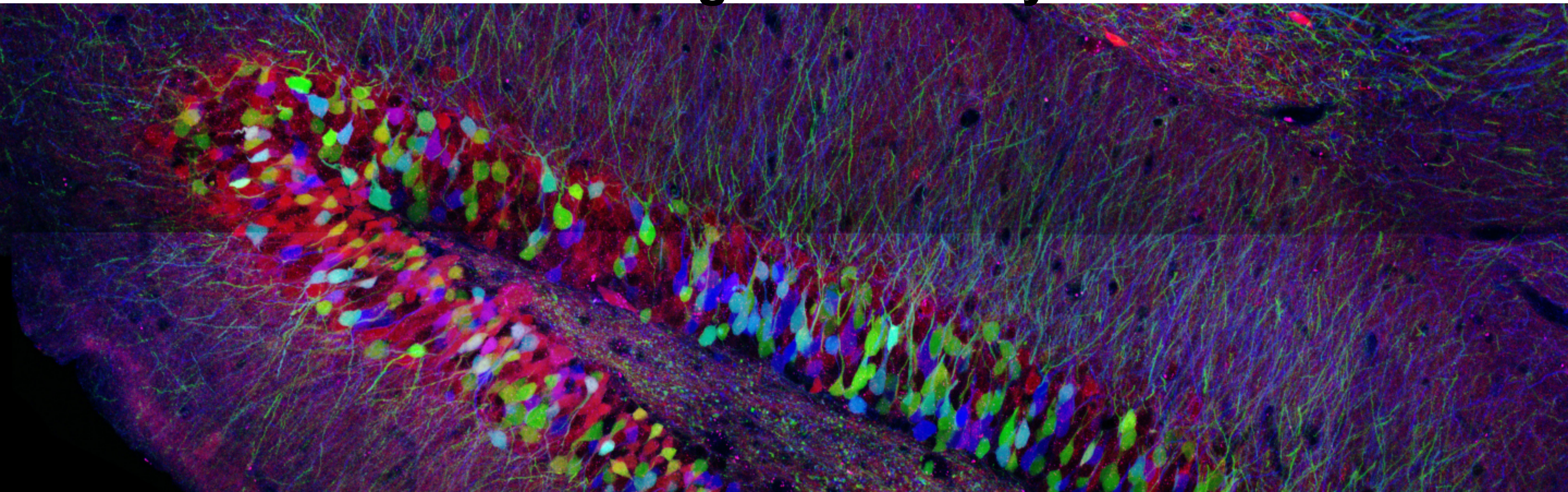
Applied Neuroscience

Columbia Science Honors Program

Fall 2017

Learning and Memory



Learning and Memory

Objective: Computational Models of Memory

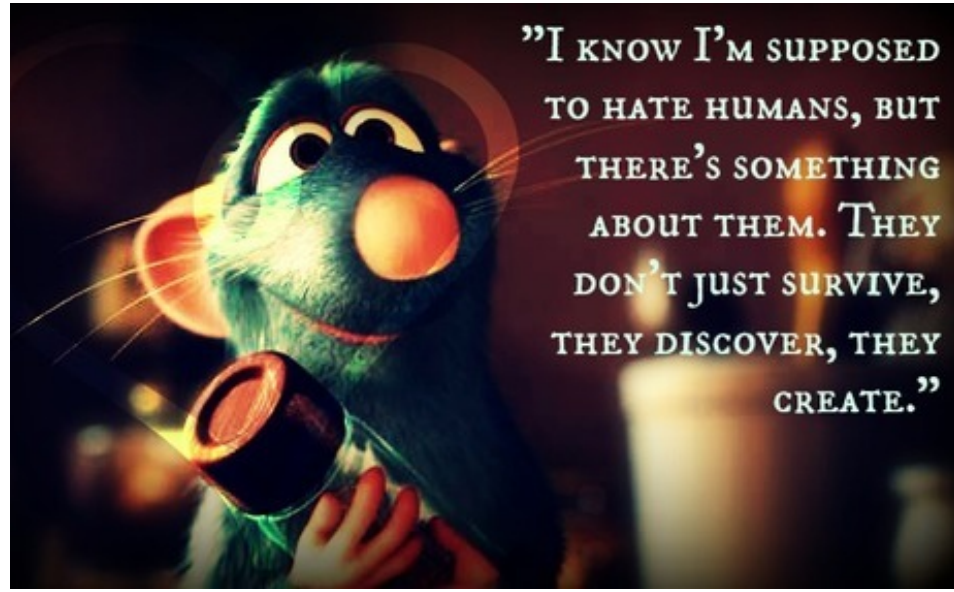
Agenda:

1. Learning and the Brain
   - Hippocampus and Cortex
   - Introduction to Neural Networks
2. Memory
   - Structure and Function of Memory
   - Memory Disorders

Introduction to Memory

What is memory?

Memory: changes in the activity or connectivity of neural systems that are triggered by stimuli or brain states and ***persist over a duration longer than triggering events***



Why do we need memory?

Memory serves an **adaptive role:**

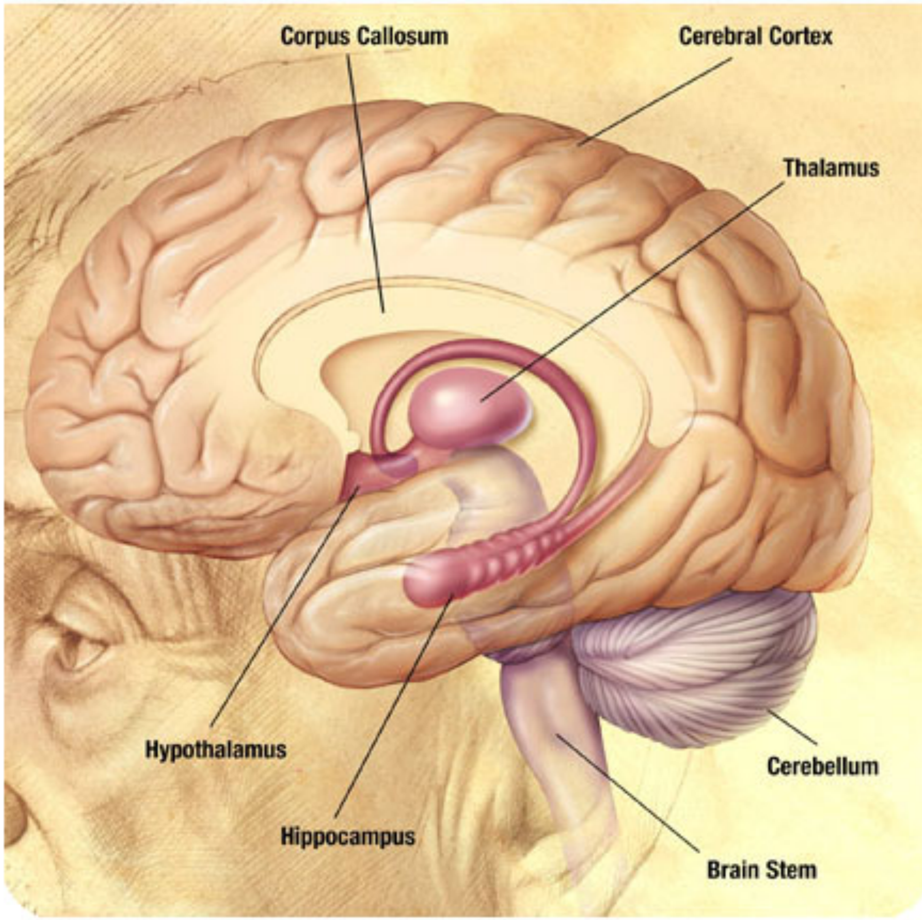
1. We learn from our experiences
2. We generalize faster
3. We can make predictions

Learning, Inference, and Prediction

Memory research uses:

1. Neuroscience
2. Computer Science
3. **Information Theory:** studies the quantification, storage, and communication of information

Introduction to Memory



Limbic System: controls emotions and instinctive behavior (includes hippocampus and parts of cortex)

Thalamus: receives sensory and limbic input and sends to cerebral cortex

Hypothalamus: maintains homeostasis and controls internal clock of body

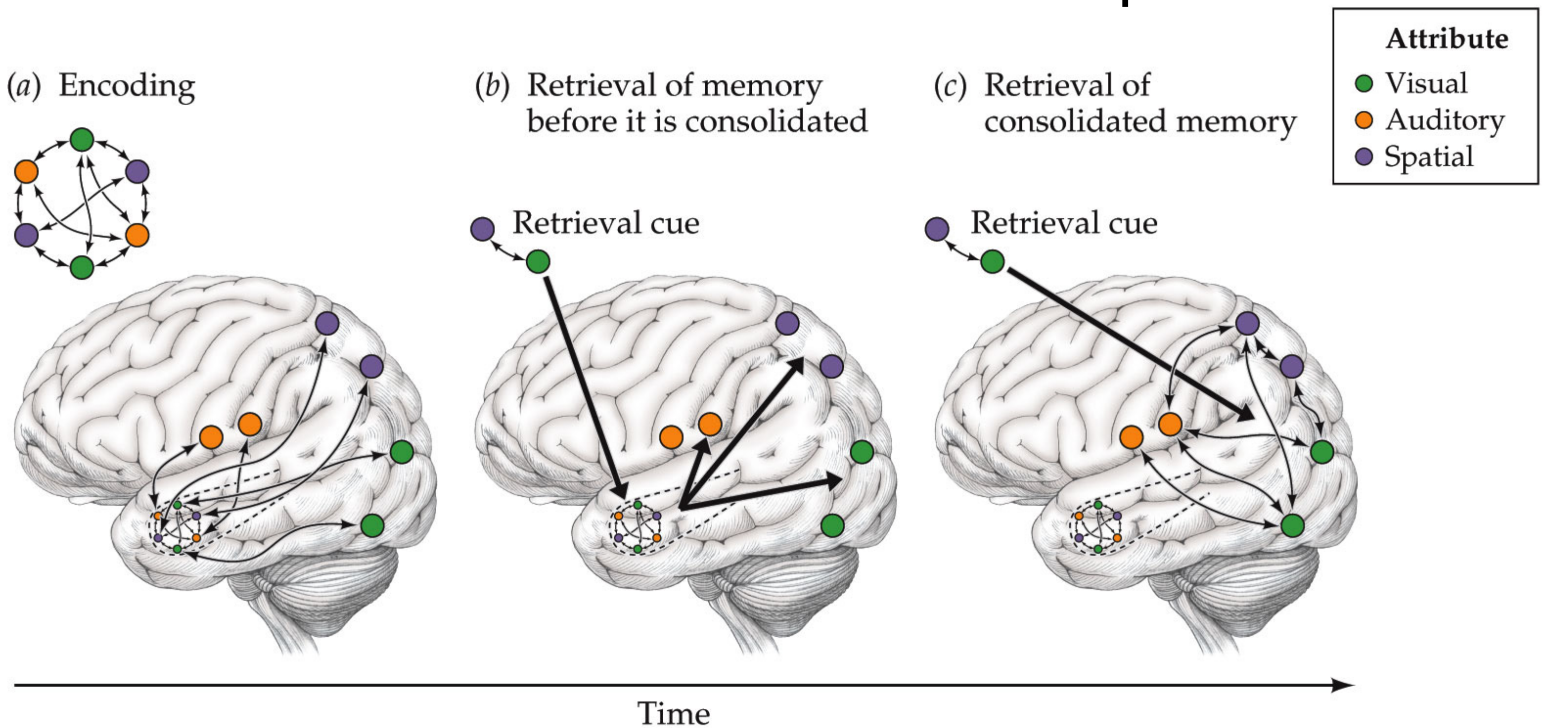
Hippocampus: where short-term memories are converted to long-term memories

Introduction to Memory

Where is memory?

