

Learning, Computation and the Brain

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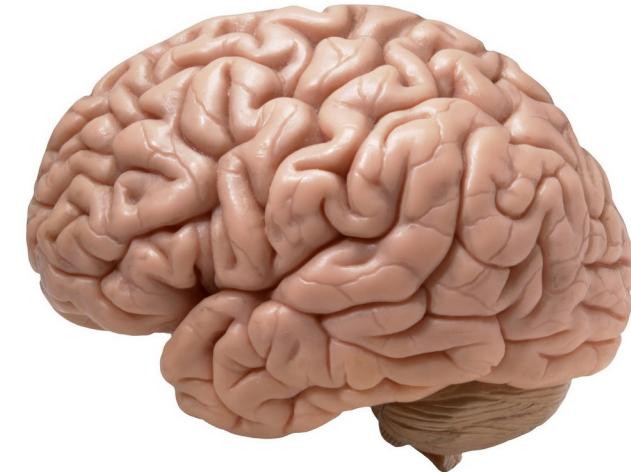
2023

Expectations

- Of you:
 - Read around subject areas, watch external lectures, learn.
 - Be respectful of your peers and me!
 - Revise diligently for the exam.
- Of me:
 - Be reasonably available to answer questions/queries.
 - Be clear about what you are to be examined on.
 - Cover the material in an interesting and engaging fashion?
- Controversial or unpleasant content:
 - Historic atrocities that helped us understand the brain.
 - Experimentation on laboratory animals.

Lecture series contents

- Overview of the human brain.
- Neurons, dendrites and synapses.
- Leaky integrate and fire.
- How are brains like computers?
- How are computers like brains?
- Shannon information.
- Neuromorphic computing.
- Neural networks.
- Consciousness and memory.
- Large language models.



The human brain

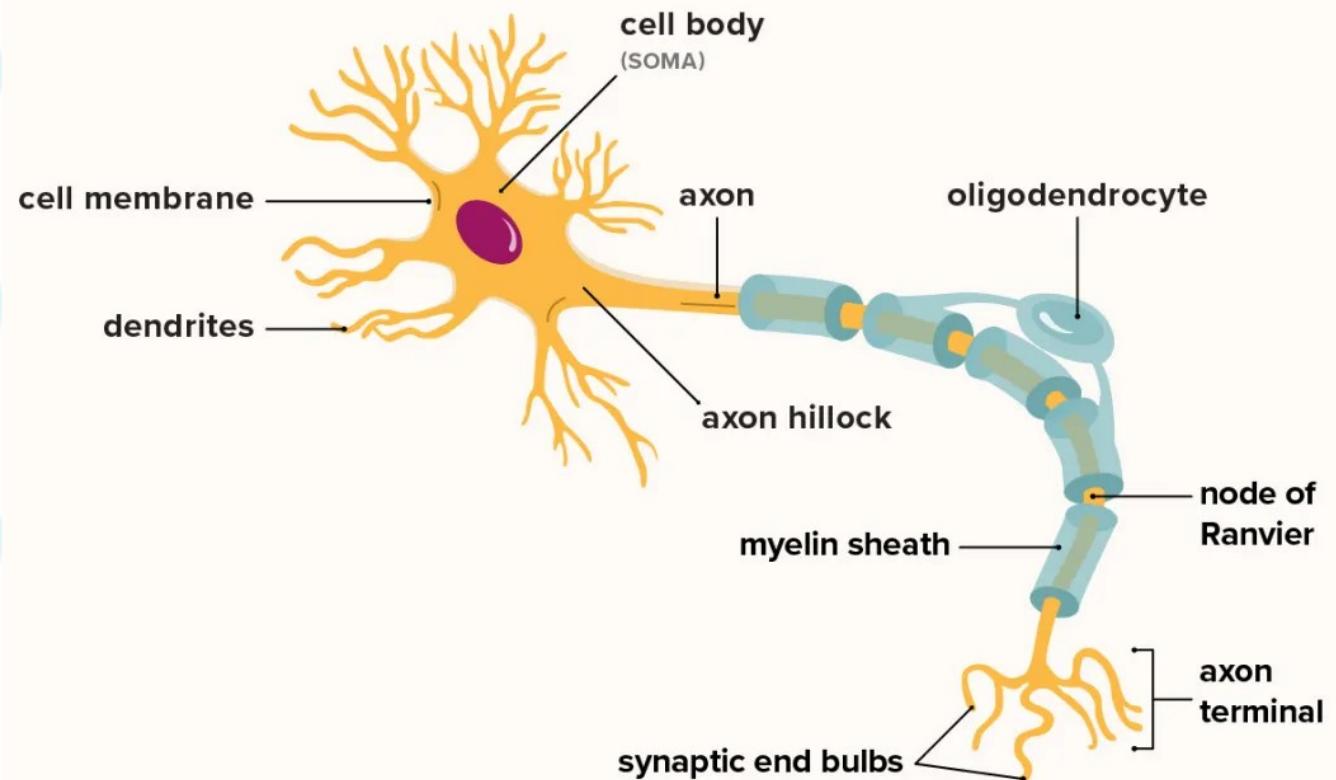
- What is the human brain?
 - 1.2 to 1.3kg of greyish, lumpy, jelly-porridge?
 - The greatest problem solving tool we know of?
 - A machine liable to break down?
- How does it work?
 - WE DON'T REALLY KNOW!
 - What do we know?
 - What it's made of:
 - Neurons, synapses, dendrites, axons etc
 - Parts of the brain:
 - Hippocampus, basal ganglia, cerebellum etc
- What am I doing when I think? Can a device have a sense of self? What computations occur in the brain and what is their mechanism?



What is the brain made of?

