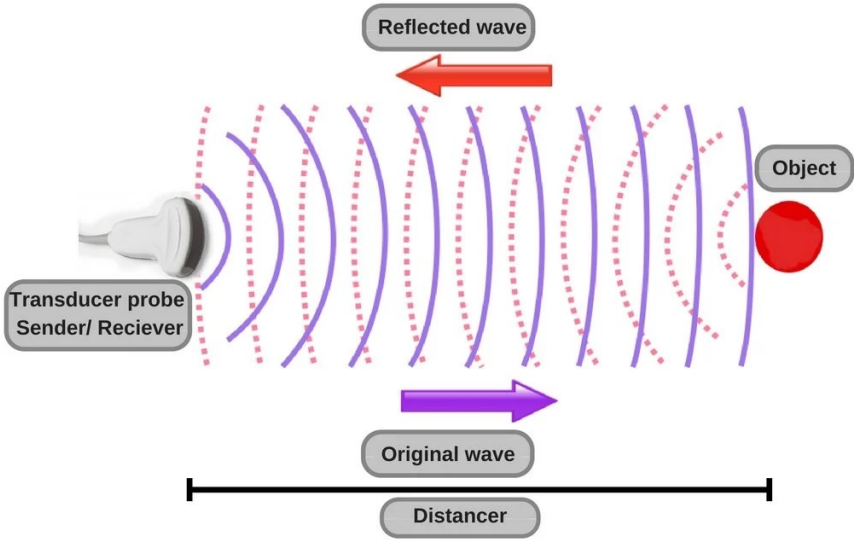
- Records electrical activity on the scalp, which relates to macroscopic activity on the brain surface (since 1924 on humans)
- Mainly used for detecting epilepsy but also diagnose of sleep disorders, depth of anesthesia, coma, encephalopathies, and brain death.



https://www.brightbraincentre.co.uk/electroencephalogram-eeg-brainwaves

Ultrasound (1942)

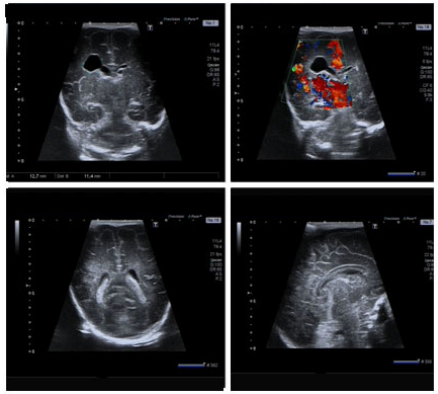
- Using high-frequency sound waves to produce sonogram images, ultrasound was first used to detect brain tumors



https://www.scienceabc.com/innovation/how-ultrasound-scanning-sonography-3d-sonogram-work-pregnancy-due-date.html

Ultrasound (1942)

- Using high-frequency sound waves to produce sonogram images, ultrasound was first used to detect brain tumors
- In the 80s, 3D ultrasounds are introduced
- In the 90s, 4D (real time) capabilities and ultrasound guided biopsies (endoscopic ultrasounds) are developed



http://www.superspecialityclinic.com/radiology/neuroimaging-brain-sonography

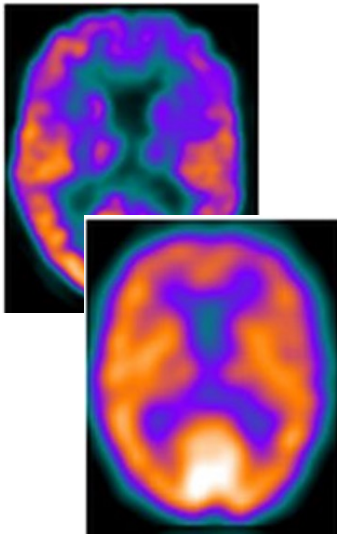
Nuclear Imaging (1951)

- Instead of recording radiation generated by an external source (like X-ray), NI records radiation emitted from within the body (by injecting radiotracers) via a gamma camera to not only capture anatomy but also brain function.

https://together.stjude.org/en-us/diagnosis-treatment/imaging-tests/pet-scans.html

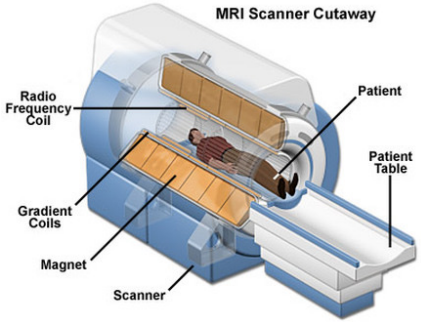
Nuclear Imaging (1951)

- Instead of recording radiation generated by an external source (like X-ray), NI records radiation emitted from within the body (by injecting radiotracers) via a gamma camera to not only capture anatomy but also brain function.
- Positron Emission Tomography (PET; 1961) detects positrons (as they annihilate with electrons resulting in gamma photons) in order to visualize biochemical changes in brain tissue (e.g., metabolism). PET is used for imaging of tumors, metastases, and certain types of dementias.
- Single-Photon Emission Computerized Tomography (SPECT; 1963) measures gamma ray emissions (visualizing path of blood) to image tumors, infections, thyroid, or bones.