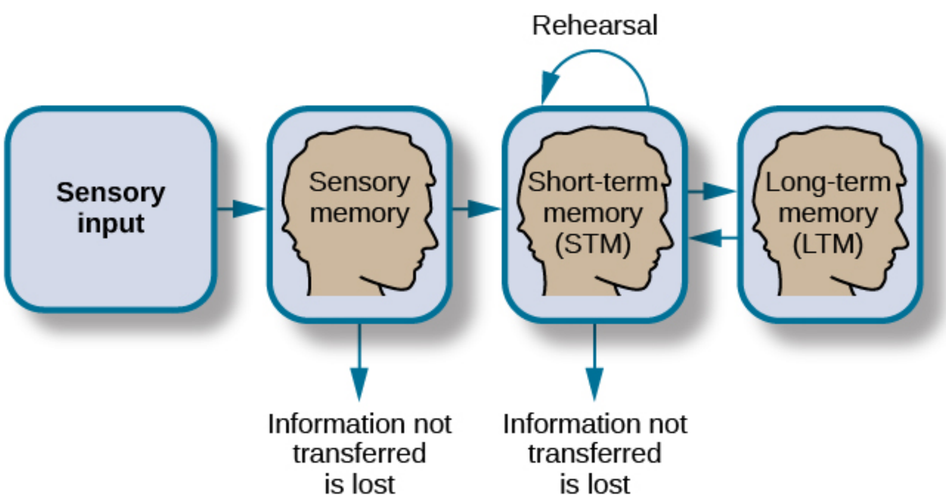
Multiple Brain Regions are involved in encoding memory as shown below by fMRI studies

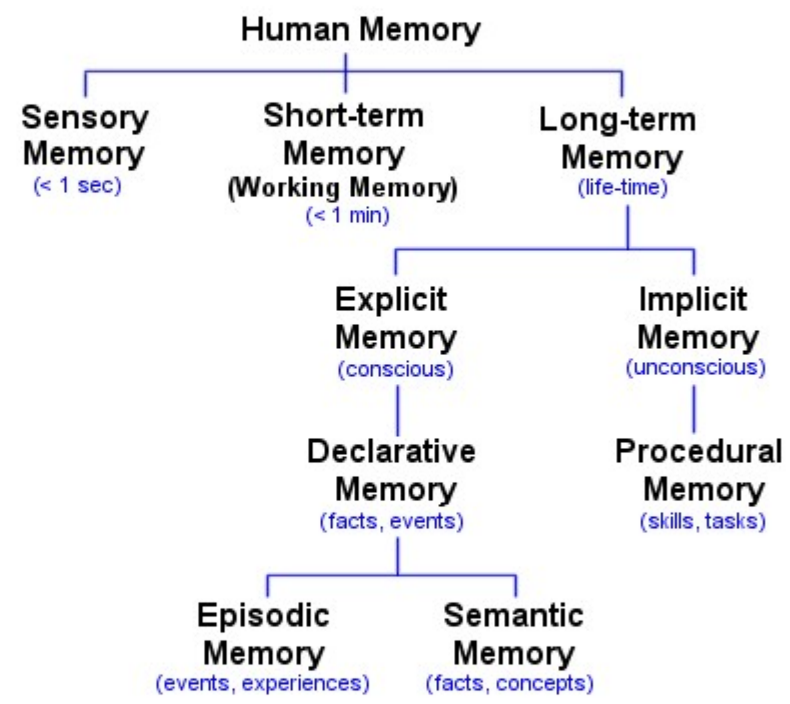
fMRI: uses MRI technology that measures brain activity by detecting changes in associated with blood flow. Cerebral blood flow and neuronal activation are coupled.



Types of Memory

- Models of memory include a sequence of three stages: **sensory, short-term and long-term memory**
- Different types of memory have their own mechanism of action
- This sequential model is called modal, multi-store or the Atkinson-Shiffrin model (developed in 1968)





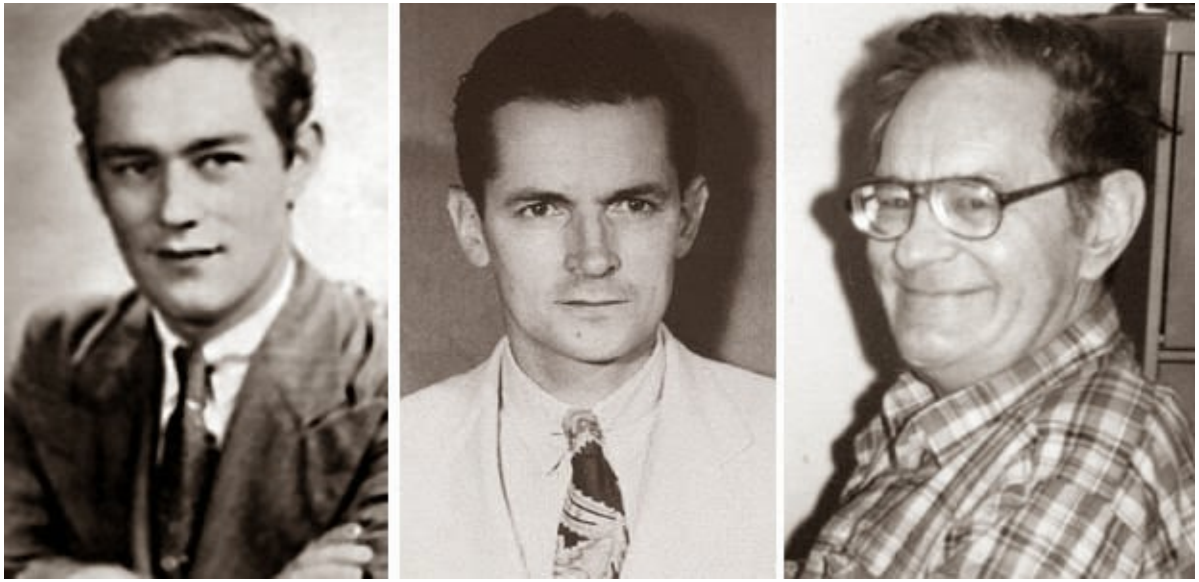
Seven Sins of Memory

Sin	Description	Example
Transience	Decreasing accessibility of memory over time	Simple forgetting of long-past events
Absent-Mindedness	Lapses of attention that result in forgetting	Forgetting location of car keys
Blocking	Information is present but temporarily accessible	Tip-of-the-tongue
Misattribution	Memories are attributed to an incorrect source	Confusing a dream for a memory
Suggestibility	Implanted memories about things that never occurred	Leading questions produce false memories
Bias	Current knowledge and beliefs distort our memories of the past	Recalling past attitudes in line with current attitudes
Persistence	Unwanted recollections that we can never forget	Traumatic war memories

Credit to Professor Daniel Schacter, Chair of Psychology at Harvard University

Case Study on Memory: Henry Molaison (HM)

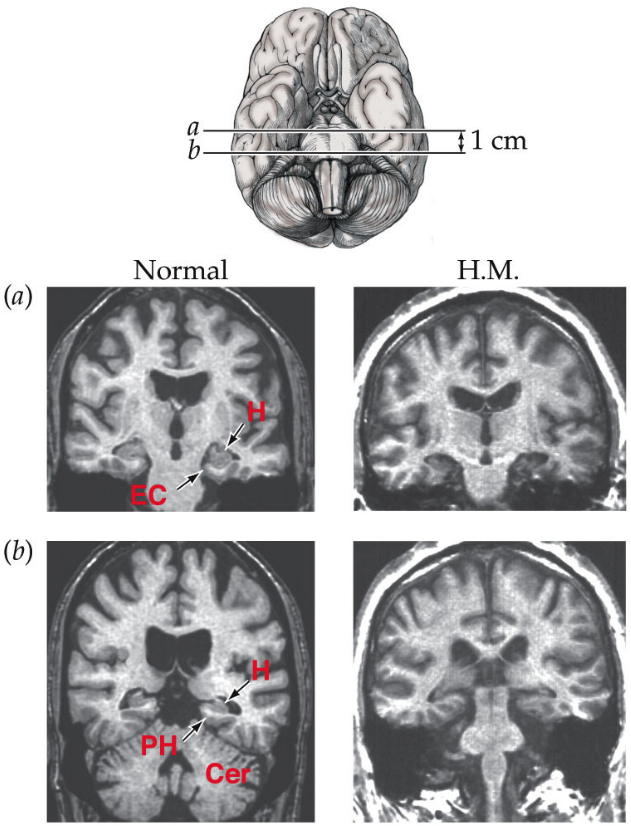
Henry Molaison and Brenda Milner

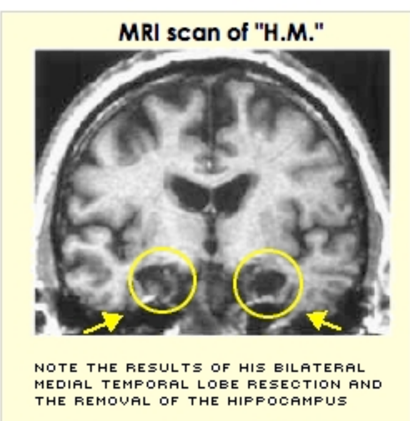


Understanding the Human Brain: A Lifetime of Dedicated Pursuit

Thank You, Professor Brenda Milner

Case Study on Memory: Henry Molaison





Anterograde Amnesia: Problems of learning new facts

- Specific to episodic memories
- Procedural memories intact
- Implicit memory performance intact
- Verbal learning disrupted

Damage to the hippocampus or to regions that supply its inputs and receive its outputs causes anterograde amnesia *as evidenced by Henry Molaison Case Study*

Role of the Hippocampus

1. **Formation of new episodic memories**

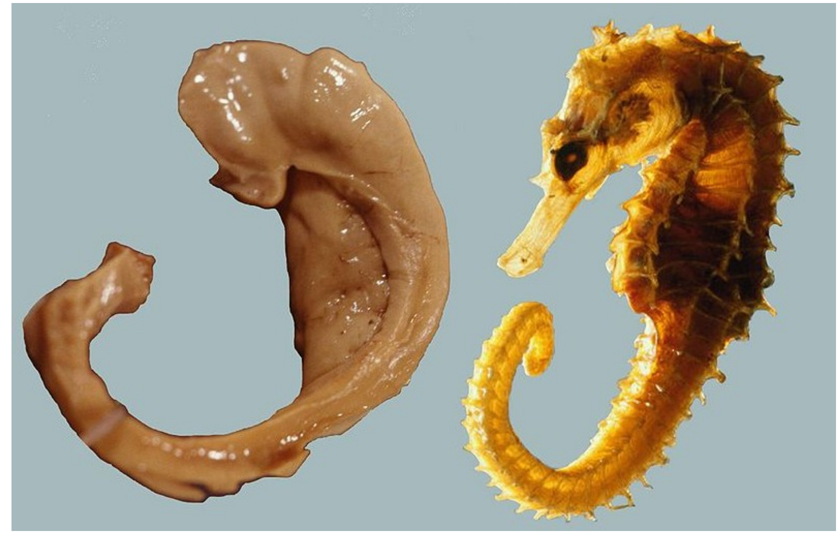
   Anterograde amnesia (HM)

2. **Cognitive Map**

   Place Cells in Rats
   Spatial Attention Cells in Monkeys

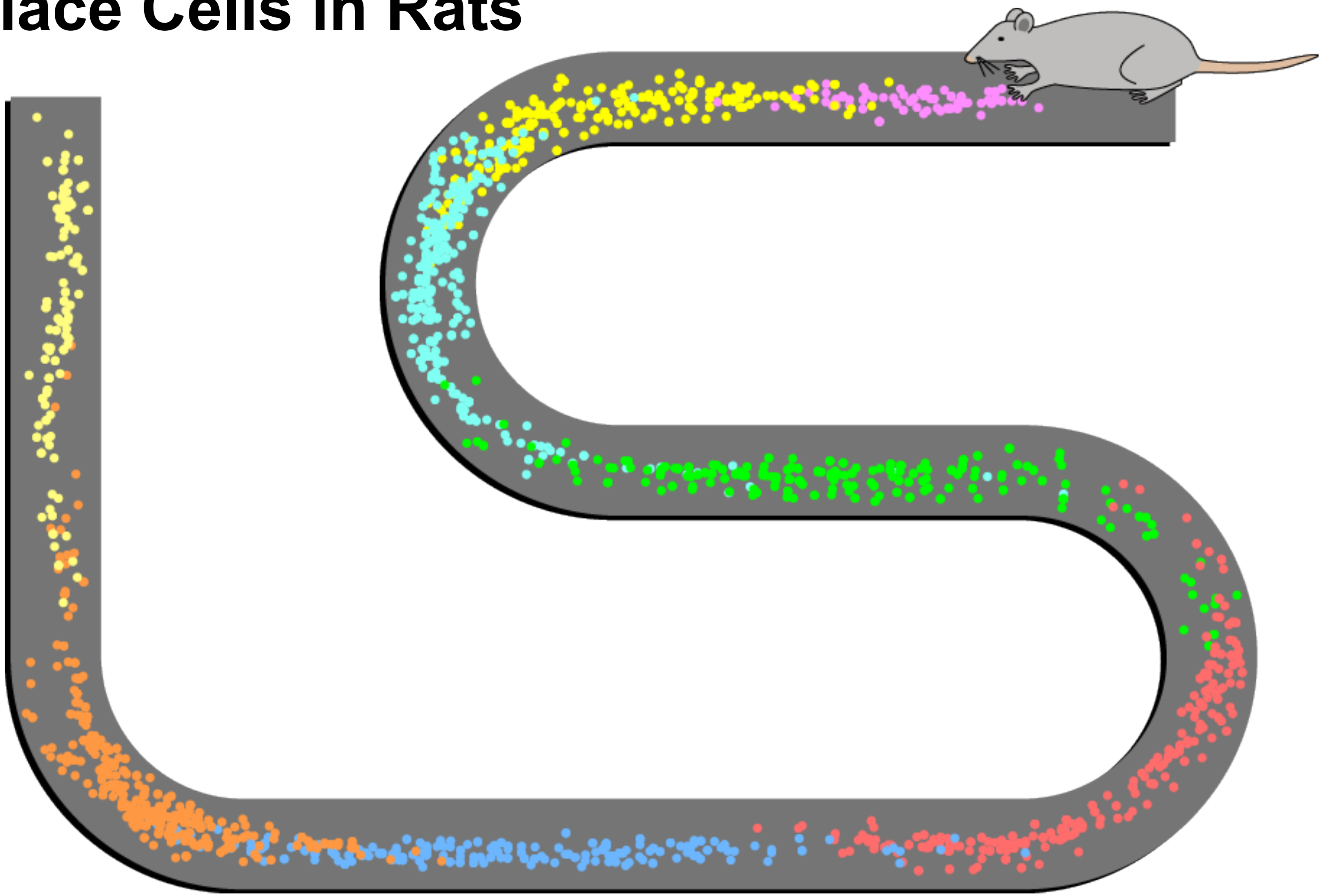
3. **Configurable Association Theory**

   Rats with hippocampus lesions are impaired on tasks requiring them to recognize cue configurations



Hippocampus means "seahorse"

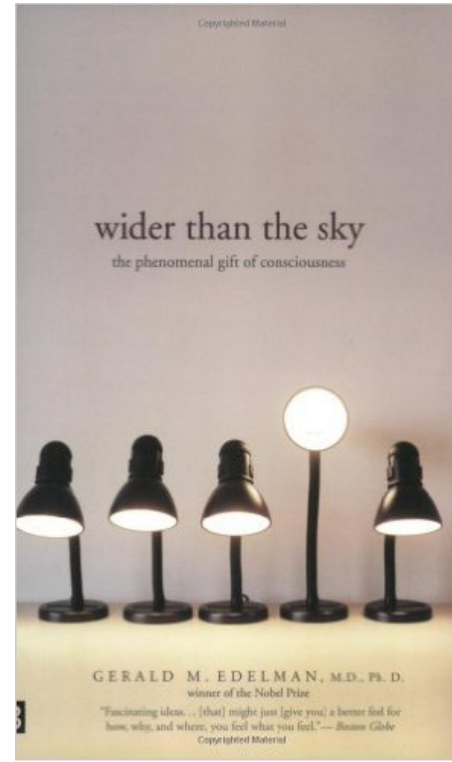
Place Cells in Rats



Place Cell: A type of pyramidal neuron within the hippocampus that becomes active when an animal enters a particular place in its environment (***place field***)

Inside Out

Inside Out: Metaphor of Neuroscience



Central Command

Control panel is operated by different emotions.