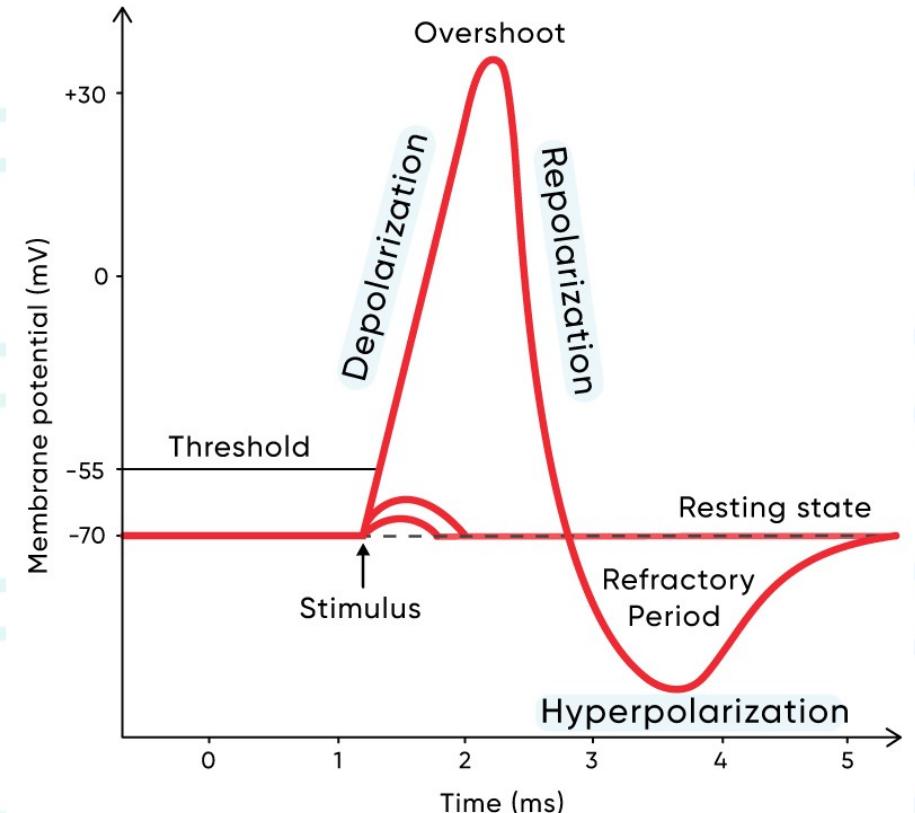
- At what length scales are we talking about?
 - Sub-nanometre: atoms, quantum effects
 - Angstrom to nanometres: compounds and chemicals
 - Micrometres: cells
 - Millimetres +: brain areas
- Lets look at the cellular level
 - Glial cells: physical, chemical and environmental support
 - Neurons: cell-to-cell signalling

Diagram of a neuron

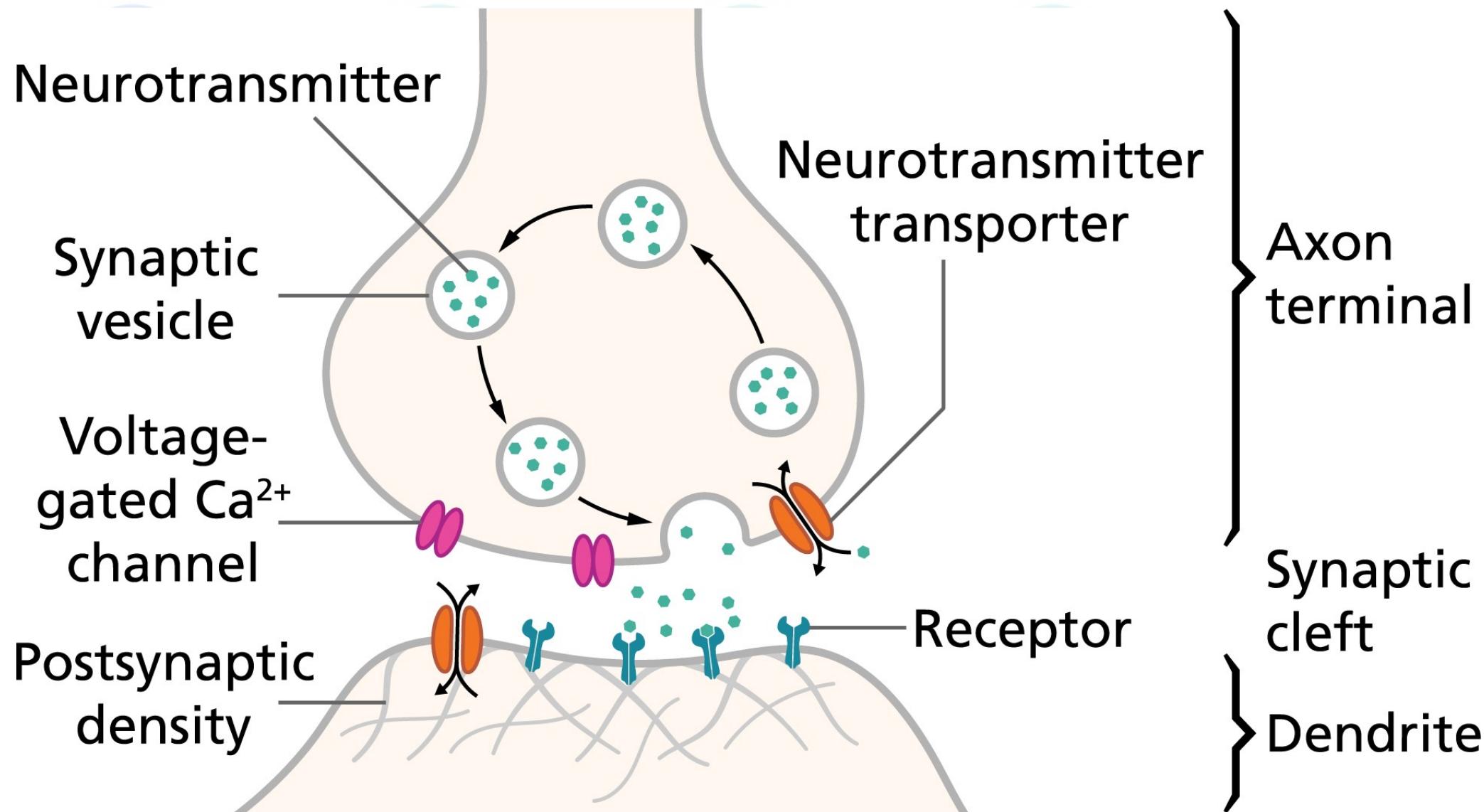


Action potentials

- There is a potential difference between the inside and outside of a neuron
 - Regard the brain fluid as zero voltage
 - Think of the fluid inside and outside the neuron as being water with dissolved salts
 - These fluids have differing types and concentrations of various ions
 - At rest the difference is around -70 mV
 - How is this difference maintained?
 - Cell membrane is an insulator
 - Pumps
- Why is this important?
 - The signaling dynamics of neurons is voltage dynamics
 - Signals are carried by action potentials or spikes
 - The spike travels along the axon and ‘splits’ at the dendrites