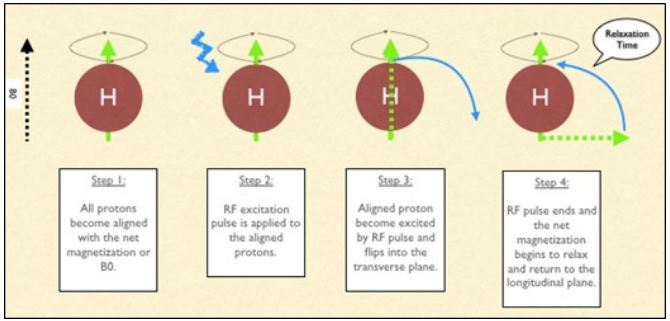


Magnetic Resonance Imaging (MRI, 1973)

- MRI scanners use magnetic fields, magnetic field gradients & radio waves to measure the spin polarization of atomic nuclei.



https://snc2dmri.weebly.com/components--functions.html

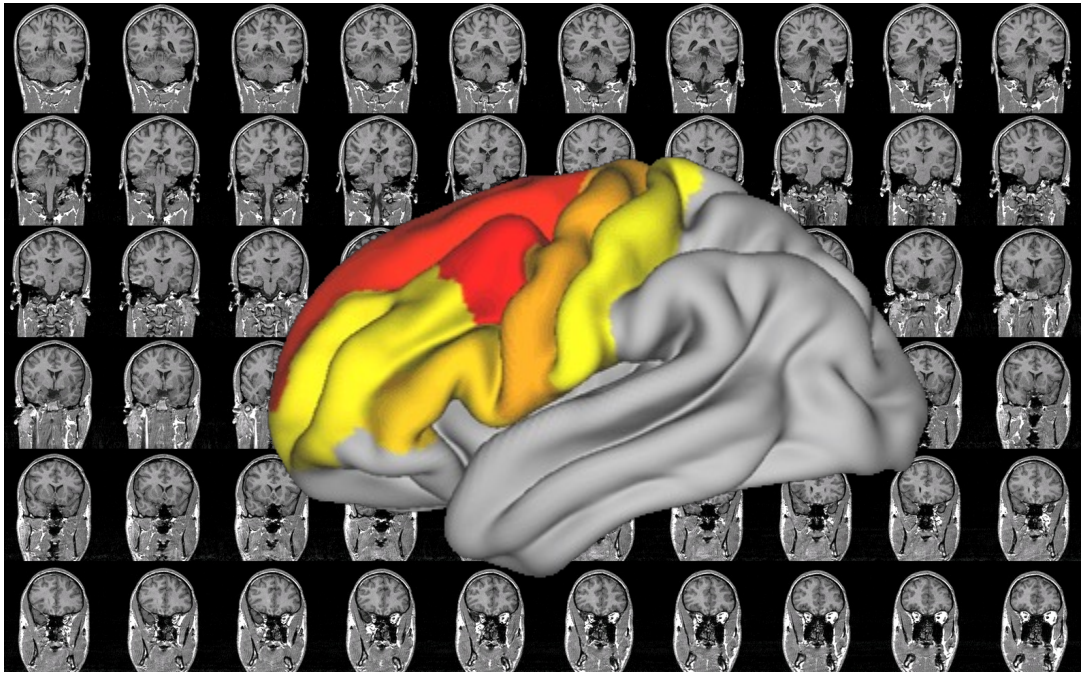


https://teachmeanatomy.info/the-basics/imaging/magnetic-resonance-imaging-mri

- MRI acquisition can capture macrostructure (e.g., brain tissue boundaries), microstructure (e.g., tissue integrity), blood flow, and brain function.

Example of macrostructural MRI

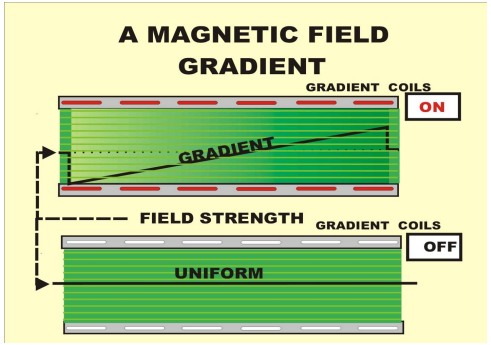
T1-weighted MRI: amount of time taken for protons' spins to realign with the main magnetic field



