Today…

Course Outline

- Brain anatomy
- Neuroimaging
- Statistical modeling
- Machine learning
Instructors and Office Hours

Ehsan Adeli, Ph.D.,
Office hours: Wednesdays 3-4pm
Location: Gates Building Rm 300 (or Zoom)

Qingyu Zhao, Ph.D.,
Office hours: Mondays 3-4pm
Location: Psychiatry Building Rm 3370 (or Zoom)

Kilian M Pohl, Ph.D.,
Office hours: Schedule only
Location: Zoom
Course Assistants

Magdalini Paschali, Ph.D. | Wei Peng, Ph.D.

Questions: Contact psyc221-aut2223-staff@lists.stanford.edu
Location

- Turing Auditorium, Rm 111, Polya Building
- Zoom (only accessible through Canvas). Please do not share the Zoom links outside the class.

Course Website:
- https://ml4n.Stanford.edu/

Canvas:
- PSYC121: https://canvas.stanford.edu/courses/162683
- PSYC221: https://canvas.stanford.edu/courses/162398
## Grading

<table>
<thead>
<tr>
<th></th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Assignments</td>
<td>10%</td>
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<tr>
<td>Mid-term (take home exam)</td>
<td>20%</td>
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<tr>
<td>Final Exam (take home exam)</td>
<td>30%</td>
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<tr>
<td>Project Proposal*</td>
<td>10%</td>
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<tr>
<td>Project delivery and poster presentation*</td>
<td>30%</td>
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</tbody>
</table>

*PSYC221 students need to have novel components in their analysis as part of their project*
References

Textbooks (Not Required)

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

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

- Python
- R / MATLAB
## Schedule and Syllabus

<table>
<thead>
<tr>
<th>Week</th>
<th>Date</th>
<th>Lecturer</th>
<th>Topics</th>
<th>Materials and Assignments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9/26 Mon</td>
<td>Kilian Pohl</td>
<td>Introduction</td>
<td>[Slides TBD]</td>
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<tr>
<td></td>
<td></td>
<td>Ehsan Adeli</td>
<td>• Course outline</td>
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<tr>
<td></td>
<td></td>
<td>Qingyu Zhao</td>
<td>• What is the brain?</td>
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<td>• Definition of neuroimaging modalities</td>
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<tr>
<td></td>
<td>9/28 Wed</td>
<td>Kilian Pohl</td>
<td>Basic operations and processing of neuroimages</td>
<td>[Slides TBD]</td>
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<td></td>
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<td></td>
<td>• Structural/diffusion/functional MRI processing</td>
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<td>• Quality control</td>
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<td>• Data curation for ML</td>
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<td>• Public datasets &amp; course projects</td>
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<tr>
<td>2</td>
<td>10/3 Mon</td>
<td>Greg Zaharchik</td>
<td>Understanding the brain through imaging</td>
<td>[Slides TBD]</td>
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<tr>
<td></td>
<td></td>
<td>(Stanford Neurology)</td>
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<td>[Assignment TBD]</td>
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<tr>
<td></td>
<td>10/5 Wed</td>
<td>Qingyu Zhao</td>
<td>Basics for statistical analysis</td>
<td>Due on 10/24</td>
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<td></td>
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<td>• Hypothesis testing and group-wise analysis</td>
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<td>• Common statistical models for neuroimaging studies</td>
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<td>• What are confounders/confounding effects</td>
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<td>• Statistical analysis of ML experiments</td>
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<tr>
<td>3</td>
<td>10/10 Mon</td>
<td>Ehsan Adeli</td>
<td>Basics for machine learning</td>
<td>[Slides TBD]</td>
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<td>• Un/semi/full supervision</td>
<td>[Assignment TBD]</td>
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<td>• Evaluation &amp; metrics of ML models</td>
<td>Due on 10/26</td>
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<td>• Traditional ML models</td>
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<td></td>
<td>• End-to-end deep learning (CNN, Transformers, generative models)</td>
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<tr>
<td></td>
<td>10/12 Wed</td>
<td>Holger Roth</td>
<td>Exploratory topics in medical and neuroimaging (tailored to help students finalize course projects)</td>
<td>[Slides TBD]</td>
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<td>(David)</td>
<td>• Federated learning</td>
<td>[Assignment TBD]</td>
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<td></td>
<td>• Active learning</td>
<td>Due on 10/26</td>
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<td>• AutoML</td>
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<tr>
<td>4</td>
<td>10/17 Mon</td>
<td>Majda Paschali</td>
<td>ML/Stats programming with Python</td>
<td>[Slides TBD]</td>
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<tr>
<td></td>
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<td>Wei Peng</td>
<td>• Intro into Jupyter notebook</td>
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<td>• Hypothesis testing</td>
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<td>• Traditional ML models</td>
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<td>• Traditional ML based on image features</td>
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<td>• CNN on 3D MRIs</td>
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<td></td>
<td>10/19 Wed</td>
<td>Ehsan Adeli</td>
<td>Applications to structural MRI</td>
<td>[Slides TBD]</td>
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<td></td>
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<td>• ML based on ROI-wise features</td>
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<td>• Deep learning on 3D MRI volumes</td>
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<td>• MRI processing (segmentation/registration/denoising/etc)</td>
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</tbody>
</table>
# Schedule and Syllabus