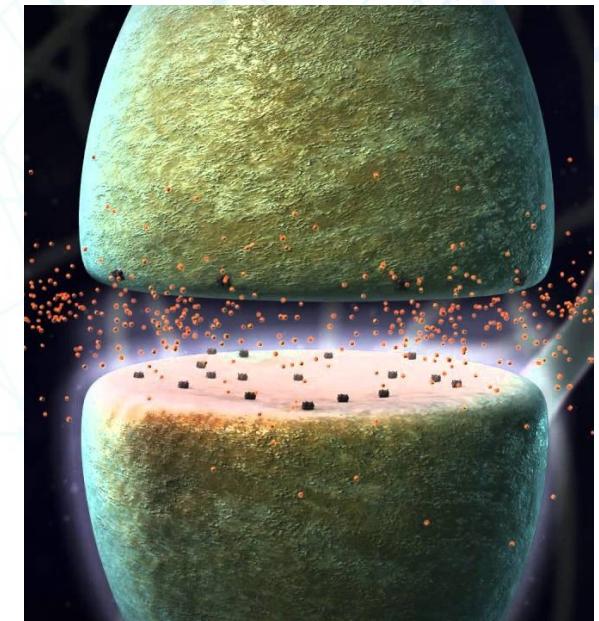


Synapses



Synapses

- How do the signals get from neuron to neuron?
 - Axon to dendrite?
 - Action potentials largely stereotypical.
 - Synapses very variable:
 - Vary over time
 - Different dynamics in response to spikes/ series of spikes
- How does it work?
 - Here we consider chemical synapses.
 - Synapses are not just connectors.
 - There is a gap (synaptic cleft)
 - What could be going on?



Synapses

- A spike arrives at the synapse:
 - Change in voltage opens channels to allow calcium to flow
 - Causes vesicles to fuse with the wall of the cleft and burst
 - Neurotransmitters are released
 - Neurotransmitters bind with channels on the opposite side
 - Ions are allowed to flow (either inwards or outwards) changing the voltage
 - Called excitatory or inhibitory synapses
- Pulses travel towards axon
 - EPSP: Excitatory post synaptic potential
 - IPSP: Inhibitory post synaptic potential
 - If enough PSPs arrive and reach the tipping point C-55mV a spike will occur in the post synaptic neuron

Synapses

- There are MANY different types of neurons and synapses.
- Dale's principle: A given neuron will only have either excitatory or inhibitory neurons.
 - Note that this refers only to out-going signals
- Neurons in the cortex
 - Inhibitory neurons tend to be small with local connections and of diverse types
 - Excitatory neurons are usually larger and have local and distal connections
 - These neurons tend to be of the pyramidal type
 - Some would postulate that the pyramidal cells do the 'work' whilst the inhibitory neurons regulate the activity ... we still don't know!

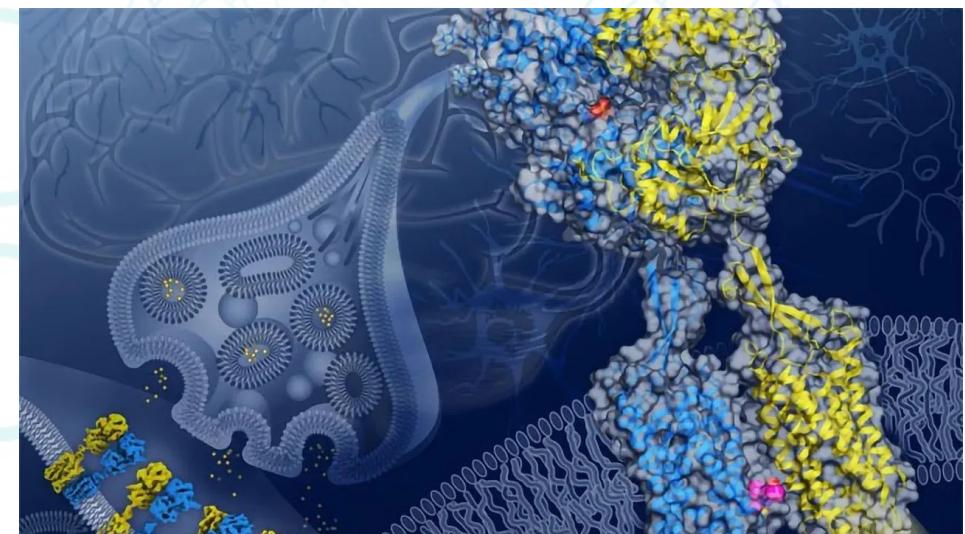
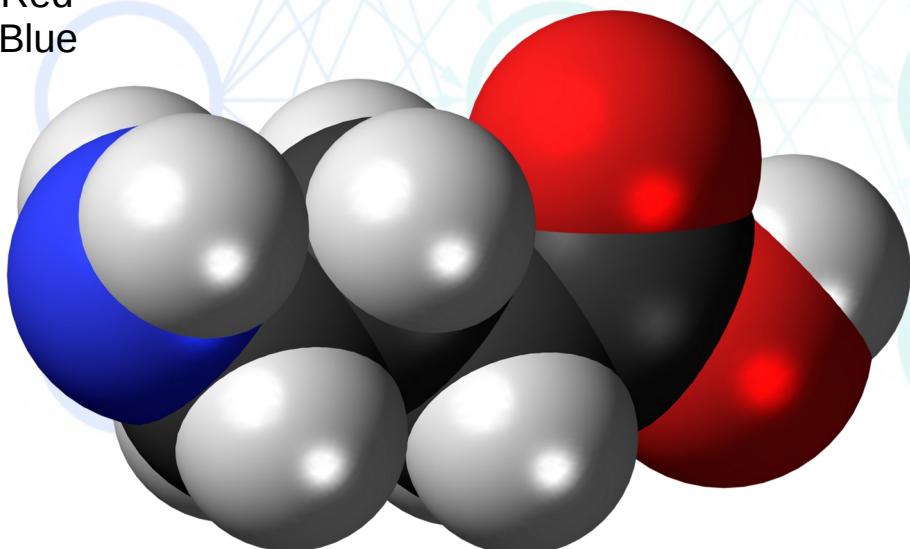