Do we have a central command?

We do not have a “seat of consciousness.” Rather, consciousness is highly distributed. We do have the limbic system that regulates emotions.

Headquarters of Inside Out: Hippocampus

Each time Riley experiences an event, a memory sphere of that event rolls into Headquarters. These memories can move into long-term storage.

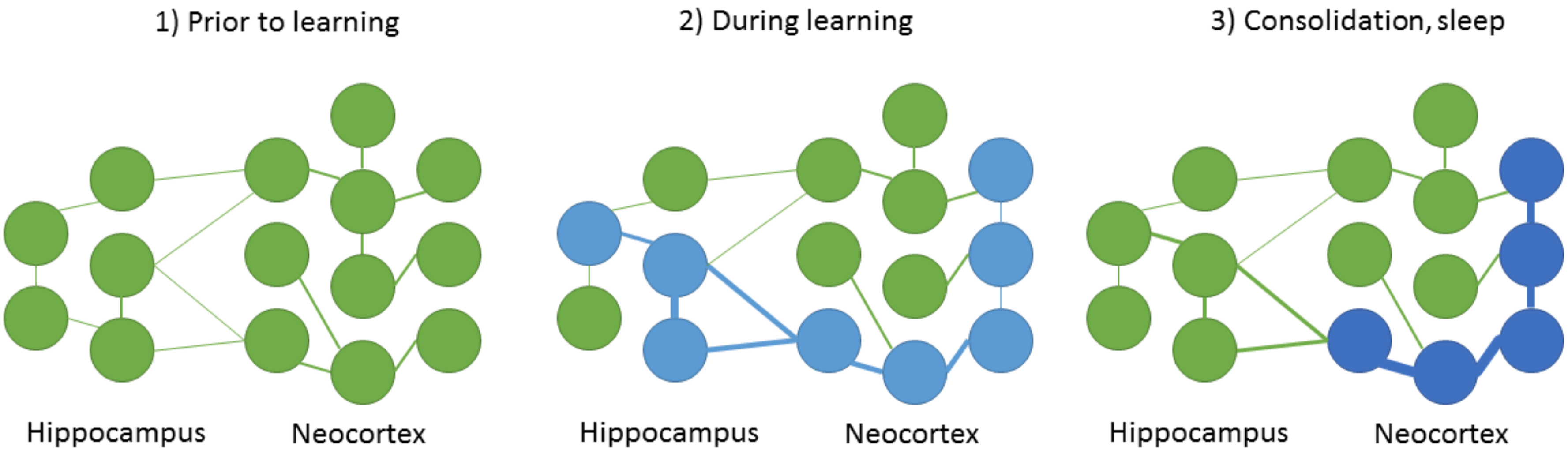
Hippocampus:
component of limbic system that is vital for the formation of episodic memories

Episodic Memories:
memory of autobiographical events (memories that consist of a what, when, and where)

Without a hippocampus, people can no longer form new episodic memories. Which patient is an example of this?

Patient HM: He had his entire hippocampus removed due to seizures.

Consolidation of Memories



Once the hippocampus has formed an episodic memory, where do these memories then go?

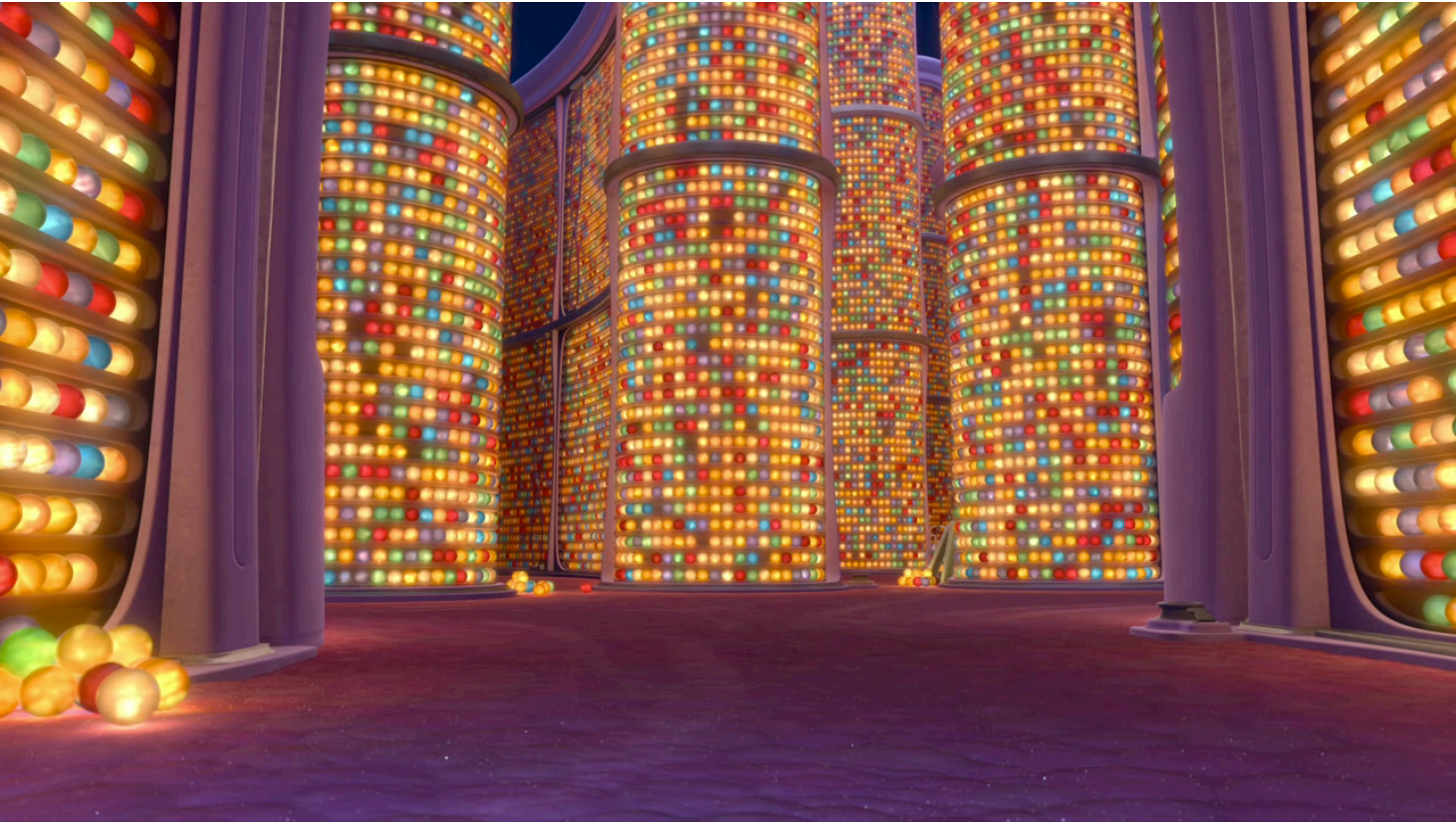
Cerebral Cortex

Consolidation:

Process of maintaining a memory for long-term storage

Sleep is believed to play an important role in consolidation of memories from the hippocampus to the cortex.

Inside Out: Long-Term Memory



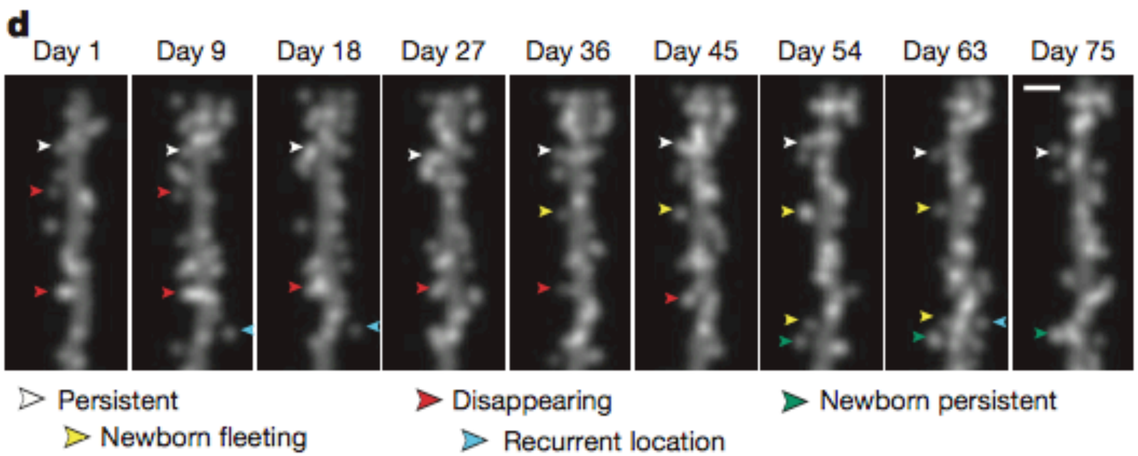
Neurobiology of Long-Term Memory

Is there evidence for the process of memories leaving the hippocampus to the cortex in vivo?

Yes: the laboratory of Mark Schnitzer at Stanford found that hippocampal synapses persist for time intervals that match the known duration of hippocampal dependent-memory.

Background:

- Mammalian hippocampus transiently retains information for about 3-4 weeks in adult mice and longer in humans
- Neural synapses are the elemental sites of information storage

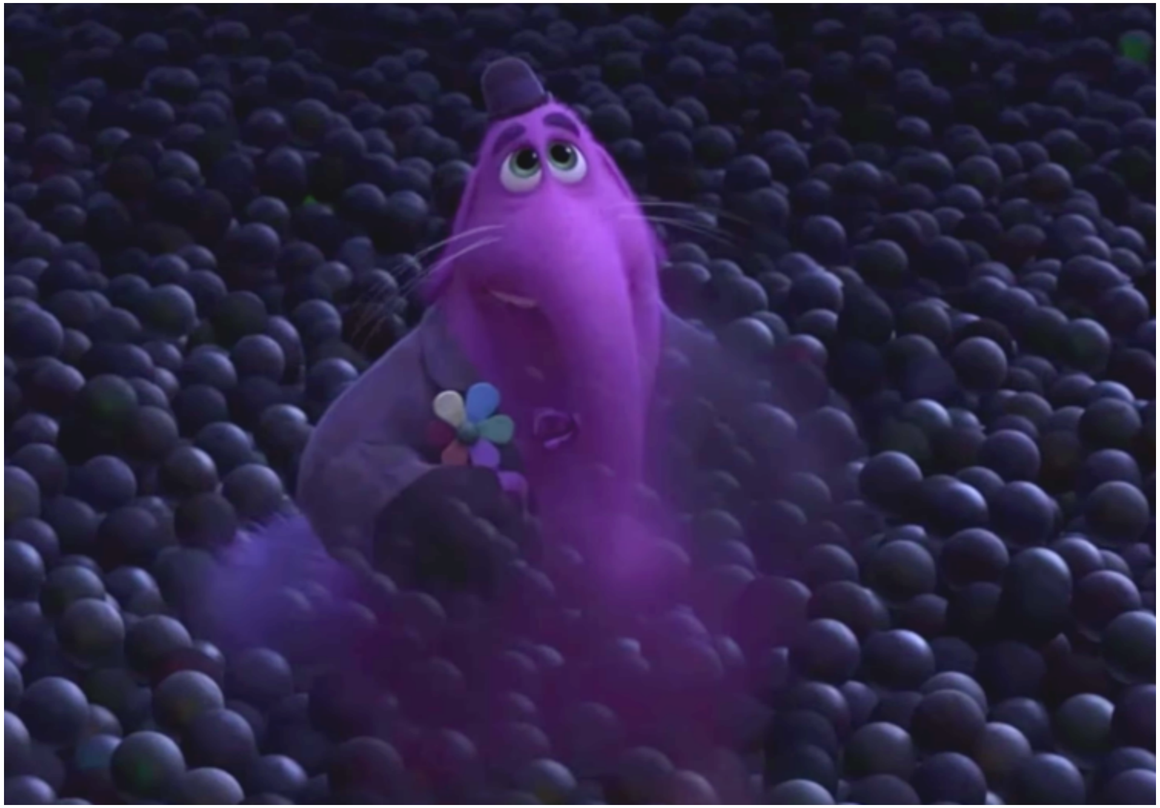


Time-lapse two-photon microendoscopy of hippocampal area of live mice was done to monitor dendritic spines of pyramidal neurons

Results:

Dendritic spine dynamics in the hippocampus was distinct from that of the cortex. In this study, spines had a mean lifetime of 1-2 weeks. This implies 100% turnover about 2-3 times.