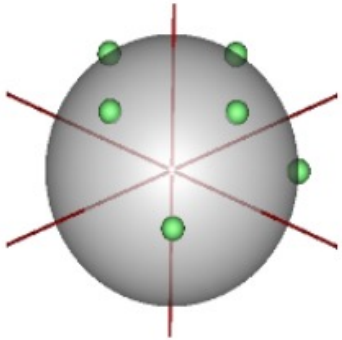
Microstructural Acquisition

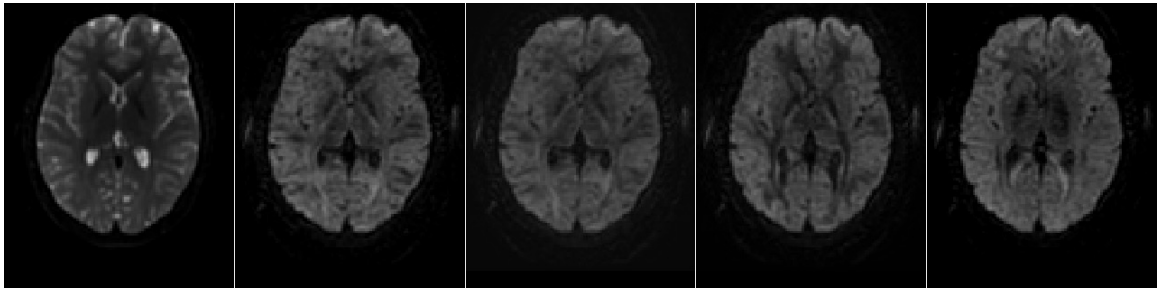
Diffusion weighted images (DWI)

Measure the rate of diffusion by varying gradient direction of scanner's magnetic field



http://www.sprawls.org/mripmt/MRI02/index.html





Microstructural Acquisition

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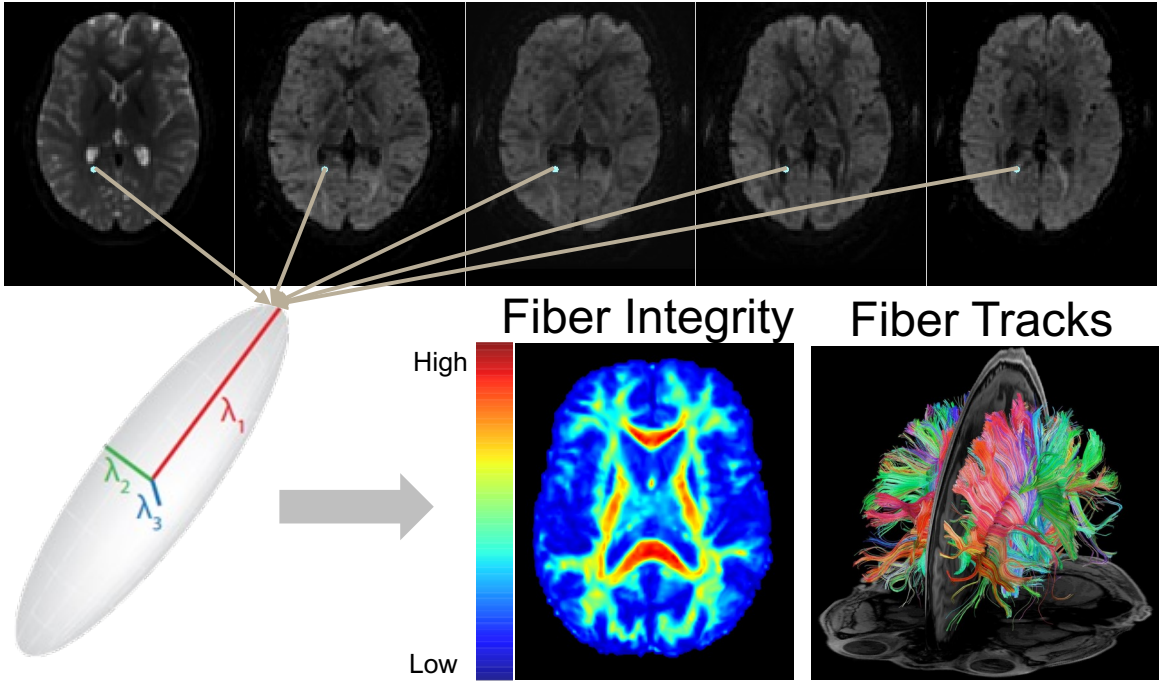