3D model of pyramidal neurons

Types of neurons and synapses

- Synapses are also classified by the sort of neurotransmitter they produce:
 - Excitatory: almost always glutamate (a small amino acid)
 - Different receptor types for glutamate eg NMDA and AMPA
 - These have different behaviours over both short and long term
 - A glutamate synapse will usually have a mix of NMDA and AMPA receptors
 - Inhibitory: the most common neurotransmitter is called GABA
 - Two classes of receptors here, ionotropic and metabotropic

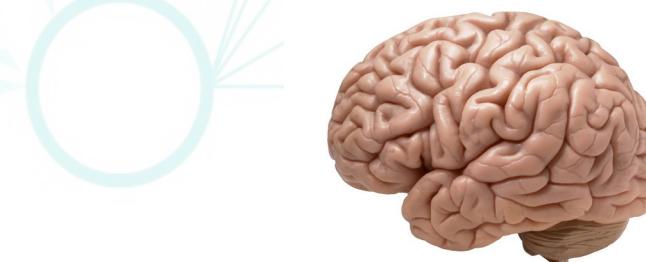
GABA
C:Black
H:White
O:Red
N:Blue



GABA synapse

More about synapses

- Several points to be made about synapses
 - Massive complexity of greatly varying biological machinery and chemical compounds
 - This complexity appears vital to brain function?
 - **You are not expected to have detailed knowledge of the functioning and variability of chemical synapses for this course. The notes represent close to the maximum level of detail required.**
 - Big questions, little questions; where are we today?
 - Consciousness
 - Memory storage, short and long term
 - Sensory processing
 - Autonomic

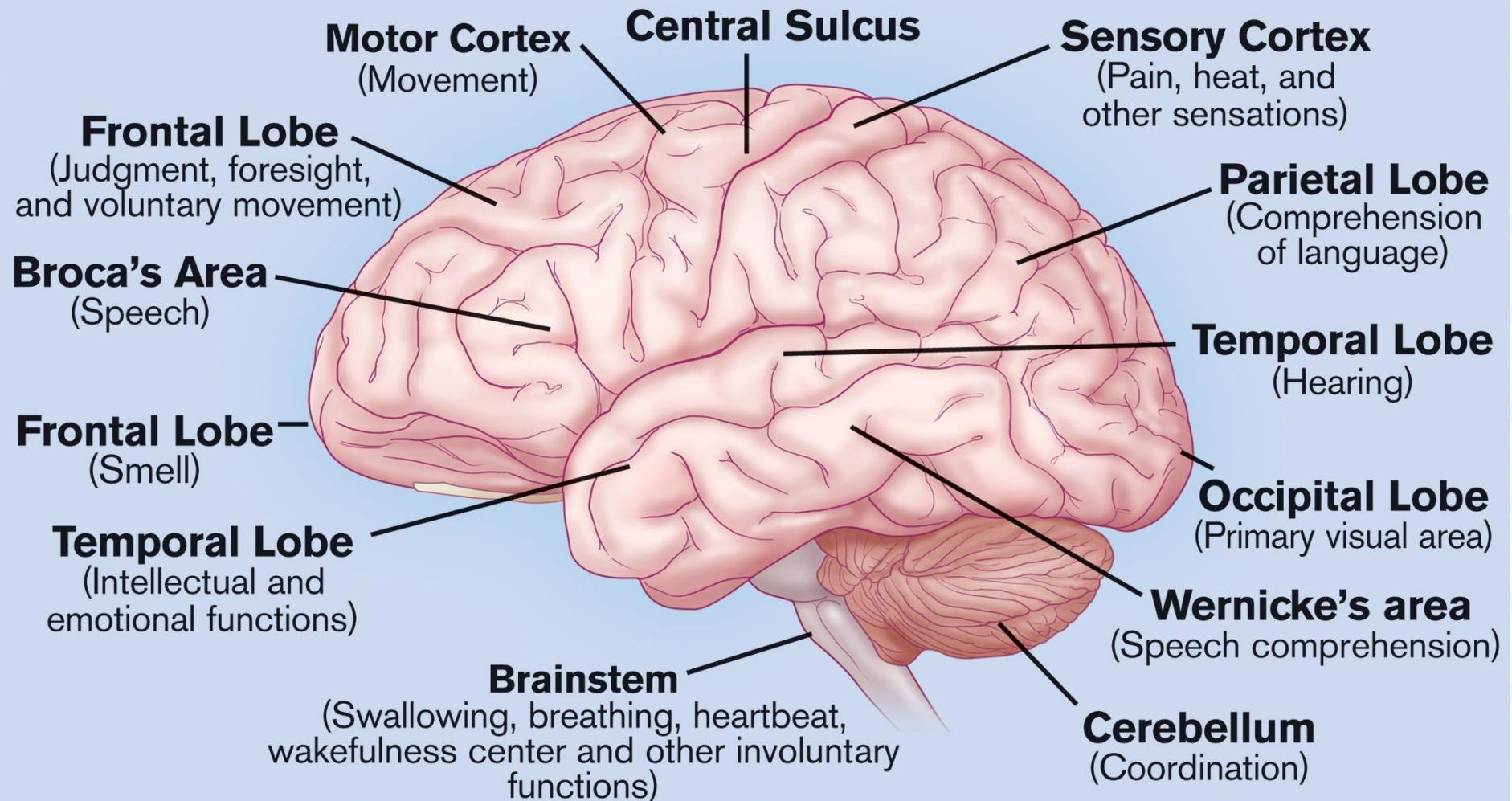


Neuromodulation

- As if things weren't complicated enough!
- Neuromodulators are chemicals which can change the behaviour of a neuron or synapse. The main four are:
 - Serotonin: modulating mood, cognition, reward, learning, memory
 - Dopamine: arousal, sexual arousal, reward motivated behaviour, motor control
 - Acetylcholine: arousal, attention, memory and motivation
 - Noradreneline: anxiety, arousal, working memory, pain
- Can be released locally to a single post-synaptic cell or into extracellular fluid so they affect a group of cells
- Some typical affects:
 - Change excitability of the neuron
 - Change the strength of a synapse
- We, as humans do this deliberately ... a lot!