Inside Out: Forgotten Memories



Inside Out depicts the degradation of a long-term memory as its loss of color and glow. Some memories turn to a puff of dust. In neuroscience, there are many theories as to how we forgot memories.

Cue-Dependent Forgetting: failure to recall memories without a cue

Rather than the memory being gone, this theory implies that it was simply hard to access.

Trace Decay Theory: memory trace decays and is lost permanently

Where are memories physically stores?

Dendritic Spines: spines can degrade and their connections can be lost. This is important in selectivity of memories.

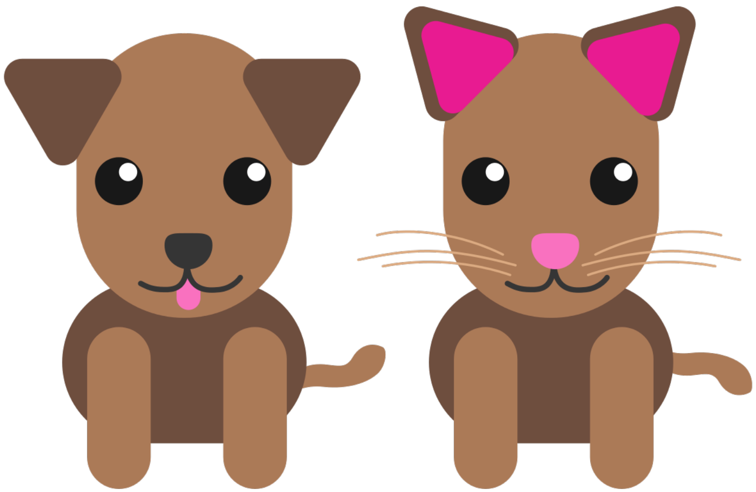
Physical Traces of Memory

Inside Out depicts memories as luminous spheres. In neuroscience, an episodic memory is represented by a neuronal ensemble.

Engram: theoretical representation of how memories are stored (physical or chemical changes in response to external stimuli)

Learning and the Brain

Dogs and cats are both furry animals with four legs and many other shared traits. Why, then, is it easy to distinguish between them?



As young people, we’re told which animals we observe are dogs and which are cats. Fairly quickly, we stop needing new examples. Our learning is powerful enough to classify a new animal as a dog or a cat, even when it doesn’t look particularly similar to one we’ve seen before. It turns out that computers learn similarly.

Learning and the Brain

A **supervised learning** algorithm attempts to model a function to relate inputs to outputs. It uses known examples to learn this relationship.

When building a supervised learning model to distinguish whether an image is of a dog or a cat, what should the inputs for the examples be?

A. The fur and eye colors of the dogs and cats
B. The lengths and weights of dogs and cats
C. Numerical data representing images of dogs and cats

Learning and the Brain

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Learning and the Brain

Suppose you have access to 100,000 images of dogs and cats that you can use to build a supervised learning model that distinguishes between dogs and cats.

After using images as examples to **train** (or teach) the model, you'll want to use images to **test** the model; that is, to determine if the model is actually successful at identifying if the image is a of a dog or cat.

Learning and the Brain

What would be a reasonable way to select your images for training and testing?

A. Use the dog pictures for training and the cat pictures for testing
B. Use the cat pictures for training and the dog pictures for testing
C. Split the images randomly into two sets: one for training and one for testing
D. Use all of the images for training and testing

Learning and the Brain

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C. **Split the images randomly into two sets: one for training and one for testing**
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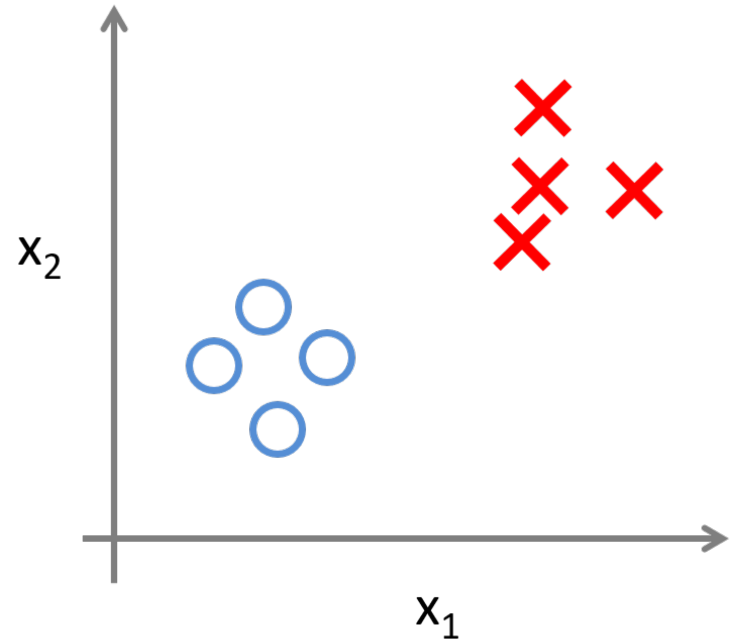
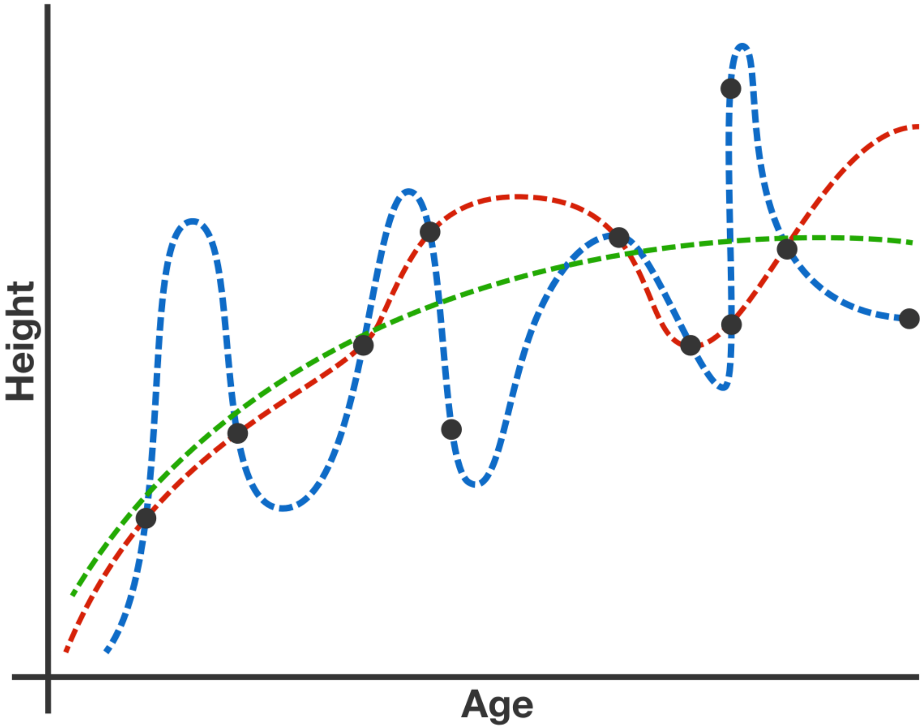
Learning and the Brain

A good supervised learning model predicts the outputs of unobserved inputs using knowledge of the outputs of observed inputs. The ability to make successful predictions on unobserved inputs from observed data is called **generalization.**



For any observed data there are an infinite number of functions that pass through all input-output pairs. The “best” function is *not* necessarily the one which fits all the observed data, but instead the one that generalizes well.

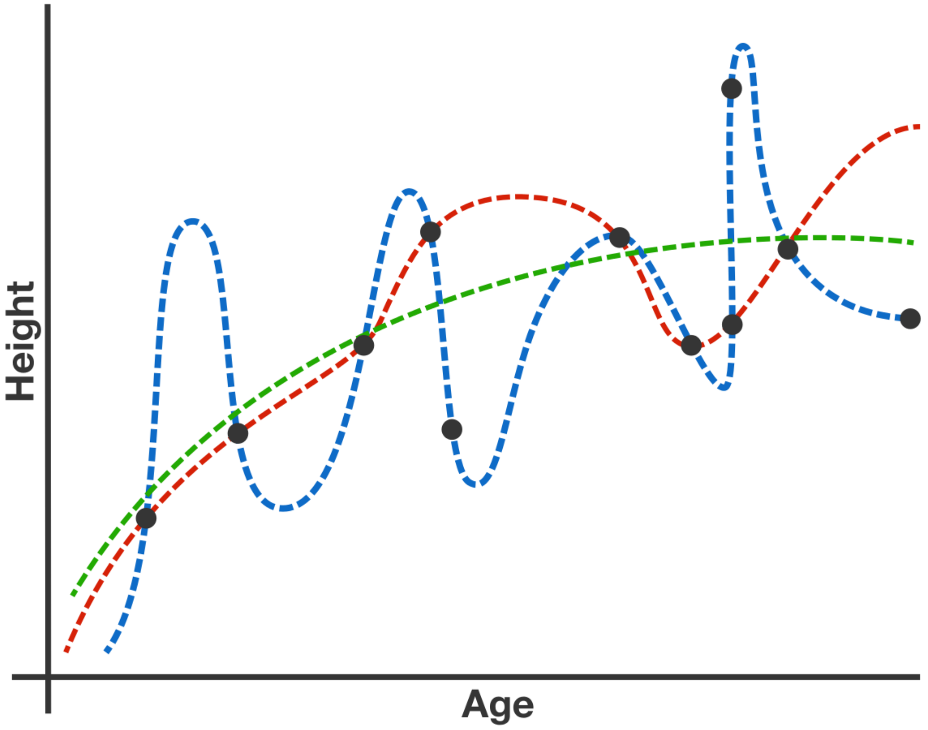
Learning and the Brain



A. Blue Model
B. Green Model
C. Red Model

You are training a height-prediction model using observed inputs of age and outputs of height, shown as points in the graph above. Which of these three functions drawn is likely to be the best model?

Learning and the Brain



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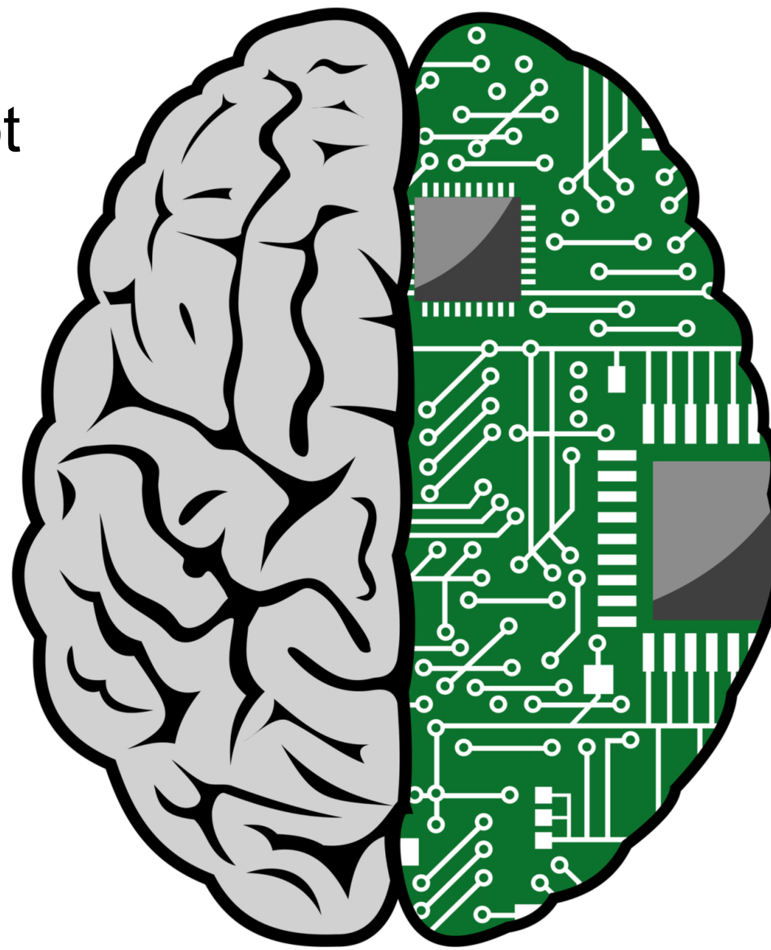
Learning and the Brain

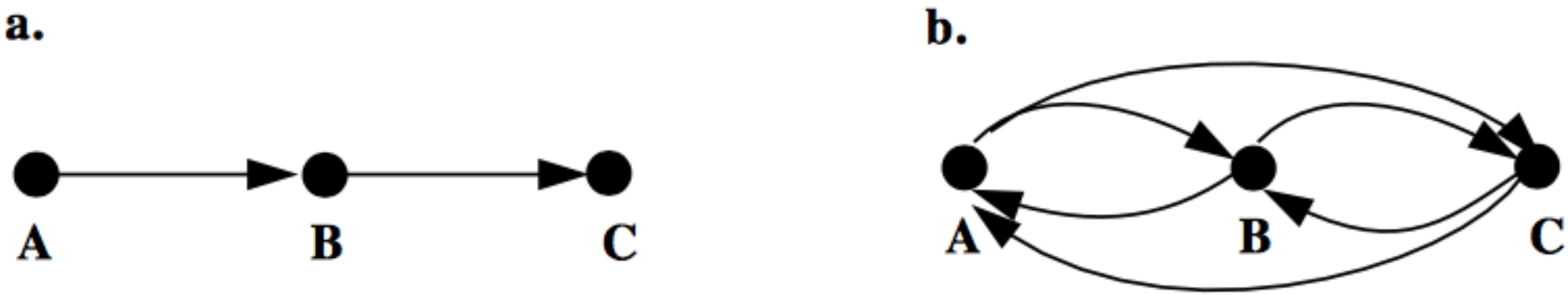
In distinguishing between dogs and cats, we wanted to classify an image into discrete categories with no numerical relationship; i.e., we cannot say a *dog* is *2 times cat.* This type of problem is called a **classification** problem.