Blood Flow

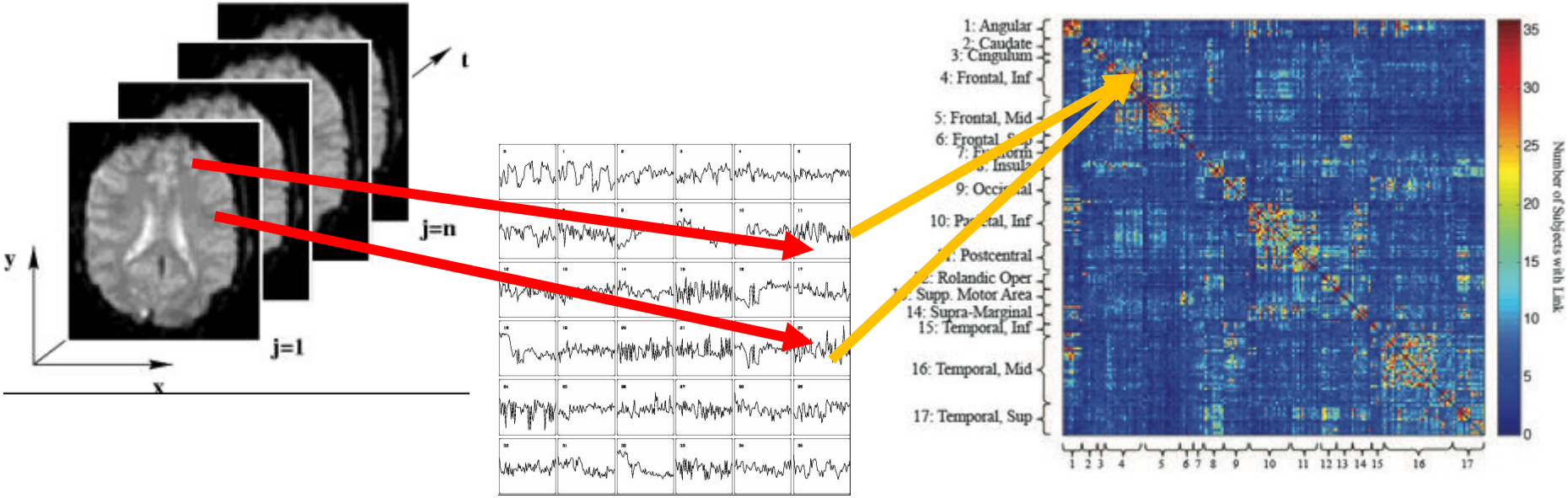
Magnetic Resonance Angiography (MRA):

- Blood entering the imaged area is not yet magnetically saturated, giving it a much higher signal when using short echo time and flow compensation
- Used for diagnosis of aneurysm, finding causes of stroke, heart disease, ….

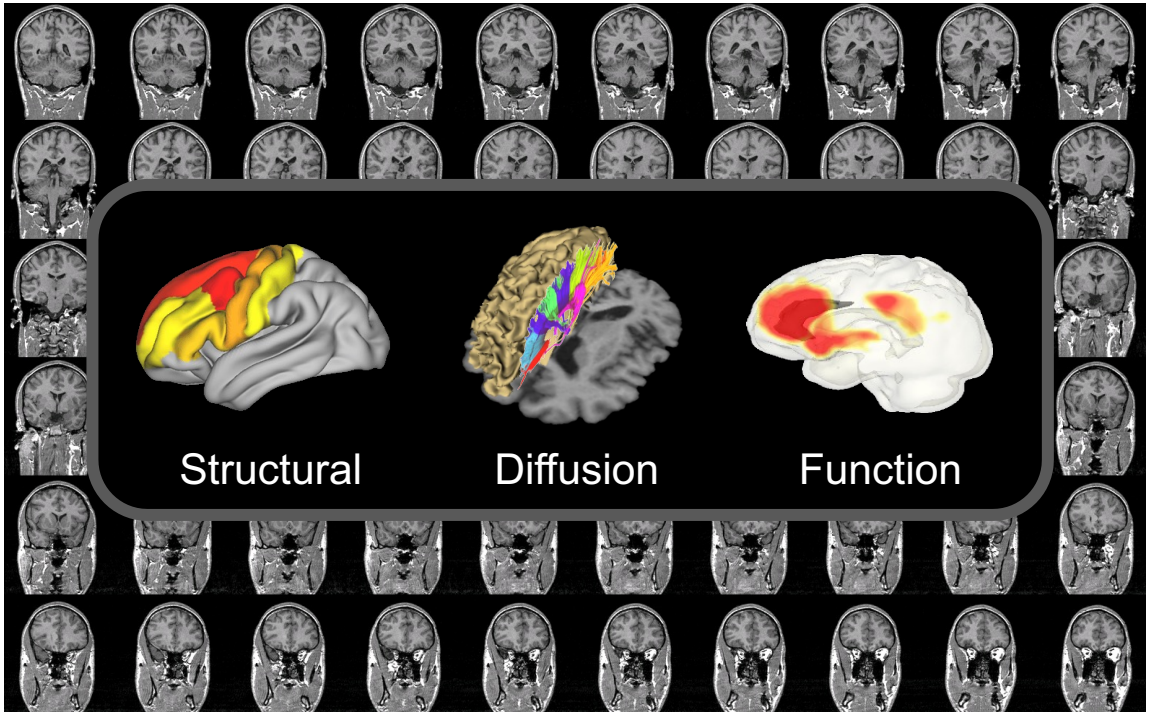
https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/magnetic-resonance-angiography-mra