Parts of the brain

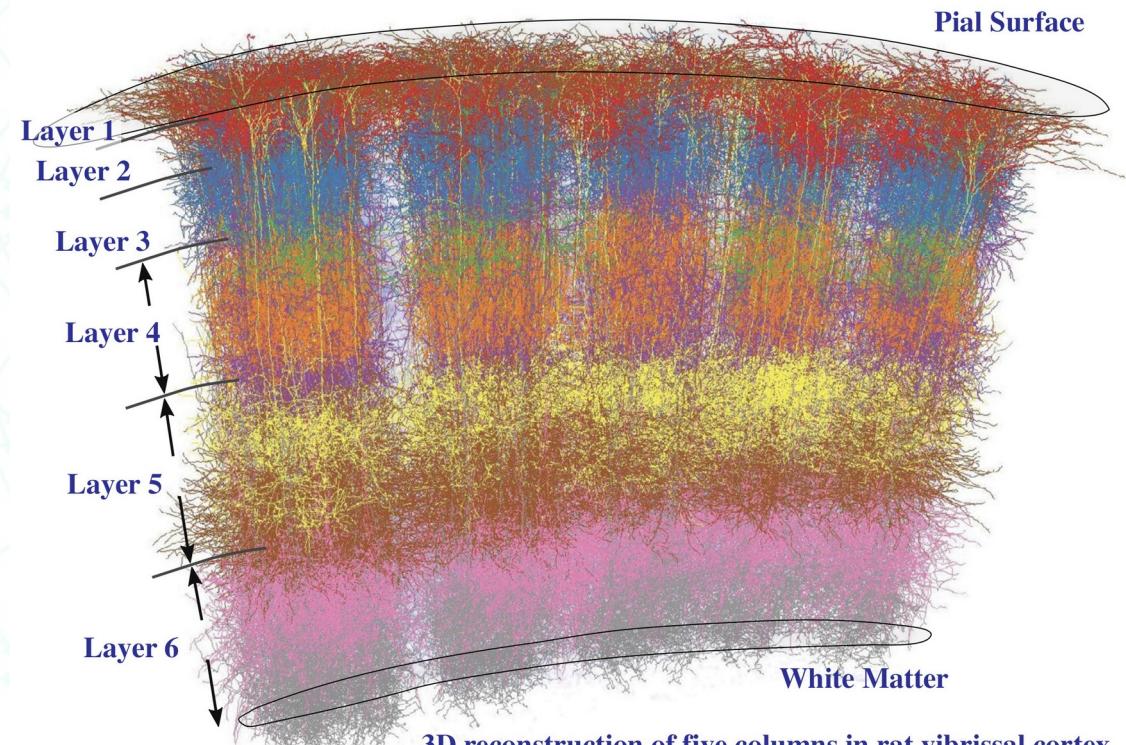


It is important to note that this is a VERY simple overview of the areas of the brain.
Check out, "The Human Brain Coloring Book: A Coloring Book", Diamond and Scheibel, 2000.

Which area does thinking? Which area does memory? Which area is me?

The cortex

- The cortex is the outer, highly ridged and folded, area of the brain.
 - 14-15 billion neurons
 - Grooves are called sulci, the ridges gyri
 - Folding allows greater area, fractal
 - 2-5 mm thick
 - Around six layers
 - Ordered into columns
 - Local processing
 - C40000 Neurons/mm³
 - C8x10⁸ synapses/mm³
 - C85% excitatory
 - Long distance connections through white matter

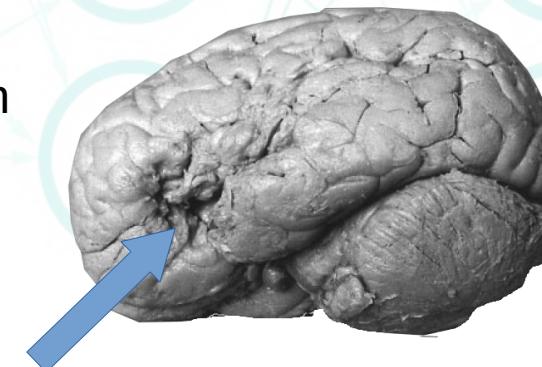


underlying image from:

Marcel Oberländer, Beyond the Cortical Column, Neuroinformatics 2012

Broca's area

- Responsible for some aspects of speech.
- Why start here?
 - Historical status
 - Early understanding of brain functions came from studying patients with brain lesions or other damage (eg see Phineas Gage (1823-1860))
 - Modern understanding concentrates more on animals but information and autopsy of those suffering brain issues still helps guides us
- Louis Victor Leborgne (Tan), at 30 years of age 'tan' was the only word he could say.
- Pierre Paul Broca (1824-1880), neurologist.
- Upon Tan's death autopsy revealed a very specific brain lesion caused by syphilis
- Expressive aphasia
- Brain areas therefore identified with function
- Today this view considered binary