<table>
<thead>
<tr>
<th>Week</th>
<th>Date</th>
<th>Speaker</th>
<th>Topic</th>
<th>Additional Notes</th>
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</thead>
<tbody>
<tr>
<td>5</td>
<td>10/24 Mon</td>
<td>James Duncan (Mole University)</td>
<td>Neuroimage Analysis in Autism: from Model-based Estimation to Data-driven learning</td>
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<td>10/25 Wed</td>
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<td>Midterm exam</td>
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<td>Project proposal</td>
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<tr>
<td>6</td>
<td>10/31 Mon</td>
<td>Elzan Adeli</td>
<td>Exploratory topics on structural MRI</td>
<td>Slides 180</td>
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<td>- Generative models</td>
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<td>- Controlling confounding effects in deep learning</td>
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<td>11/2 Wed</td>
<td>Ender Kanukoglu (ETH Zürich)</td>
<td>Applications to structural MRI</td>
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<td></td>
<td>- Historical view of how ML evolved for structural neuroimaging, covering univariate,</td>
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<td>multivariate ML, RF and DL models</td>
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<td>- What can current DL models (not) do for structural neuroimaging?</td>
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<td>- Challenges ahead</td>
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<tr>
<td>7</td>
<td>11/7 Mon</td>
<td>Qingyu Zhao</td>
<td>Applications to functional MRI</td>
<td>Slides 182</td>
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<td>- Correlation-based analysis</td>
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<td>- Independent component analysis</td>
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<td>- Auto-regressive models</td>
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<td>- Deep learning on 4D BOLD signals</td>
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<td>11/9 Wed</td>
<td>Thomas Wolters (University of Tübingen)</td>
<td>From Estimating Activation Locality to Conceptualizing Disorder: Machine Learning for Brain</td>
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<td>Imaging Psychiatry</td>
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<tr>
<td>8</td>
<td>11/14 Mon</td>
<td>Qingyu Zhao</td>
<td>Applications to diffusion MRI</td>
<td>Slides 180</td>
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<td>- ML based on diffusivity measures</td>
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<td>- ML-based DSI estimation and tractography</td>
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<td>- Tensor-based convolution</td>
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<td>11/16 Wed</td>
<td>Lauren O’donnell (Harvard University)</td>
<td>Machine learning in diffusion MRI tractography</td>
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<tr>
<td>9</td>
<td>Thanksgiving</td>
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<td>No Classes</td>
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<tr>
<td>10</td>
<td>11/23 Mon</td>
<td>Martin Styner (University of North</td>
<td>Machine Learning for predictive, longitudinal studies of infant MRI data</td>
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<td>Carolina at Chapel Hill)</td>
<td>- Image imputation/generation for missing infant MRI data in longitudinal studies</td>
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<td>- Age and contrast-agnistic image segmentation for infant MRI</td>
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<td>- Classification/learning from cortical surface data for prediction in early brain</td>
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<td>development</td>
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<td>11/30 Wed</td>
<td>Ismail Idelk (Imperial College London)</td>
<td>Exploratory topics</td>
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<tr>
<td>11</td>
<td>12/5 Mon</td>
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<td>Final exam</td>
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<td>Project presentation</td>
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Projects

- 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)

  - MICCAI 2023 (Vancouver, Canada)

- Find you teammates (Canvas, Slack if requested)

- 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)
Today…

- Course Outline
  - Brain anatomy
  - Neuroimaging
  - Statistical modeling
  - Machine learning
The Human Brain

- One of the largest organs (1300~1400g), but also the least understood organ
- 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

Human Nerve Cell

Structure of the Synapse

Spinal cord

Basic Neuron Types

Human Brain

Human Brain Anatomy

Neurosciences Anatomy Core

By Rita Carter

PSYC 121 / PSYC 221

NEPR 205: Neurosciences Anatomy Core
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 …
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
- **Occipital lobe**: visual processing
- **Temporal lobe**: auditory processing, language
Finer and finer Parcellations

- **Frontal lobe**: Executive functions, thinking, planning, organising and problem solving, emotions and behavioural control, personality
- **Motor cortex**: Movement
- **Sensory cortex**: Sensations
- **Parietal lobe**: Perception, making sense of the world, arithmetic, spelling
- **Occipital lobe**: Vision
- **Temporal lobe**: Memory, understanding, language

HCP MMP
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
Today…

Course Outline

Brain anatomy

Neuroimaging

Statistical modeling

Machine learning
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
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
- 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
X-Ray (1895)

- Measures high-speed electrons (generated via electromagnetic 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.