Functional MRI

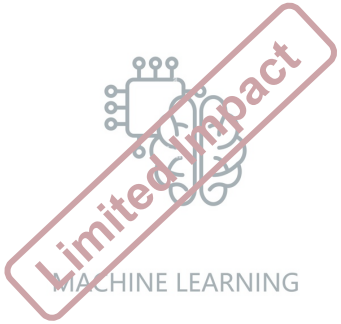
Resting-state fMRI: measures spontaneous low-frequency fluctuations in the blood-oxygen-level-dependent (BOLD) signal



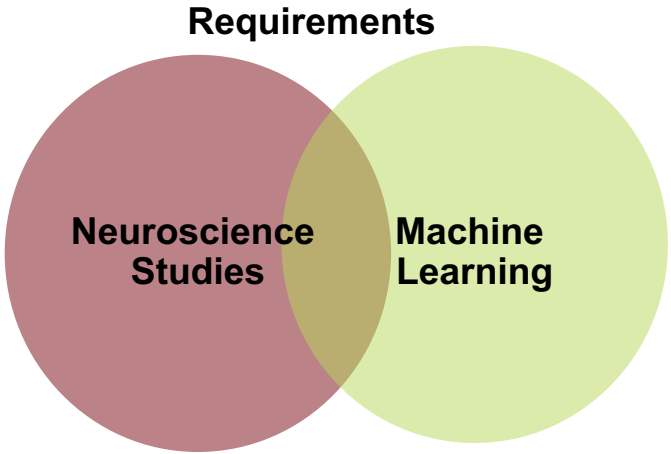
Focus of course



Why Create New Machine Learning Models for Neuroscience Discovery ?



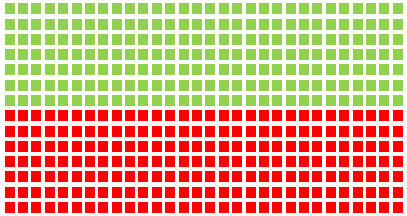
Baker, M.: 1,500 scientists lift the lid on reproducibility, *Nature,* 533, 452–454, 2016



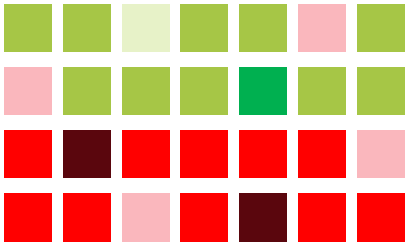
Limiting Impact

Assumptions of neuroscience studies rarely accommodate those of machine learning models and vice versa:

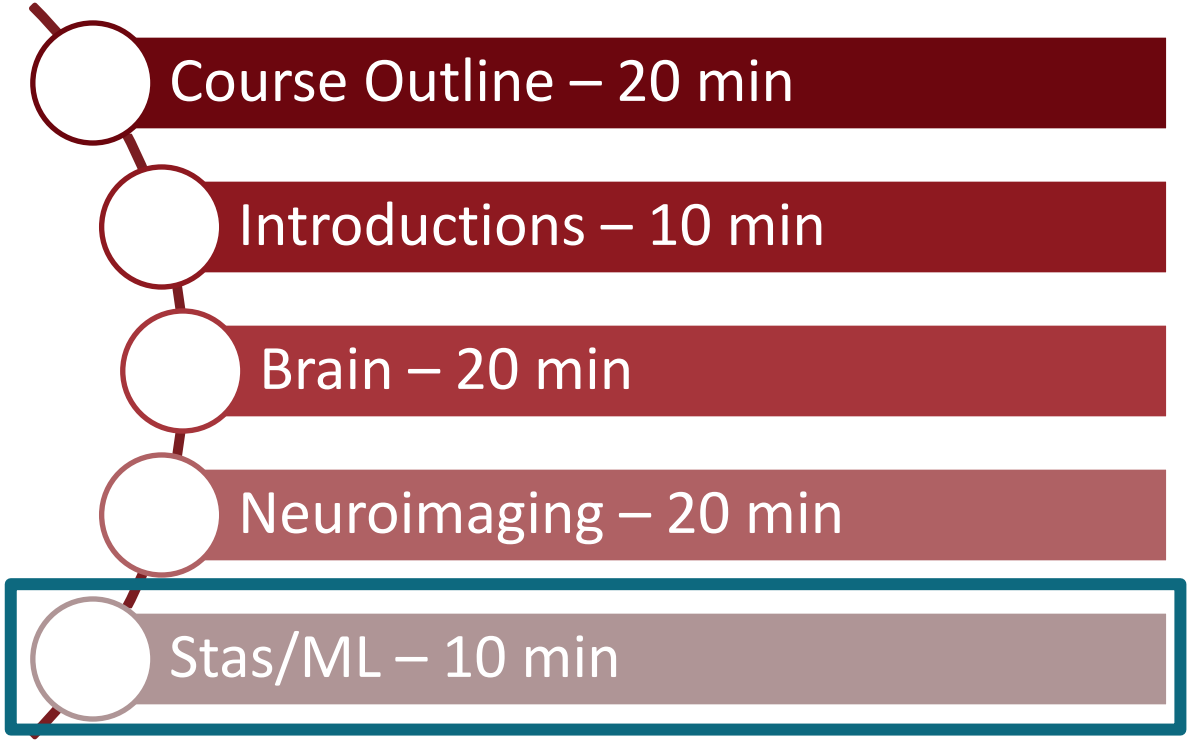
- **Machine learning models require data sets to be**
  - well curated
  - large sample size
  - diverse cohort composition
  - small number of measurements per sample from a single modality