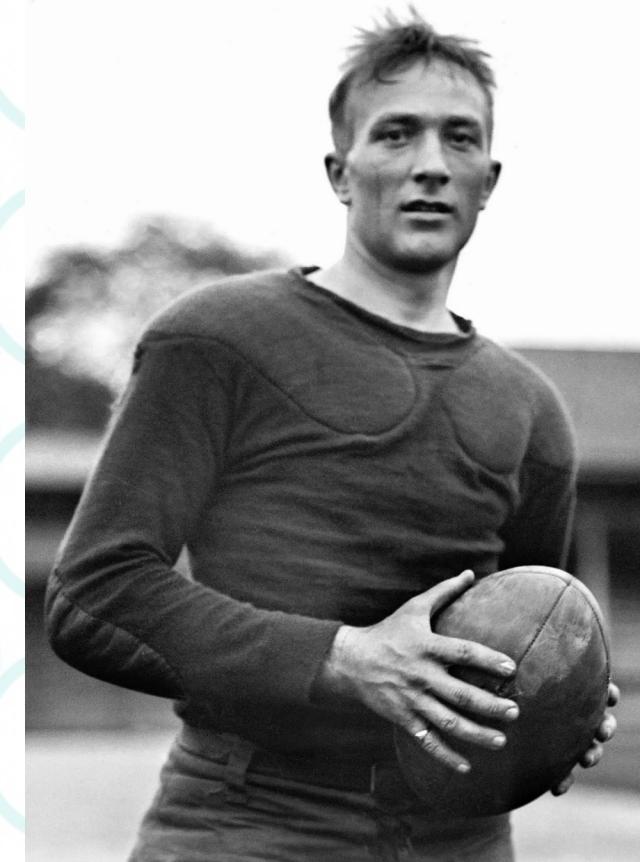
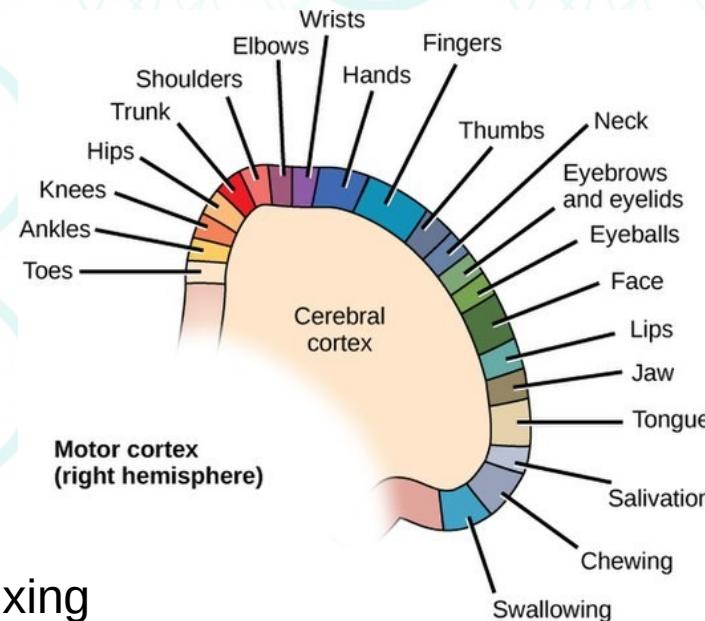
Tan's brain showing lesion



Broca

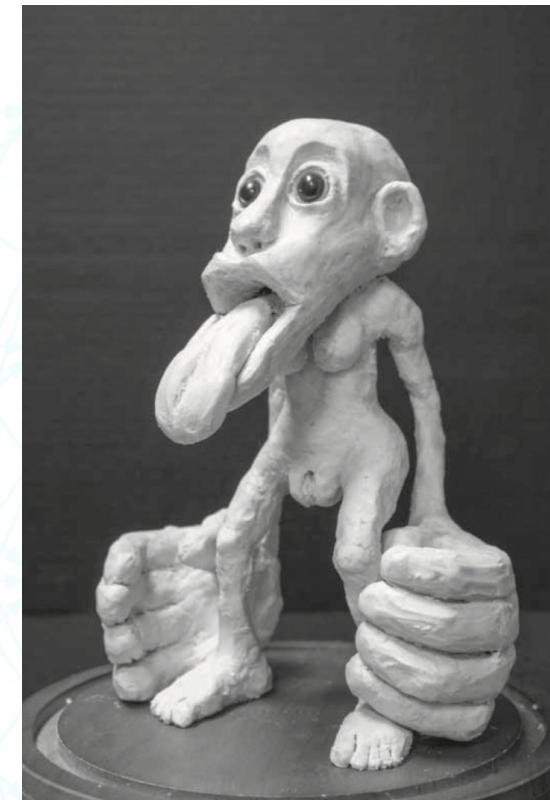
Motor and somatosensory cortices

- The somatosensory cortex is associated with the postcentral gyrus of the parietal lobe
- Responsible for processing sensations from various parts of the body
- Wilder Penfield (1891-1976), neurosurgeon
- Woke patients during neurosurgery and stimulated parts of the brain
- Brain has no sensory nerve endings
- Allowed him to work out which parts of the brain he could operate on or remove
- Touching parts of the brain caused fictive sensations
- Hence he was able to map the motor and somatosensory cortices
- Other parts of cortex dedicated to hearing and vision
- Initial processing and mixing



Wilder Penfield

Cortex continued



Male and female homunculus. The female homunculus is a newer addition reflecting the fact that female neuroanatomy is less well studied. This gender gap is still common but becoming less so, see Beery and Zucker 2012. (10.1016/j.neubiorev.2010.07.002) Note boulderisation.

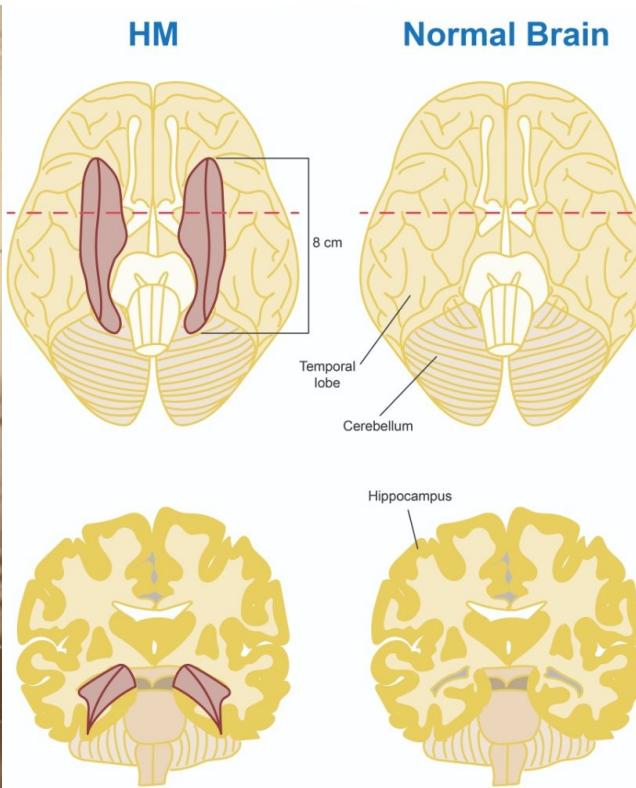
Cortex and memory:

- Scientists initially assumed that long term memory had a location in the cortex
- A series of experiments by Karl Lashley, who taught maze tasks to rats and then lesioned parts of their cortex showed no clear relationship.
- So where does memory live?