In the last question, we found a function to relate an input to a numerical output (height). These outputs have a clear numerical relationship. This type of problem is known as a **regression** problem.

Artificial neural networks can be used to solve both types of problems.

Introduction to Neural Networks



A. Feed-forward network: Information flows directly from one layer of neurons to the next without feedback
In the brain, the existence of such network connectivity is rare (an example of it is between the retina and the LGN)

B. Recurrent network: Information is connected with feedback
In the brain, these networks are ubiquitous.

Role of Feedback in Neural Networks

What difference does feedback make in a neural network?
Feedback is a way to create a memory from memory-less components. More specifically, we create a persistent state through non-persistent parts with **feedback.**

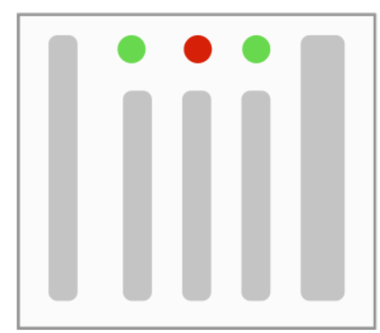
"Reverberating Activity Loops" *were proposed by Rafael Lorente de No and Donald Hebb. The idea is that excitation among units in a circuit* ***enables*** *excitation to persist* ***beyond the duration of exciting stimulus.***

Short-term memory *uses changes in activity*
Long-term memory *uses changes in synaptic connections (**Long-term potentiation (LTP)** is used for memory acquisition)*

Learning and the Brain

Of the following three learning problems, how many should be treated as **regression** problems?

- Identifying which zip-code digits have been written on an envelope
- Predicting the total number of points scored by two teams in a basketball game
- Determining the *probability* that a given person will get heart disease



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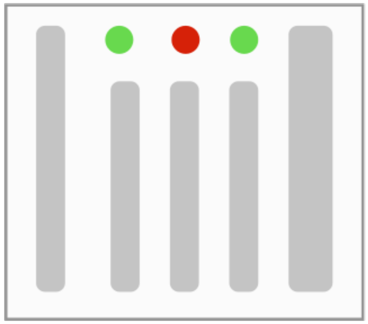
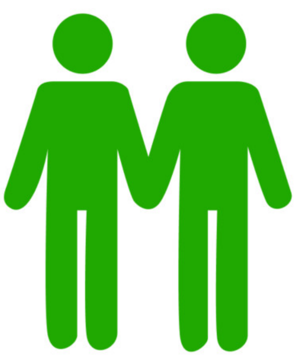


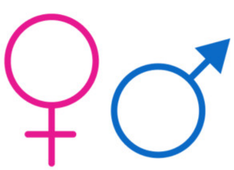
Learning and the Brain

We have focused on supervised learning problems. However, there is another type of learning: **unsupervised learning.**

Unsupervised learning attempts to determine relationships between inputs without using an example outputs (such as “dog” or “cat”). Which of the following would **not** be a good fit for unsupervised learning?

- Determining possible friendship matches from interest profiles
- Predicting someone’s gender from their name
- Grouping news articles about similar topics





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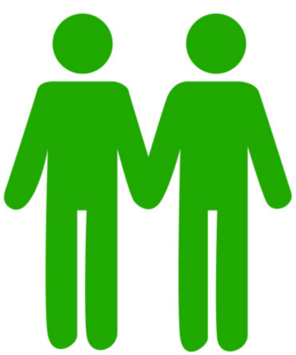
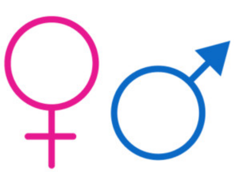


Learning and the Brain

Learning and the Brain

- Batch Learning
- Online Learning

When training a learning model, there are two main processes that can be used with respect to how the training data is handled: batch learning and online learning.

In **batch learning**, the model learns from batches of data- often the entire training set at once. In **online learning**, the model learns from data processed sequentially over time, as it becomes available. Which type of learning does the human brain use?

Learning and the Brain

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- **Online Learning**

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Learning and the Brain

Based on your intuition, which of the following is **not** an advantage of online learning over batch learning?

- It is more efficient for data storage
- It allows for gradual improvement over time
- It makes performance evaluation of the learning model easier

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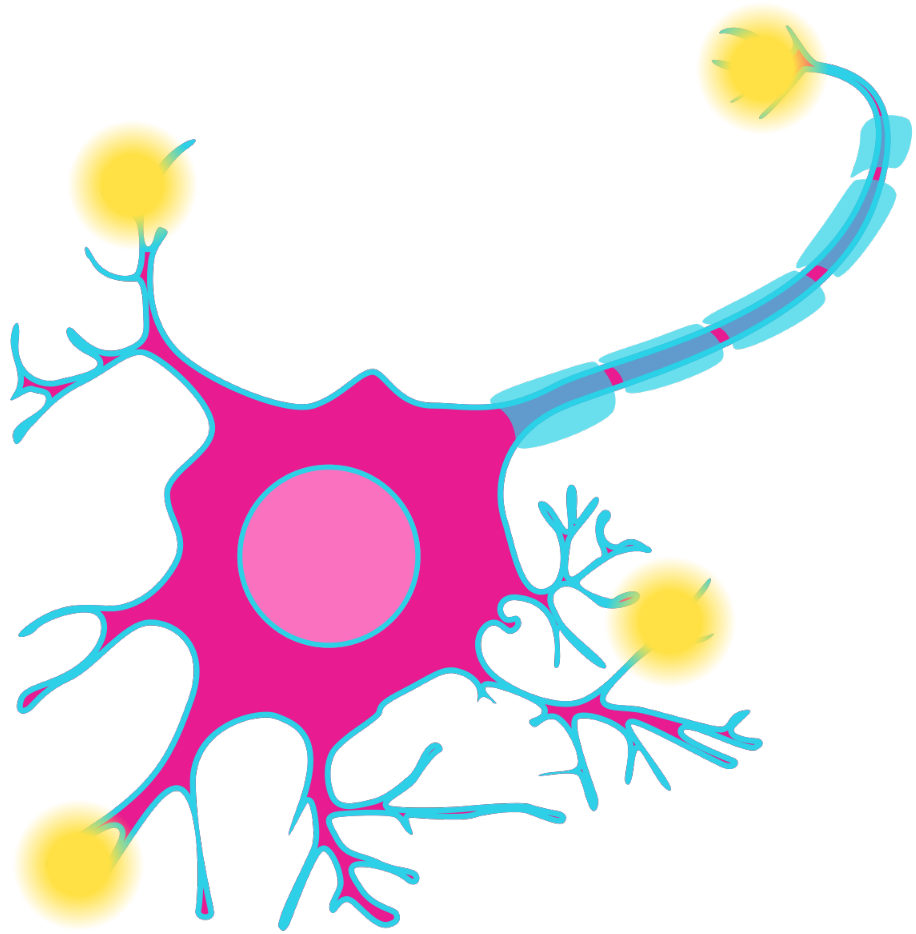
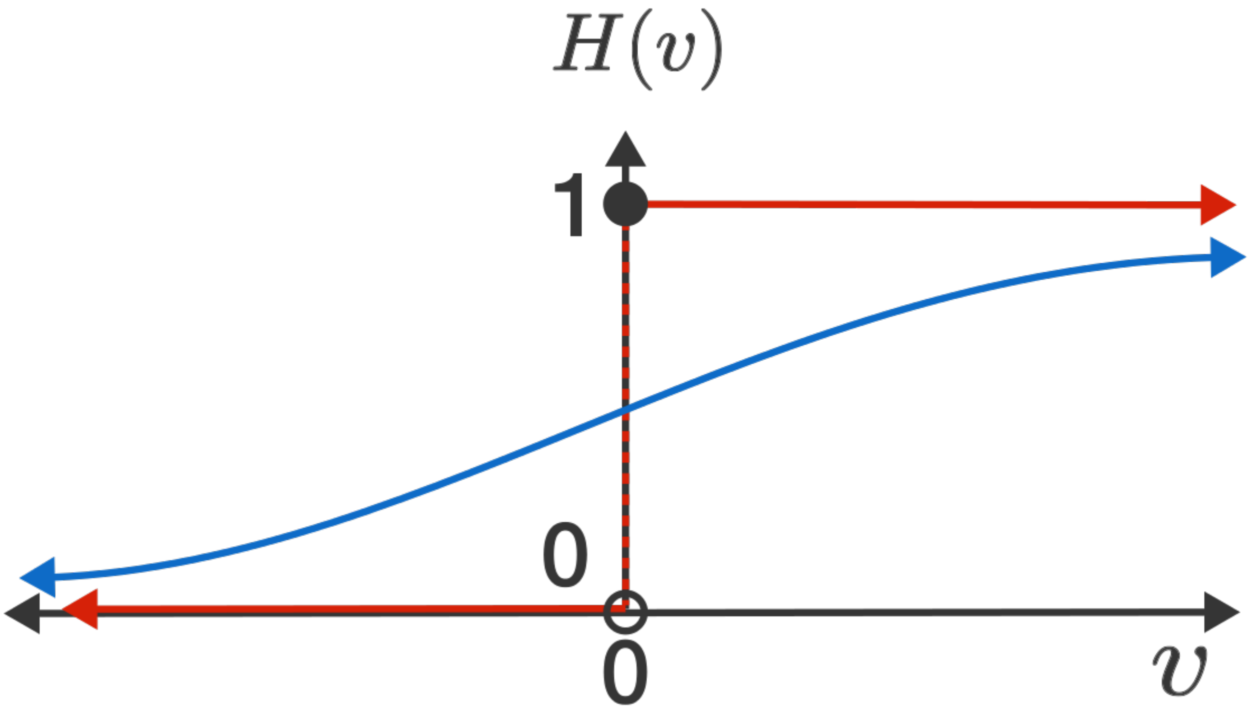
Learning and the Brain

Artificial neural networks can use both online learning and batch learning.

Neurons are the simplest units of the computation in the human brain. While the actual dynamics of a neuron's computation are complex, a simplified view of them is that they **integrate and fire.** That is, a neuron performs a computation with its inputs, and then fires if that computation passes a certain threshold.