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.

- 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
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

Focus of course

Structural  Diffusion  Function
Today…

Course Outline
Brain anatomy
Neuroimaging
Statistical modeling
Machine learning
Data Science in Neuroimaging

Classical Statistics
- Statistical significance
- p-value
- Hypothesis testing
- Univariate analysis
- Goodness of fit
- High interpretability

Machine Learning
- Training/testing
- Classification
- Big data
- Clustering
- Multivariate analysis
- Prediction accuracy
- Low interpretability

Neuroimaging Data
- Applied to “larger” data set
- Higher “complexity and compacity”
- Less mathematically explained
- Less interpretable

From classical statistics to machine learning

Concept of Hypothesis Testing

Healthy controls → Extract Measurement → Region of Interest 1

Patients

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

Null distribution:

Pre-defined threshold e.g. 5%
p=0.2
p=0.01

Machine Learning for Neuroimaging - Autumn 2022
Multiple Comparisons

Healthy controls

Patients

Extract K Measurements

Measurement 1

Measurements K

Controls Patients

Significant regions

One false positive every 20 test

Push to a more stringent threshold

5%/K

Machine Learning for Neuroimaging - Autumn 2022
Voxelwise Analysis

- Healthy controls
- Patients
- Voxelwise measures

$\times 1 \text{ million?}$

- How to choose specific statistical model for each hypothesis testing?
- How to extract measurements?
- How to relate the multiple (non)independent tests?
Today…

Course Outline
Brain anatomy
Neuroimaging
Statistical modeling
Machine learning
Concepts

Image Credit: https://www.sumologic.com/blog/machine-learning-deep-learning/

Following slides, courtesy of D. Batra, Georgia Tech

Ehsan Adeli, Ph.D. (eadeli@stanford.edu)
What is (general) intelligence?

- Boring textbook answer
  *The ability to acquire and apply knowledge and skills*
  - Dictionary

- My favorite
  *The ability to navigate in problem space*
  - Siddhartha Mukherjee, Columbia
What is artificial intelligence?

- Boring textbook answer
  
  *Intelligence demonstrated by machines*
  
  - Wikipedia

- My favorite
  
  *The science and engineering of making computers behave in ways that, until recently, we thought required human intelligence.*
  
  - Andrew Moore, CMU
What is machine learning?

- My favorite

*Study of algorithms that improve their performance (P) at some task (T) with experience (E)*

- Tom Mitchell, CMU
What is machine learning

Without Machine Learning

With Machine Learning

Image Courtesy of Interpretable ML Book
What is deep learning?

Deep Learning = Hierarchical Compositionality
Deep Learning = Hierarchical Compositionality

Feature visualization of convolutional net trained on ImageNet from [Zeiler & Fergus 2013]
Types of Learning

<table>
<thead>
<tr>
<th>Supervised Learning</th>
<th>Unsupervised Learning</th>
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<tbody>
<tr>
<td>Discrete</td>
<td></td>
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<tr>
<td>classification or</td>
<td>clustering</td>
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<tr>
<td>categorization</td>
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<td>Continuous</td>
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<tr>
<td>regression</td>
<td>dimensionality</td>
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<tr>
<td></td>
<td>reduction</td>
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</table>

Ehsan Adeli, Ph.D. (eadeli@stanford.edu)
Predicting neurodevelopmental outcomes

Brain fingerprinting

Age prediction, relations clinical test scores

Supervised Learning
- classification or categorization
- regression

Unsupervised Learning
- clustering
- dimensionality reduction

Tumor segmentation

Clustering brain functional states

1. Tractometry
2. Dimensionality reduction
3. Feature extraction

Computer-aided diagnosis of dementia

Ehsan Adeli, Ph.D. (eadeli@stanford.edu)
Thank you!

- [https://ml4n.Stanford.edu/](https://ml4n.Stanford.edu/)
- [psyc221-aut2223-staff@staff.stanford.edu](psyc221-aut2223-staff@staff.stanford.edu)

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