Hippocampus

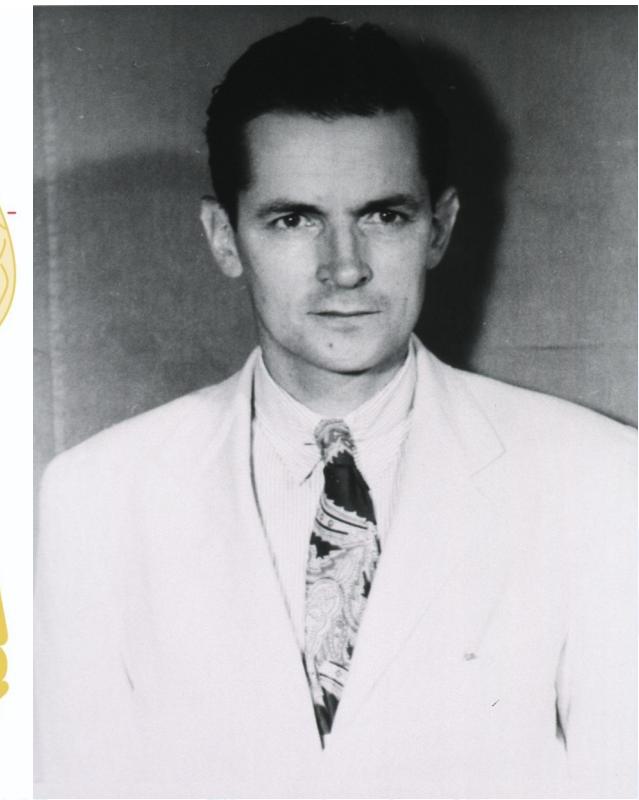
- Little was known of the Hippocampus until 1953
- From the early thirties to the late forties there had been a ‘fashion’ in psychiatry to perform frontal lobotomies as a treatment for mental health problems.
 - A spike would be pushed into the brain from the eye socket and the frontal lobe severed!
 - Had no medical benefit but made people more passive.
 - Nobel prize awarded for its discovery.
 - Today this can only be considered monstrous.
- Henry Molaison (HM) (1926-2008) suffered from intractable epilepsy
- In 1953 surgeon William Scoville (1906-1984), who believed the source of the seizures was the hippocampus, removed the majority of HM’s hippocampus.

Hippocampus



Henry Molaison

Surgery

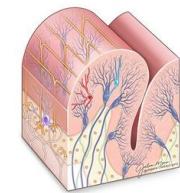
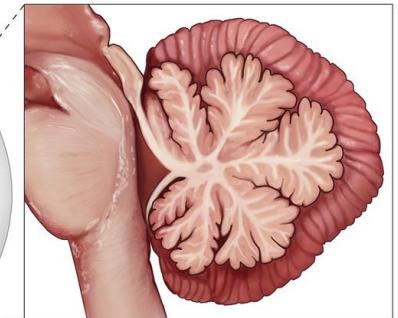
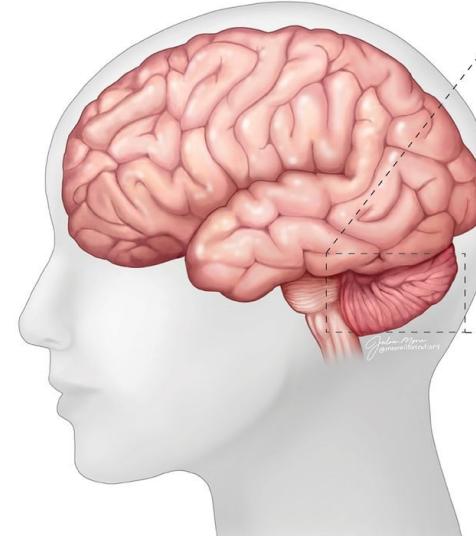


William Scoville

- Molaison was no longer able to form new memories.
- He remembered his past and was able to form short term memories on the order of a few seconds.
- We now know that the hippocampus stores memories from minutes to weeks and supports quick memory and recall
- Distinct from long term memories which we think are stored in the cortex and consolidated there from the hippocampus.

Cerebellum

- Cerebellum, or hindbrain, is at the back of the head
- It has a very distinctive structure
- Jean Pierre Flourens (1794-1867), removed the cerebellum from living animals
- The animals where still able to move but without there usual grace



- Consistent with observations of human patients.
- Today we think the cerebellum performs very precise predictions in aid of motion control
- Motor controls need to be based upon estimates
- One solution is a forward model ...

JP Flourens

Basal ganglia

- The basal ganglia are a complicated group of subcortical brain areas.
- Thought to act as a gate to decision making and the rewards associated with actions.
- Includes the substantia nigra, one of the two main areas where dopamine producing neurons are found.
- The other area, the ventral tegmental area (VTA), produces dopamine in reaction to rewarding events.
- Parkinsons disease, associated with stiff or frozen movement, is associated with the loss of cells in the basal ganglia.
- L-dopa, a dopamine precursor, can alleviate this.
- Awakenings (1990), movie