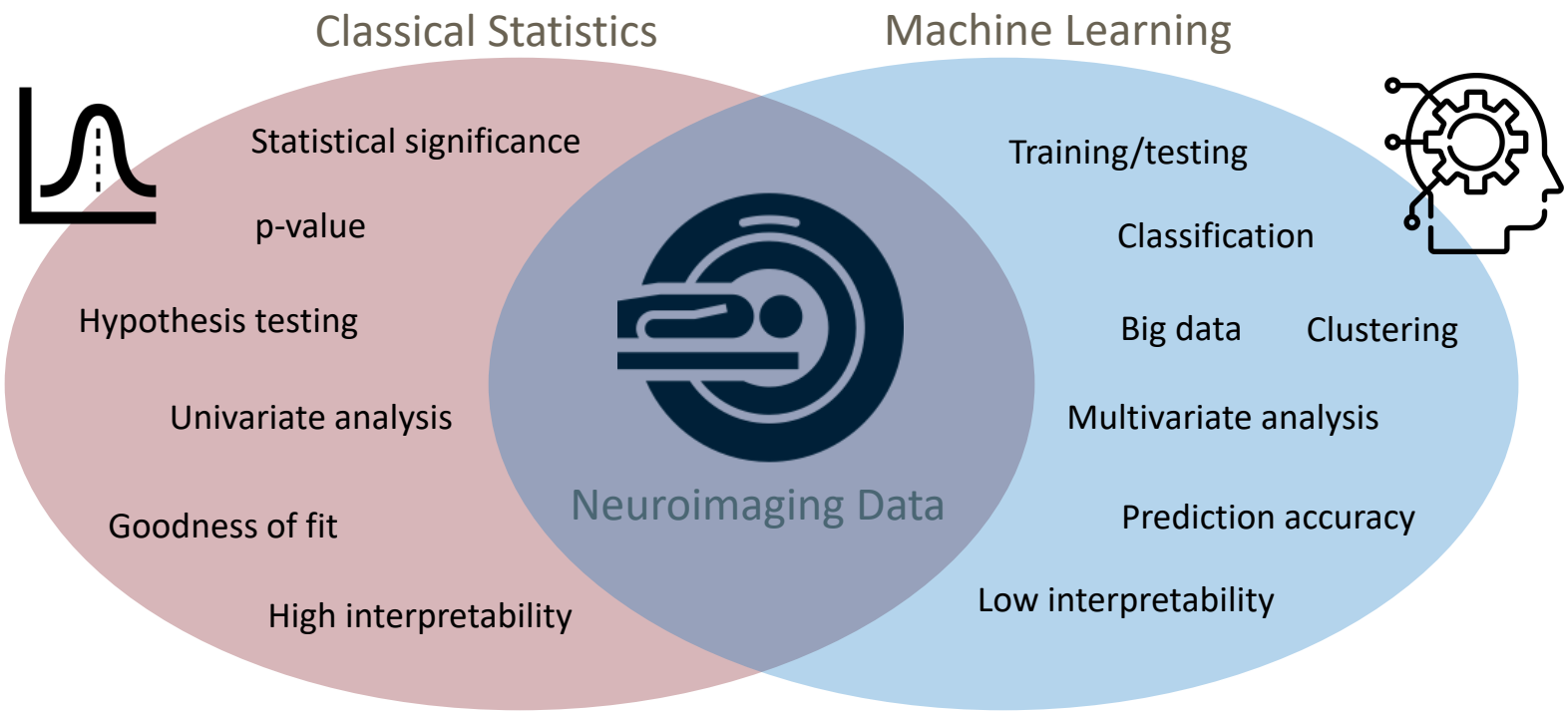
- **Neuroscience studies often analyze data sets that are**
  - imprecise definition (lacking ground truth)
  - small sample size
  - carefully recruited cohorts
  - large number of multimodal measurements per sample