Learning and the Brain

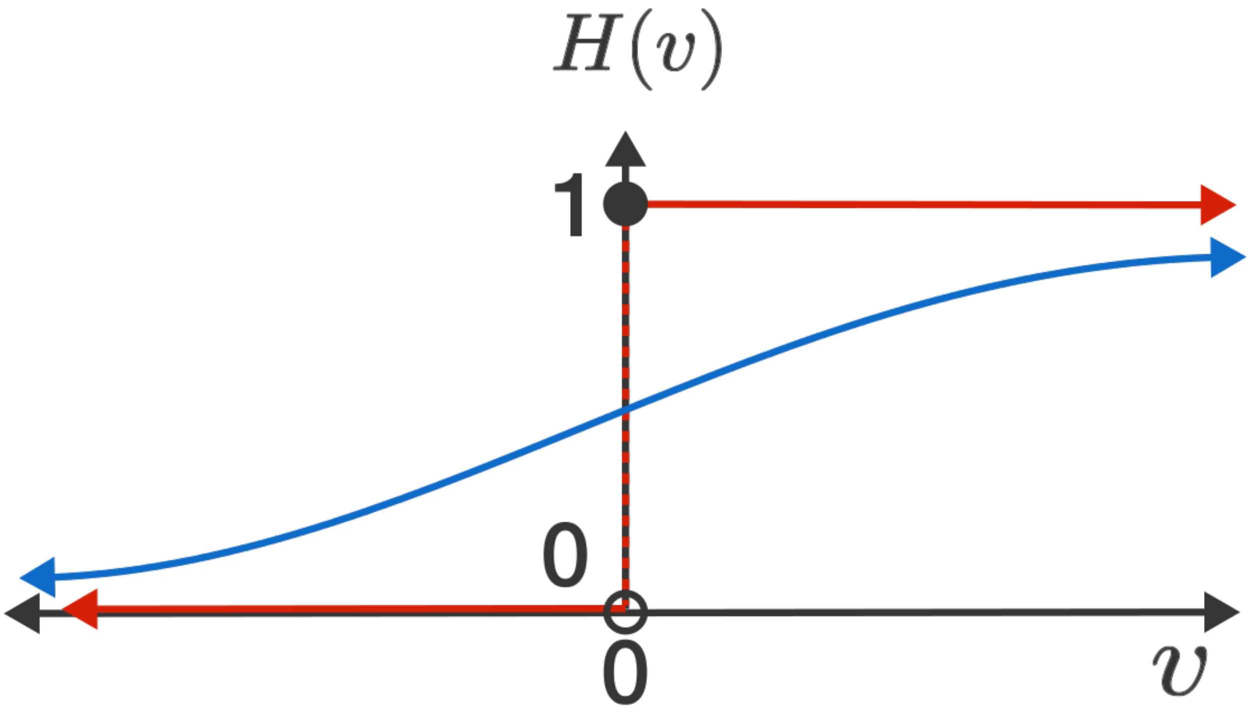


- Red Model
- Blue Model

In an artificial neural network, the inputs are combined as a weighted sum into a single value, *v.* Then, an activation function, *H(v)*, is applied to determine whether or not the neuron fires.

What activation function would best model a physical neuron?

Learning and the Brain



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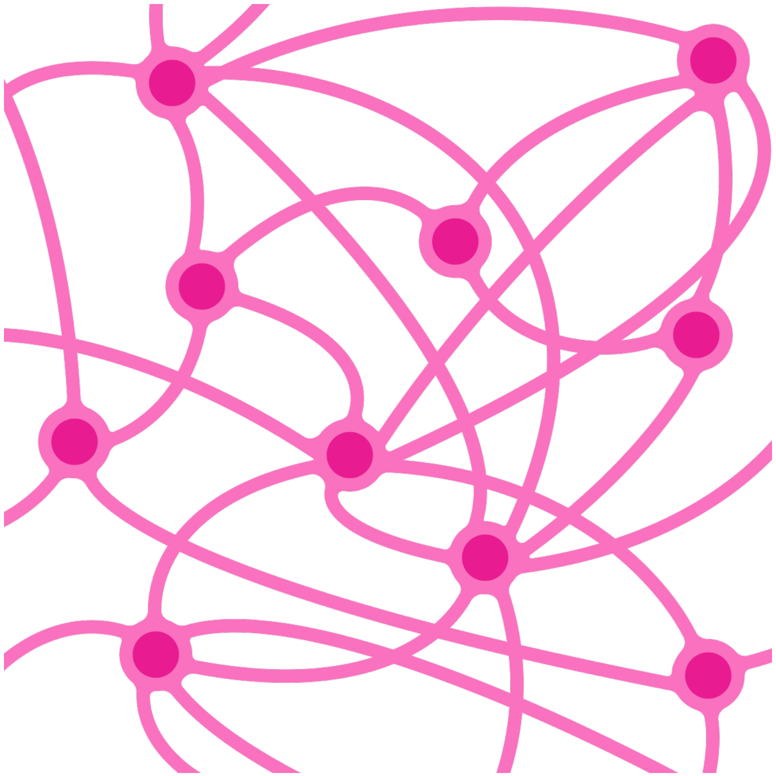
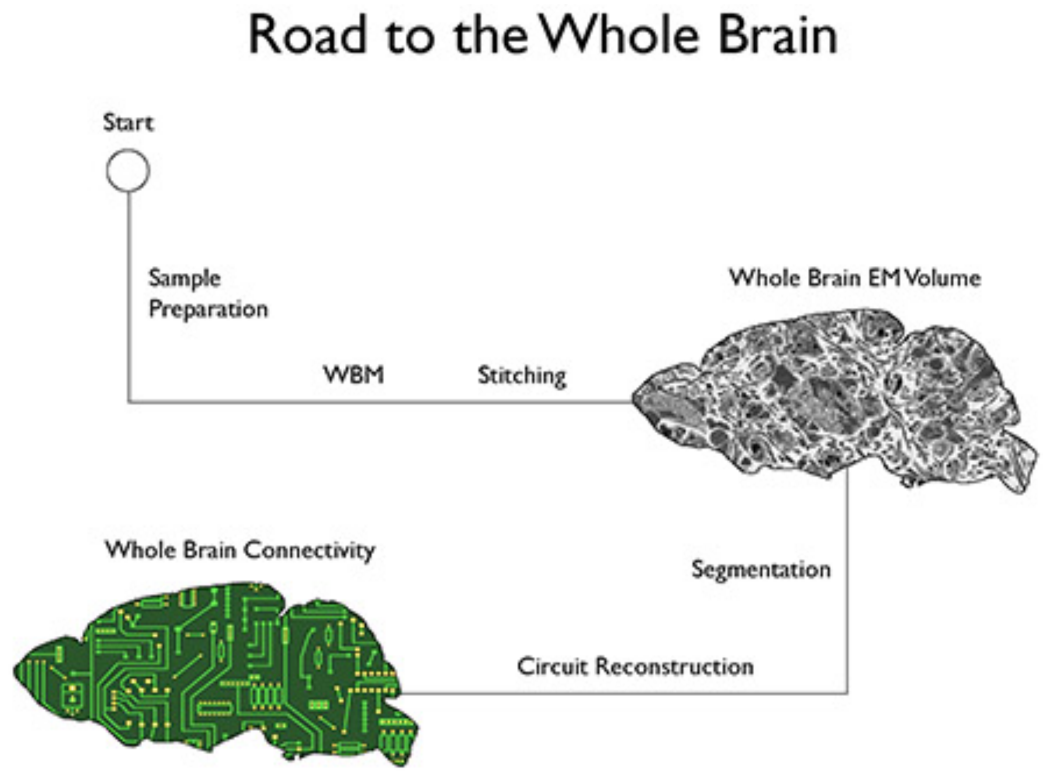
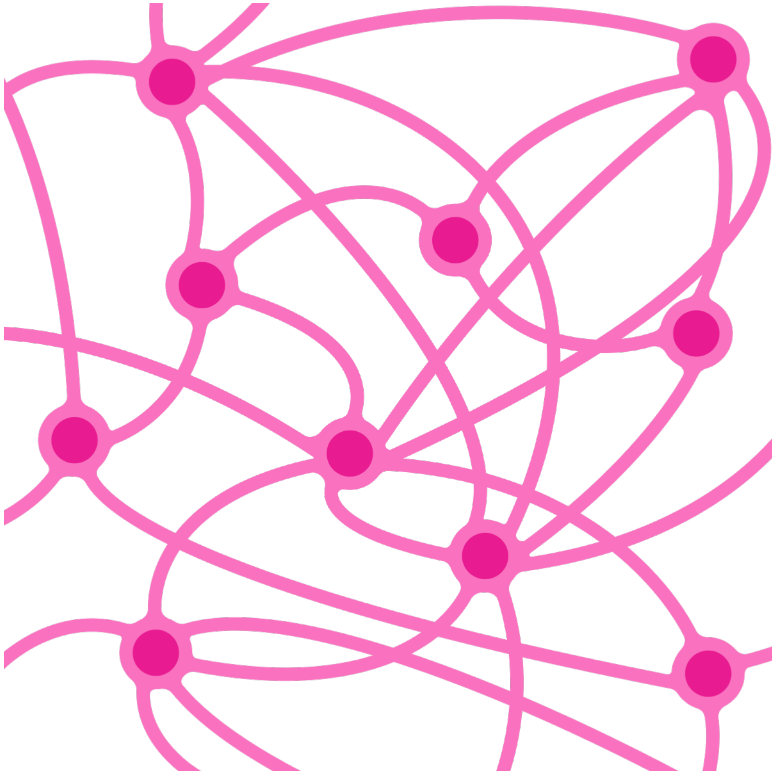




Connections (or synapses) between neurons are used to pass information from the outputs of some neurons to the inputs of other neurons. Not every neuron is connected to every other neuron, and certain neurons have stronger connections than others.

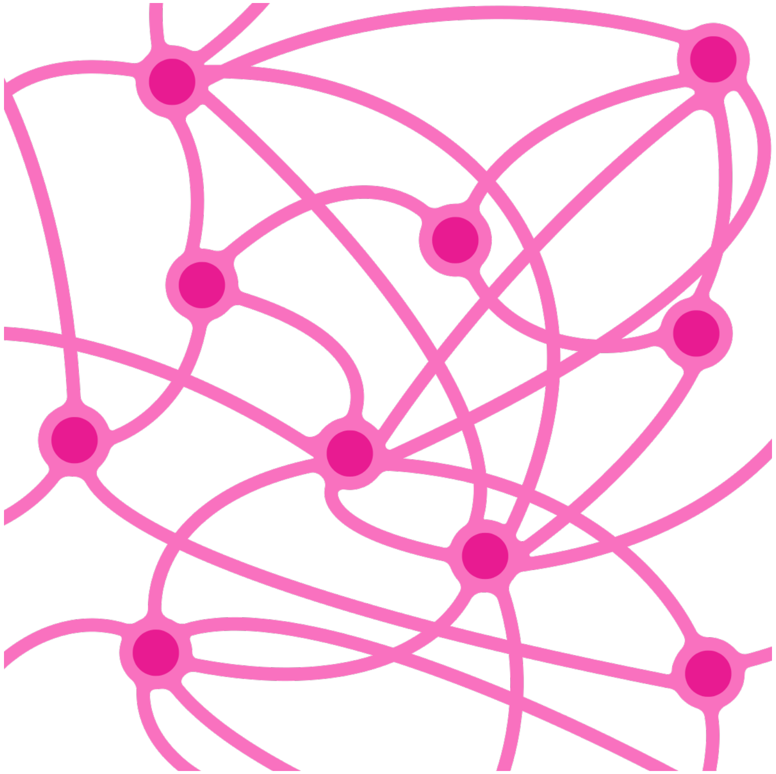
Learning and the Brain



If there are approximately **10^{11}** neurons in the human brain and between **10^{14}** and **10^{15}** synapses, which of these values is a reasonable estimate for the average number of connections per neuron?

- 10
- 1,000
- 100,000
- 1,000,000

Learning and the Brain



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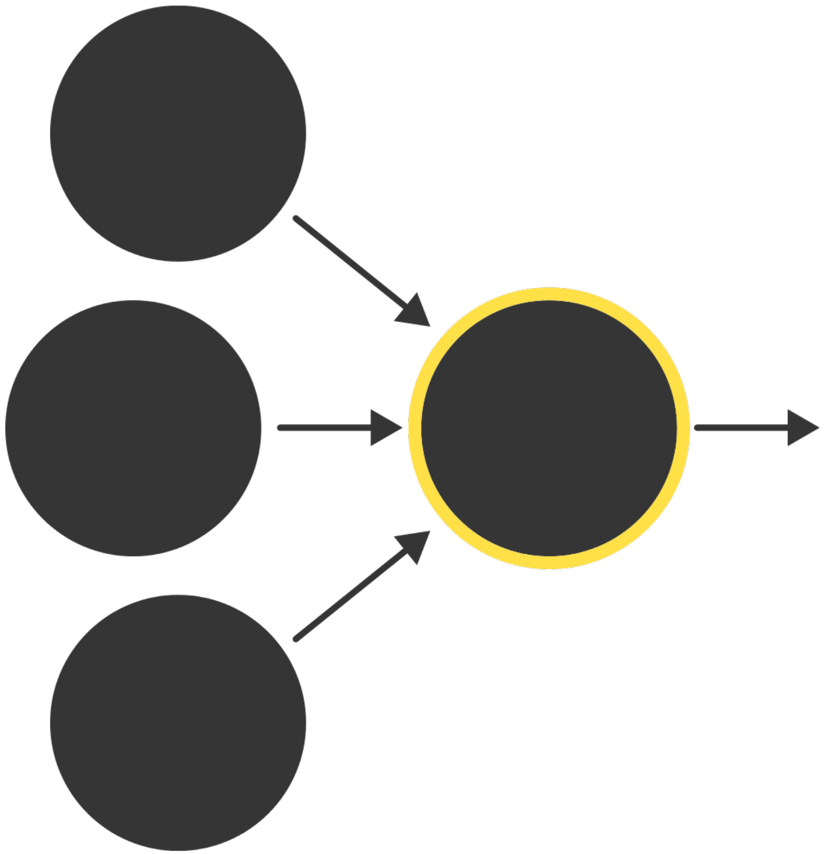
Learning and the Brain



By adjusting which connections exist and how strong they are, the human brain is able to learn a huge variety of complex functions. Thus, a computational model of the human brain should include simple computational units (like neurons) which are connected to one another (like synapses). If the model can learn to adjust the strengths of those connections appropriately, it may be able to approach the power of the human brain.