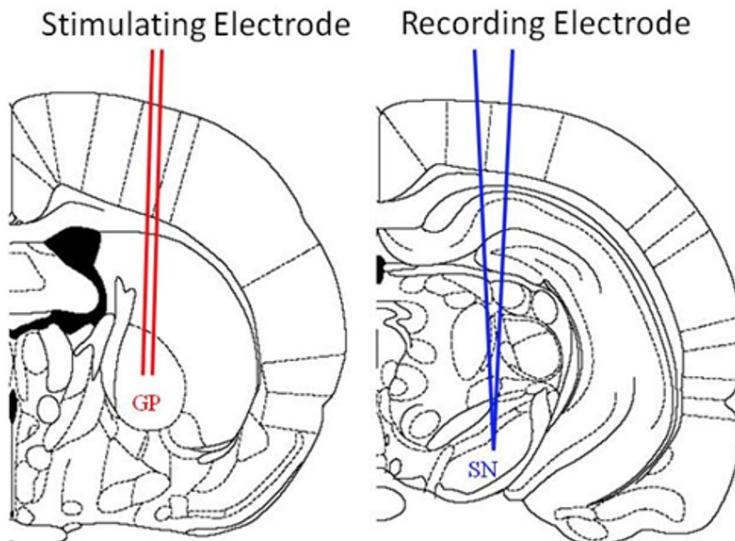
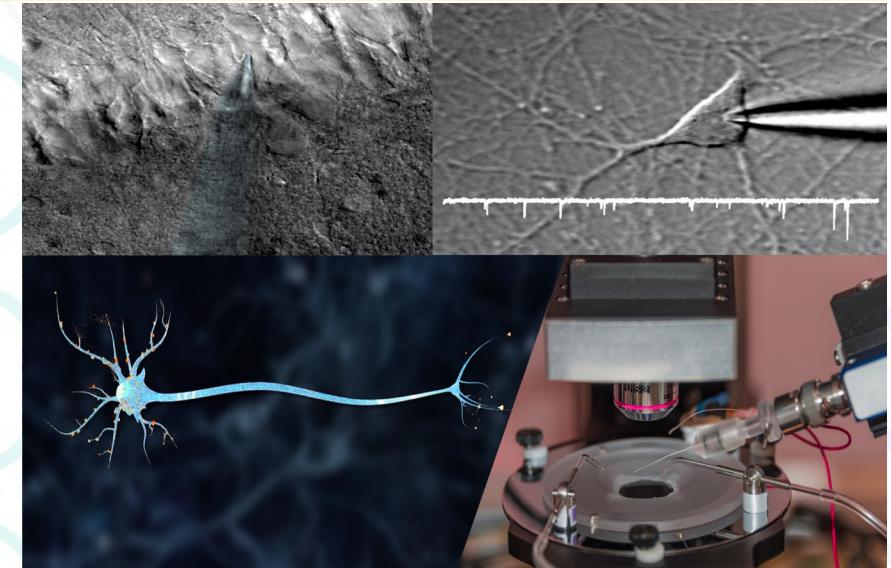


How do we understand our brains?

- We can think about thought, structured introspection. Borders upon philosophy, see eg Thomas Metzinger (1958 -) Being No One (2003).
- Today we concentrate more on observing the dynamics of neural matter.
 - Big question or small question again.
 - In the past we relied upon studying living patients and dissecting them after death.
 - We would like to record the whole brain.
 - We would like to measure the voltage changes in every neuron in real time.
 - Compromise between spatial and temporal resolutions and the invasiveness of the techniques.
 - From in vitro examinations of brain slices to electroencephalography which will get conductive gel in your hair but the data is very noisy

Modern(ish) methods

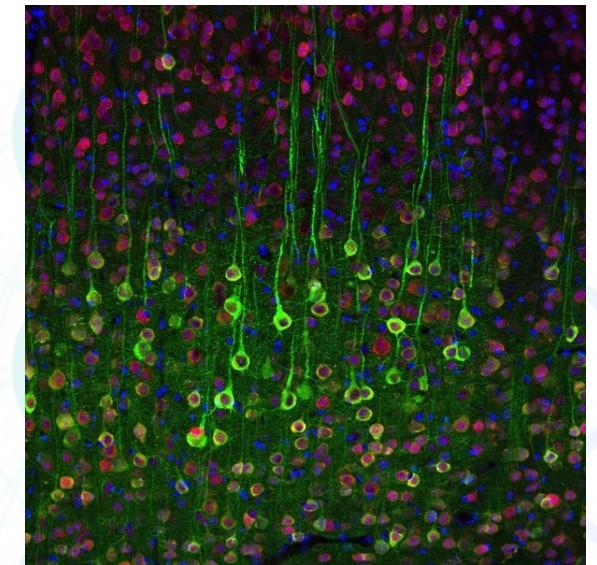
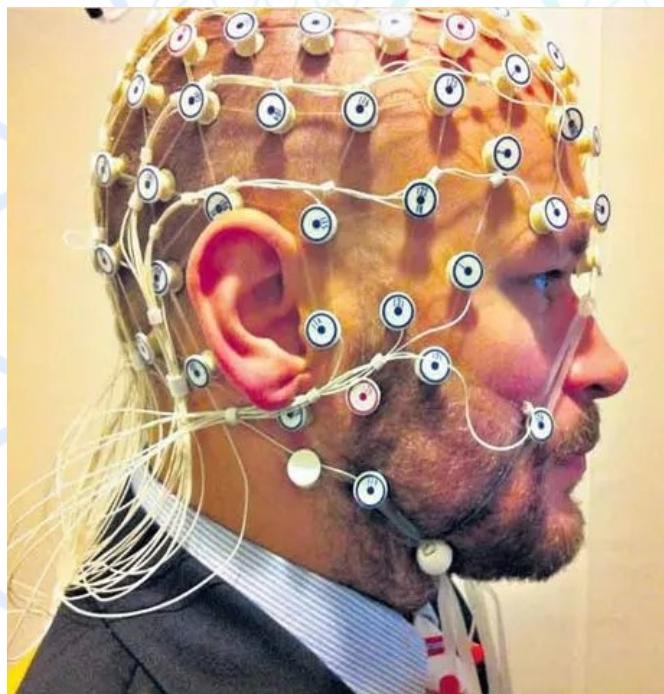
- In vitro electrophysiology
- Slice living tissue and keep alive in special fluid
- Insert electrodes, devices etc
- Very detailed but not natural environment



- In vivo electrophysiology
- Silicon probe or electrode in living brain
- Only spikes recorded not voltages
- ‘Natural’ state
- Great deal of post processing
- Highly invasive, morally questionable

Modern(ish) methods

- Calcium imaging; calcium also plays a role in mammalian brains signalling
- Chemicals that bond with calcium and emit photons
- Can measure voltage of neurons
- Dye is slow, window to brain required



- Electroencephalography (EEG)
- Electrodes on scalp
- Telepathy!!!
- ‘Natural’ state
- Bias in field, activity does not cancel
- Signal noisy, resolution awful

Learning computation and the brain

Thank you :)