Today…

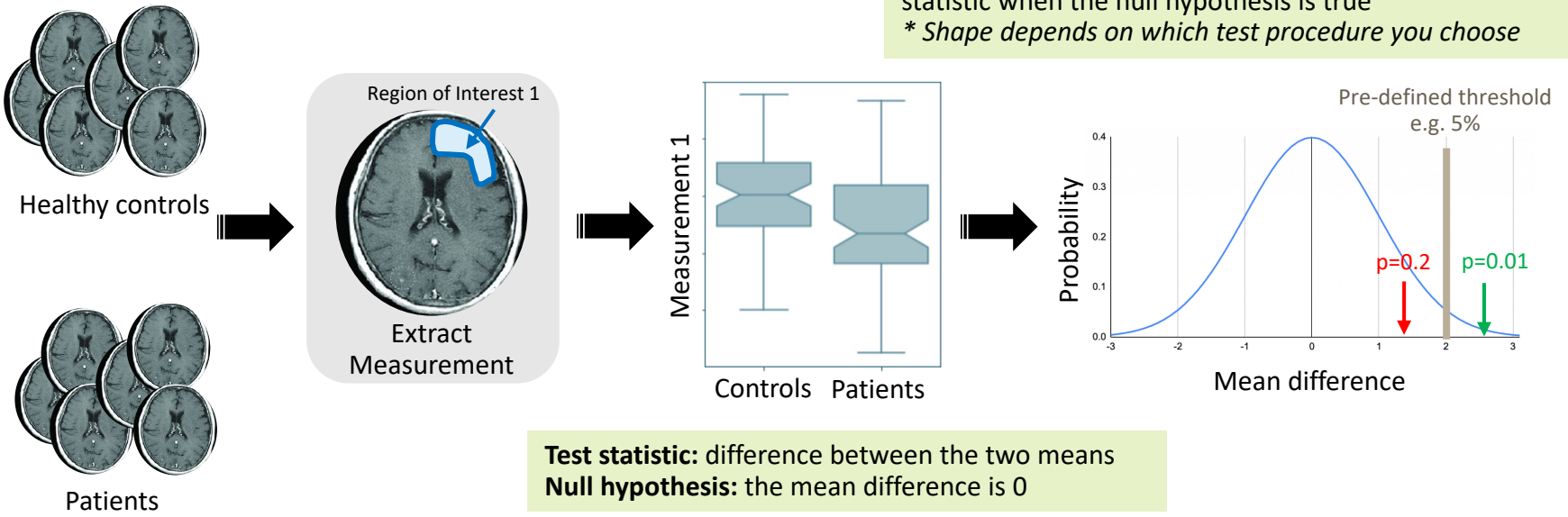

Course Outline – 20 min
Introductions – 10 min
Brain – 20 min
Neuroimaging – 20 min
Stas/ML – 10 min

Data Science in Neuroimaging



Statistical Analysis (Hypothesis Testing)

Null distribution*: probability distribution of the test statistic when the null hypothesis is true
** Shape depends on which test procedure you choose*



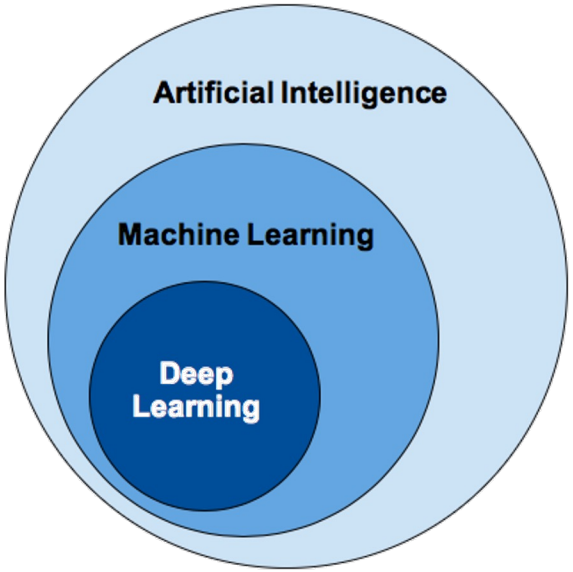
Test statistic: difference between the two means
Null hypothesis: the mean difference is 0

☑ Reject the null hypothesis (patients have lower measurements **on average**)

☒ Cannot reject the null hypothesis

Machine Learning

Study of algorithms that
improve their performance (P)
at some task (T)
with experience (E)
- Tom Mitchell, CMU