Case Study on Memory: Alzheimer's Disease

Alzheimer's Disease (AD)

- Cortical and Progressive Dementia

  Pre-Clinical AD

  - Signs of AD are first seen in entorhinal cortex and then proceed to the hippocampus
  - Affected regions begin to shrink as nerve cells die
  - Changes can begin 10 to 20 years before symptoms appear
  - **Memory Loss** is the **first** sign of AD

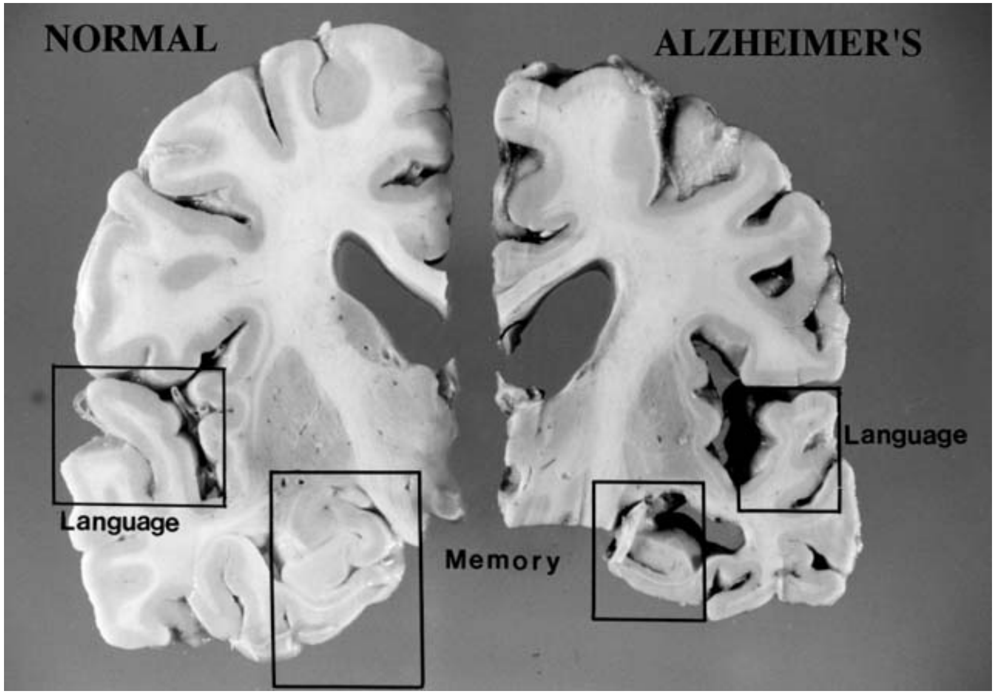
  Mild to Moderate AD

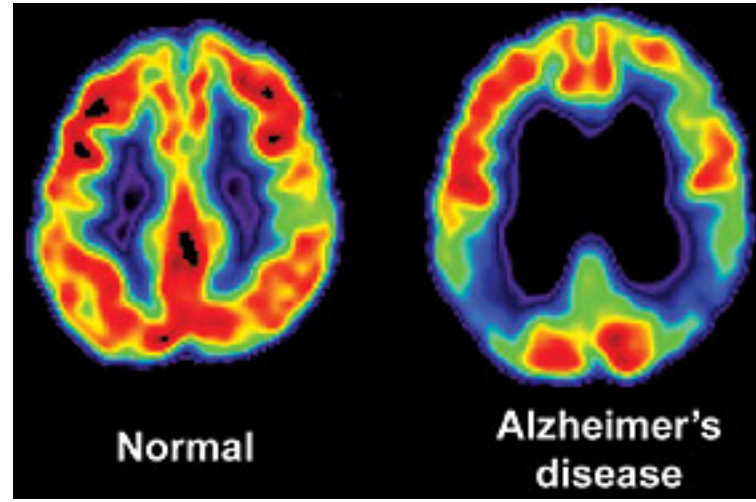
  - AD spreads through the brain and the cerebral cortex begins to shrink as more and more neurons die

  Severe AD

  - Extreme shrinkage, patients are completely dependent on others for care.
  - Death from pneumonia and other infections

Alzheimer's Disease (AD)



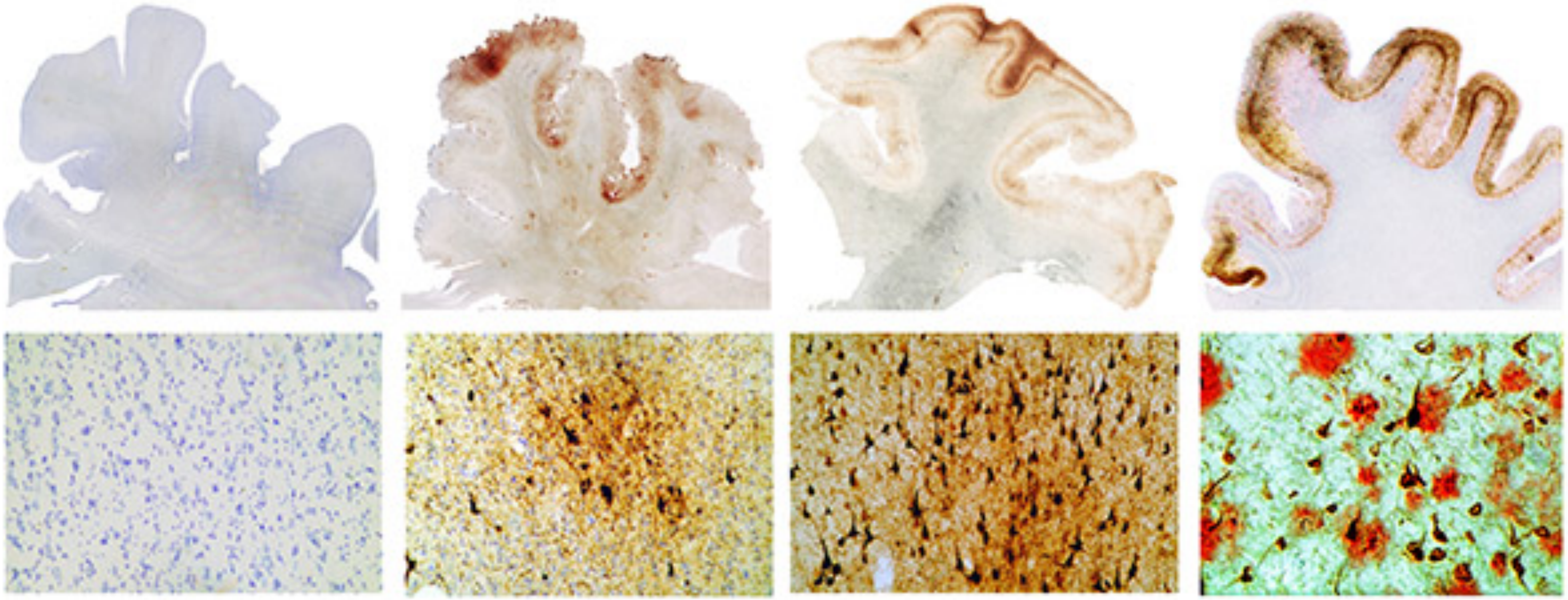


1. Extreme Shrinkage of Cerebral Cortex
2. Extreme Shrinkage of Hippocampus
3. Severely enlarged ventricles

Positron Emission Tomography (PET):
Uses a small amounts of radiotracers (analog of glucose, *fludeoxyglucose*) to evaluate organ and tissue function

Intense labeling of organs that use glucose extensively

Alzheimer's Disease (AD)



Neurofibrillary Tangles (NFT): aggregates of hyper-phosphorylated tau protein (changes in cytoskeleton)

B-Amyloid Plaques: Peptides of 36-43 amino acids that aggregate as plaques (incorrectly folded proteins)

Case Study on Memory: Jill Price

Case Study on Memory: Jill Price

Jill Price

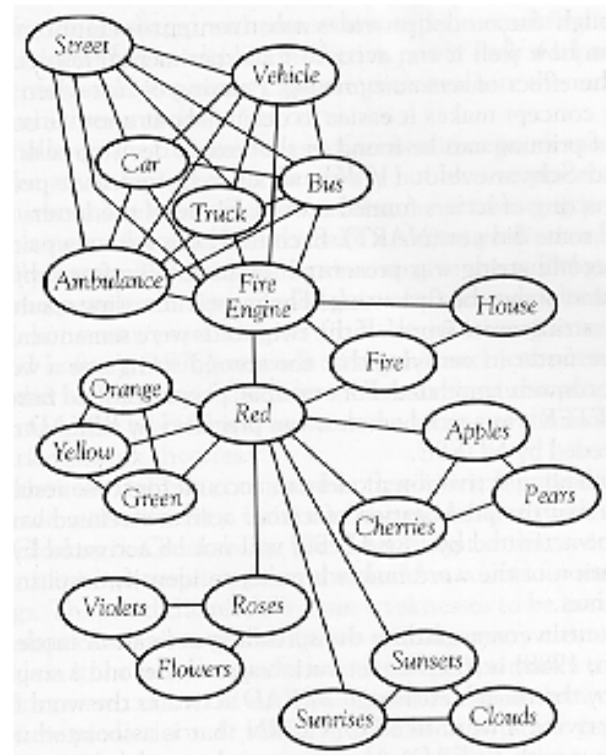
Hyperthymesia

- Condition of possessing an extremely detailed autobiographical memory
- Studied by three UCI neurobiologists: Elizabeth Parker, Larry Cahill and James McGaugh
- Attributed it to two defining characteristics:
    - Spending an excessive amount of time thinking about one's past
    - Displaying an extraordinary ability to recall specific events from one's past
- Causes:

  Psychological: information coded is semantic, so semantic clues are used in retrieval

    - Once memory is retrieved, it is episodic and follows a spreading activation model

  Biological: temporal lobe and caudate nucleus were both enlarged – can be attributed to atypical neural development



Brain Regions for Memory

Case studies have taught us what brain regions are involved in encoding memories:

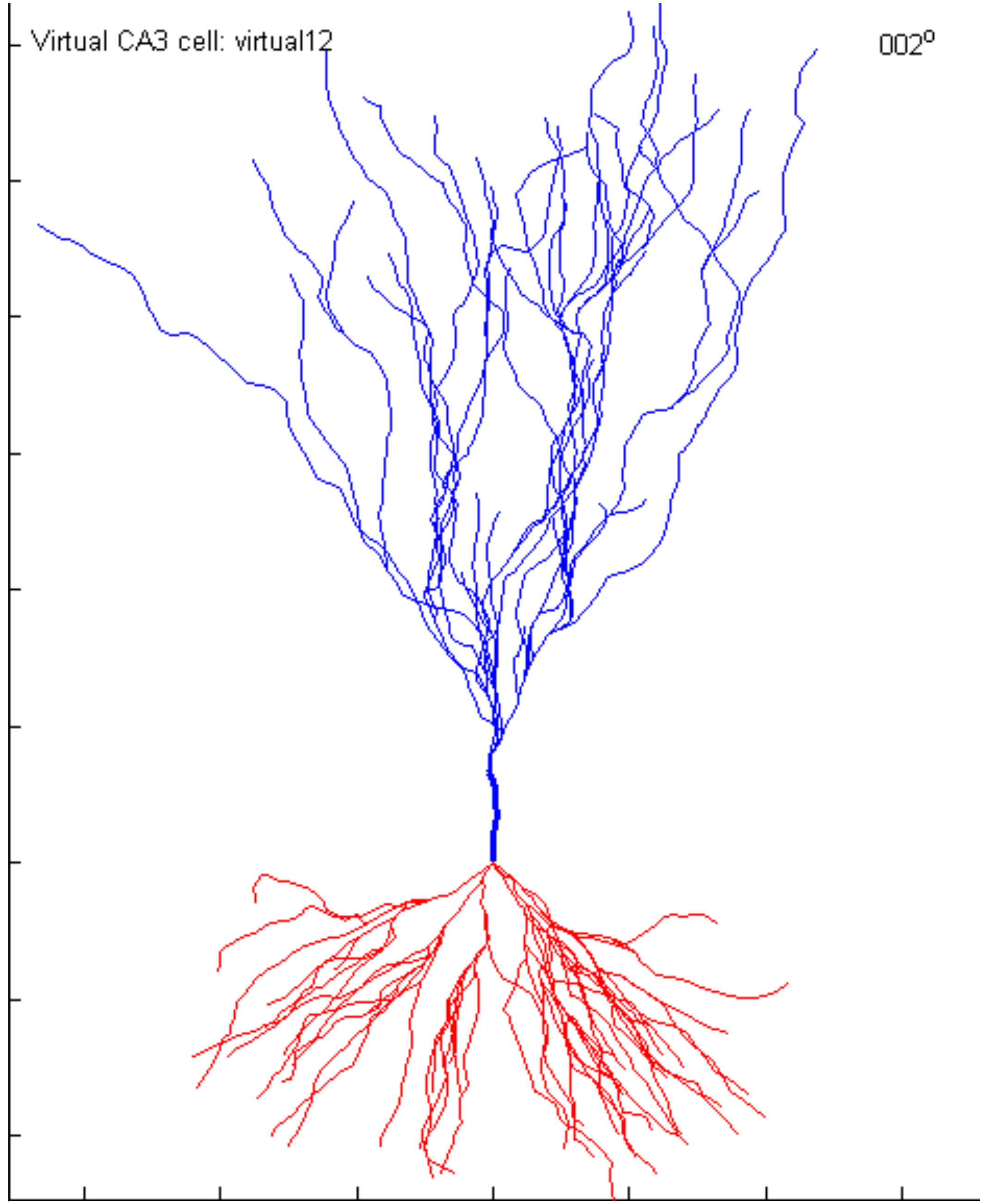
Memory	**Brain Regions Involved**
Recalling pictures	Right prefrontal cortex and parahippocampal cortex of both hemispheres
Recalling words	Left prefrontal cortex and left parahippocampal cortex are activated
Consolidation of Memory	Hippocampus
Storage of Long-Term Memory	Cerebral Cortex (near where memory was first processed and held in short-term memory)

Summary:
1. Pre-Frontal Cortex
2. Hippocampus
3. Cerebral Cortex
4. Amygdala (Memory Modulation and part of **Temporal Lobe**)

Memories are made of this

"He was still too young to know that the heart's memory eliminates the bad and magnifies the good, and that thanks to this artifice we manage to endure the burden of the past."
Gabriel Garcia Marquez

Pyramidal Neurons: found in the cerebral cortex, the hippocampus, and the amygdala
Pyramidal neurons are the primary excitation units of the mammalian pre-frontal cortex and the cortico-spinal tract.