Machine Learning

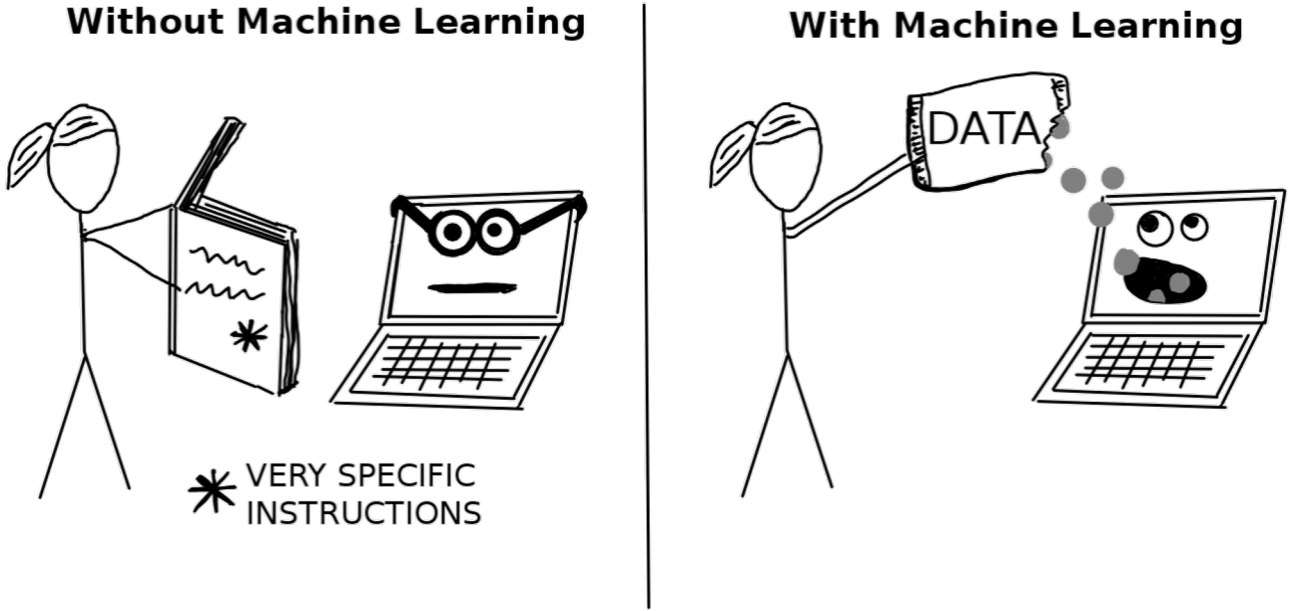
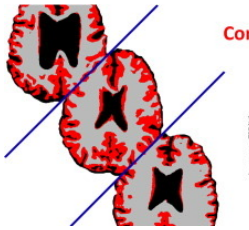
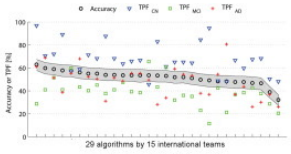


Image Courtesy of Interpretable ML Book

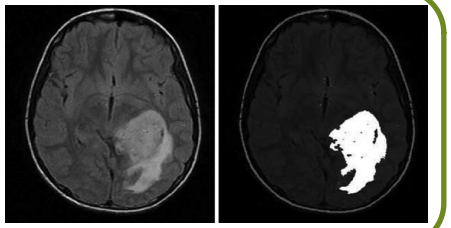


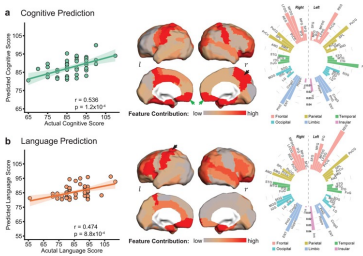
Computer-aided diagnosis of dementia



	Supervised Learning	Unsupervised Learning
Discrete	classification or categorization	clustering
Continuous	regression	dimensionality reduction

Tumor Segmentation





Predicting neurodevelopmental outcomes

Brain Fingerprinting

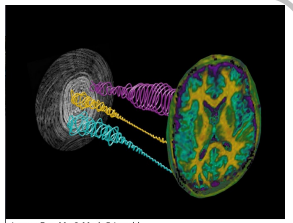
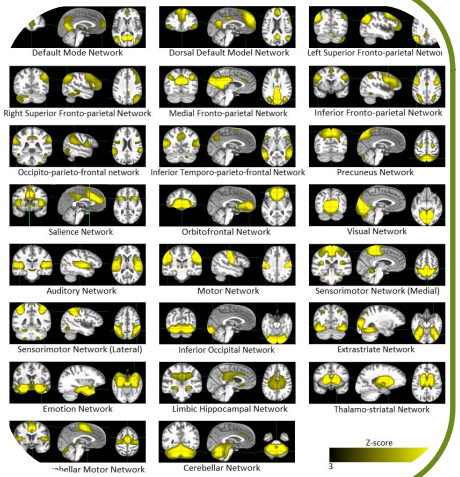
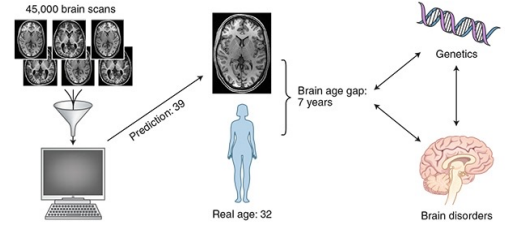


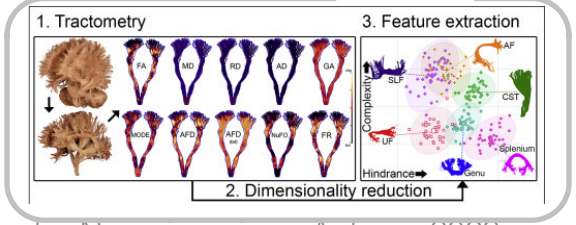
Image: Dan Ma & Mark Griswold

Clustering brain functional states



Age prediction, relations clinical test scores





Thank you!

- https://ml4n.stanford.edu/
- psyc221-aut2324-staff@staff.stanford.edu

- Start thinking about an exciting project topic
- See http://cnslab.stanford.edu/publications for examples