What creates a memory in the brain?

Many biophysical variables are involved, including:

- *Neural voltage*
- *Synaptic activation, strength, and connectivity*
    - *How does a chemical synapse work?*
- *Pre-synaptic vesicles*
    - *What variable in regards to action potentials controls the amount of neurotransmitter release on the pre-synaptic neuron?*
- *Phosphorylation levels*
    - *What does a phosphate group look like?*
- *mRNA concentrations*
- *Transcriptional regulation*
- *Neuro-modulatary signals*
    - *What part of the brain is involved in modulation of memory?*
- *Glia*

Man v. Machine

How can we compare the forms of memory in humans and computers?

Structures of Memory:

- **Random Access Memory (RAM) and the Hippocampus**
- **The Hard Drive and the Cerebral Cortex**
- **Central Processing Unit (CPU) Cache and Neuronal Network Attractors**

Features of Memory:

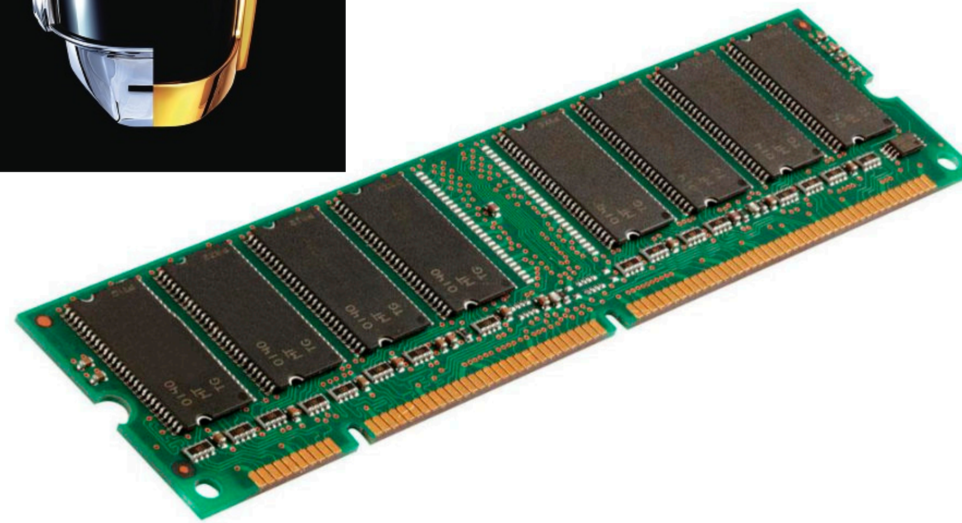
- **Protected Memory and Explicit Memory**
- **Memory Swapping and Writing**

Random Access Memory (RAM) and the Hippocampus

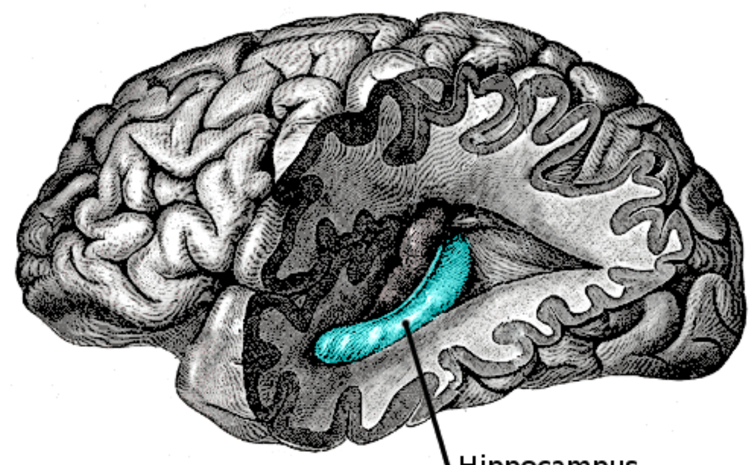
Random Access Memory: place in a computing device where the OS, application programs and data current in use are kept so they can be reached by the device's processor

Data remains in the RAM as long as the computer is running*. *If you turn off a computer, the RAM is gone.

RAM provides a quick access to a memory in any location.



Humans have a form of RAM: **Short-Term Memory** (used to recall immediate actions). Both share **structural homogeneity.**

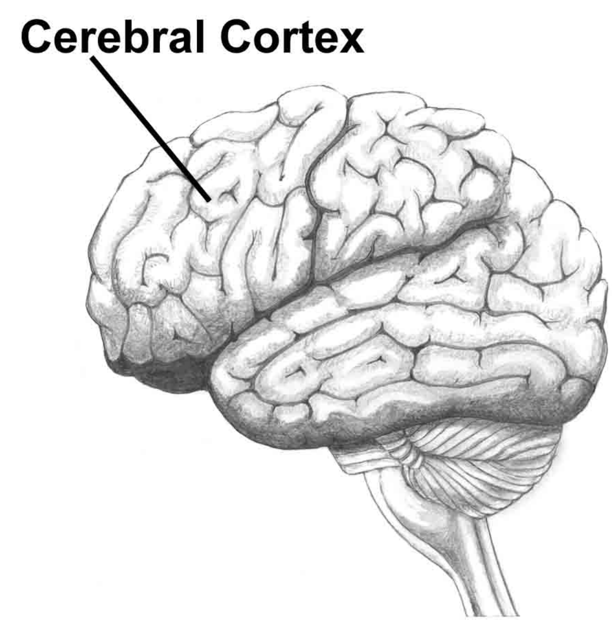


The Hard Drive and the Cerebral Cortex

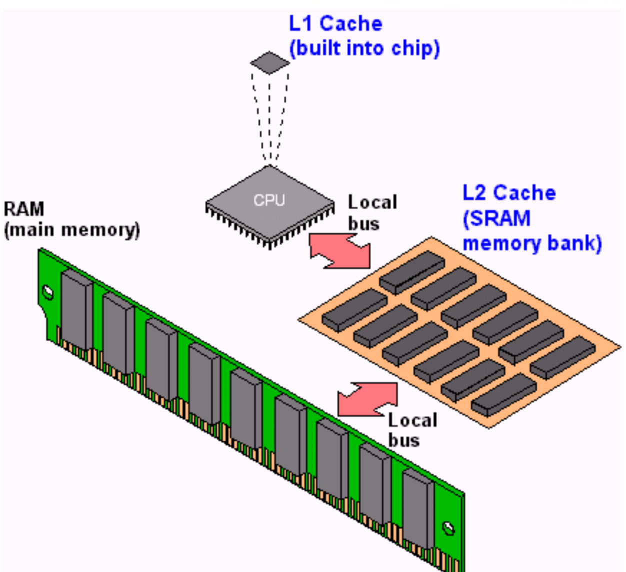
In addition to RAM, a complimentary form of storage for long-term memory in computers is **the Hard Drive (HD).** A hard drive has lower bandwidth (100 Mbytes/s) but can store much more (500 Gbytes). **This is where all of your data and programs are located.**

Bandwidth:
[1](Computer) Range of frequencies used for transmitting a signal
[2](Human) Energy or mental capacity required to deal with a situation

Cerebral cortex is the presumed site of human long-term memory. Recollecting old memories varies in timescale for both the cortex and HD (read/write speed depends on where memory is stored).



Central Processing Unit (CPU) Cache and Neuronal Network Attractors

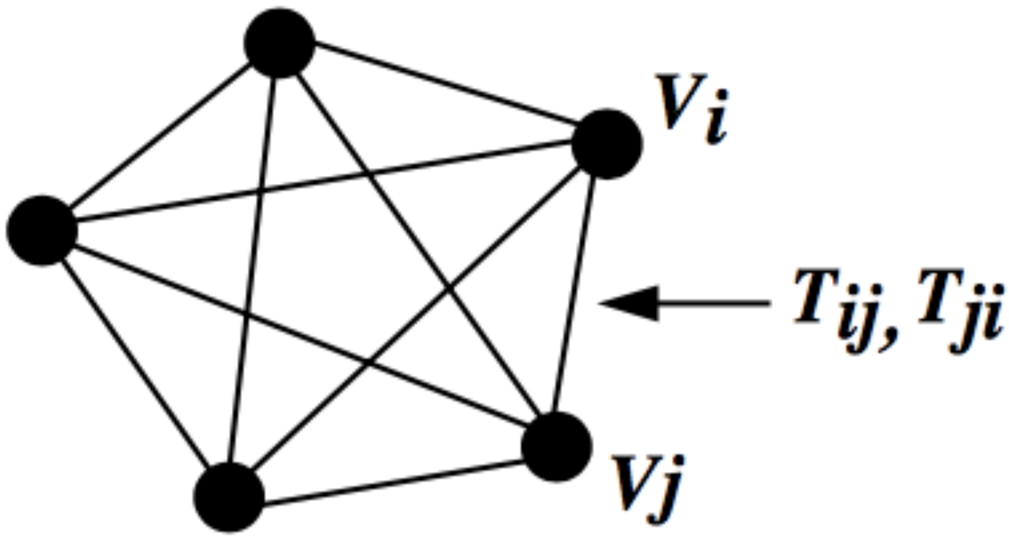


CPU Cache: a smaller, faster memory which stores copies of data from frequently used main memory locations

How Caching Works (Transfer of RAM)
CPU caches are small pools of memory that store information the CPU is most likely to need next. **L1 Cache** is built into microprocessor chip itself and performs **cache hits.**
A cache miss, however, means the CPU must find data elsewhere. The **L2 Cache** is used for this (It is slower but larger than L1 Cache).

A CPU Cache is the main difference between a computer and a human. Our brains do not have multiple levels of storage working at distinct speeds. Memory storage is distributed all over cortex (a giant cache).

Modeling Memory: Attractor Neural Networks



V_i**:** *denotes activity state of* ***neuron i*** *in the network*

T_{ij}**:** *denotes strength of the connection from* ***neuron j*** *to* ***neuron i***

Attractor Neural Network: recurrent neural network with symmetric connections that act in two ways

$$V_i \rightarrow 1 \quad \textit{if} \quad \sum_{j \neq i} T_{ij} V_j > 0$$

$$V_i \rightarrow -1 \quad \textit{if} \quad \sum_{j \neq i} T_{ij} V_j < 0$$

Each neuron has two states, **+1 and -1**, and changes its state, V_i, according to rule on left

Features of Memory: Protected Memory and Explicit Memory

Explicit Memory: Memory used consciously
Implicit Memory: Memory not necessarily used consciously
(Example: We know how to walk but we don't have to think to walk)
This separation of between explicit and implicit memory is done at neuronal level and happens in computers.

Memory Protection: way to control memory access rights on a computer that is built-into an OS
When you write a program that needs some memory for its behavior, the OS allocates some space into it. Why? To prevent the program from accessing any other memory and rewriting it

Distinguishing our memories is a way to protect them.

Features of Memory: Memory Swapping and Writing

What is memory swapping?

When a program asks for memory then what is available in the RAM, the OS uses the hard drive (HD) to allocate space needed. This is known as **memory swapping.**

Since hard drives are slower than RAM, this leads to a great loss in performance.

This is why MATLAB programs can slow down. Your program cannot tell if its data is being stored on the hard drive or the RAM. In other words, memory swapping is not transparent.

Do humans do memory swapping?

No, the human brain was well-designed to work within its memory limits. However, we compensate for our memory by taking notes *(we swap data to a piece of paper using a pen).*

Memory Storage System

Based on what we see in computers and humans, we can define features we desire in a **memory storage system:**

1. States that can persist over time
2. Adequate storage capacity (can hold a great number of states)
3. Different inputs to be remembered should trigger ***persistence*** of different memory states
4. Memory states are robust to noise
   What are examples of noise in the brain?
   Signals can fail and neurons can spike stochastically.
5. Memories are retrievable given appropriate cues

Which feature would differ between short-term memory and long-term memory?