Week 1

Lecture 1 –*Why have a Nervous System?*

What do you know for sure? –could be dreaming (brain in a bucket and only our thoughts exist)

- all we know for certainty is that we're thinking; therefore we exist
- we recognise our mental existence → part of the nature of thought is that it seems to be a private experience; "you".

What else are we aware of?

- Knowledge of an external and internal
  - a universe in which we are embedded in
  - variety of attributes about ourselves (internal state/feelings)
  - and then, a capacity for action
- All these properties (attributes of the mind) are a product of operation of the NS

It wasn't always known, so how did we get to know this?

Aristotle

- **cardio-centric view** (brain had little consequence for function
- Ancient Egyptians → health of body and mind followed symbolic properties e.g. Nile river cannot be too low or too high in flow of water
- Hence, heart pumps fluids around body so is the centre of the soul
- made sense logically → e.g. feeling nervous affects HR and visceral areas
- Heart moves, brain does not; simple animals move, but have no brain; warmth emanates from heart (body's core)

Hippocrates

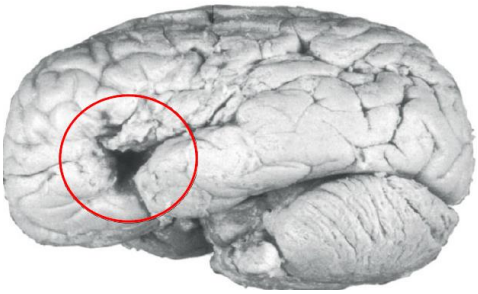
- "…from nothing else but **the brain** comes joys, delights, laughter and sports, and sorrows, griefs despondency and lamentations …"
- change of thinking → based on evidence

Understanding complex systems via simplistic mechanism

Descarte

- a view of brain function as a mechanism of fluid and tubes (brain included but still the heart centre –the pump)

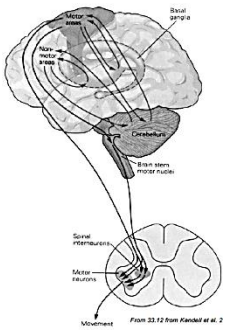
Prof. Paul Broca



- Correlated regions of the brain to different functions
- Post mortem brain of patient –"Tan" –studied
  - unable to produce speech
  - Lesion in L Frontal Lobe → region now known to produce speech
  - correlate structure of brain to function

A Capacity for Action

- Nervous system controls movement
- *Arabidopsis thaliana* → very distant relative of ours genetically,; a plant that has more genes than us but no nervous system → no movement
- *Corynactis californica,* a simple invertebrate –has a nervous system network that has sensory ends that case contraction when stimulated

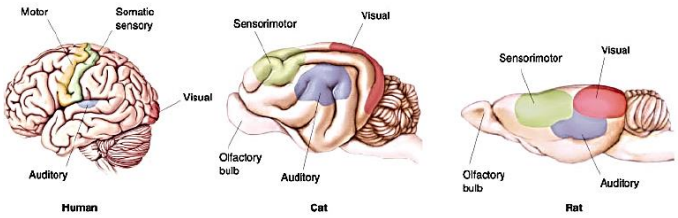


- Human brain has large regions dedicated to movement –cerebellum, basal ganglia and in the cerebrum

Ego-centric External Universe

- The universe is just material (energy and light), it is our nervous system that detect it, and appreciates it; forms the sensory stimulates we know and love
  - Seeing? → a construction of an image by a brain from light reflecting at different wave lengths
  - We tend to think that the external or real world has the properties we perceive, but these properties are the conscious experiences generated by the actions of the nervous system. So one of the things our nervous system does is generate our experiences of ourselves and the external world.

Exteroception-



Human brain has comparatively smaller regions associated with sensory and motor actions

- we have larger regions for thinking and imaging beyond

Homeostatic Regulation

- nervous system regulates a stable internal environment by detecting and causing a response e.g. NS controls BP fluctuations within narrow ranges

Summary-

1. Reveal the universe and ourselves in it –detect energies out there impinging on us
2. Provide a capacity for action
3. Homeostatic regulation

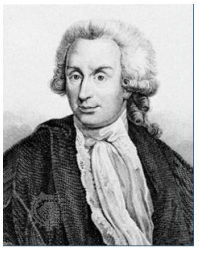
Lecture 2 –*Cellular Basis of Neural Function*

- Initially (1700s), the nervous system was still largely misunderstood, and how neurons worked with the brain specifically, came down to 3 abstract theories:
  - Spirits running through hollow nerve fibres
  - Mini explosions from fermentation
  - Vibrations caused by light of different energies
- Experimentation easily refuted these theories

- Early 18th Century –ELECTRICITY was a big thing
  - Leyden jar (like batteries) replaced electric animals (fish and eels)
  - Is the nervous run electrically too??

Luigi Galvani –Italian doctor

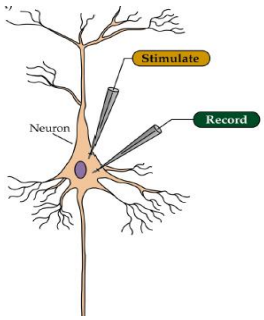
- experiments to show that nerves convey “animal electricity” and by this signal activate muscles
- concluded that the electrical spark must have activated natural processes (biological signal) by which nerves activate muscles
- previously concluded that a spark directly on muscle would cause movement



Aldini –Galvani’s nephew

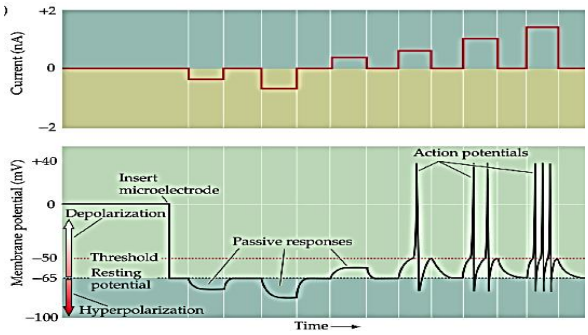
- attempted (largely unsuccessfully) to electrically stimulate the brain to cause a response in muscles

- did manage to stimulate facial muscles by sparking the brain



Neurons

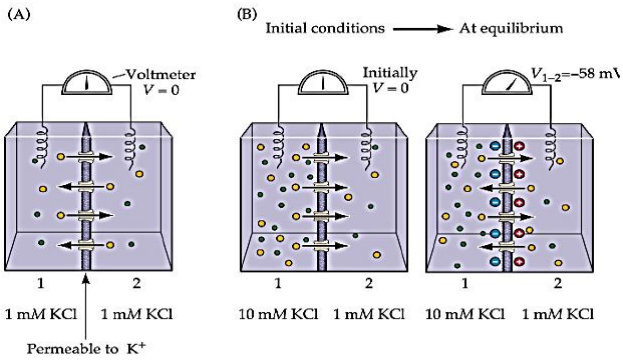
- structure suggests their function –transmit electrical signals
- measured with tiny microelectrodes → placed intra- and extracellularly to measure potential differences



Microelectrode inserted, Cl- ions pumped in, to further hyperpolarise the potential

Na+ then pumped to depolarise, enough pumped in to reach threshold and generate an action potential → the more Na+ pumped didn't change the magnitude of the AP, only the frequency

Electrochemical equilibrium

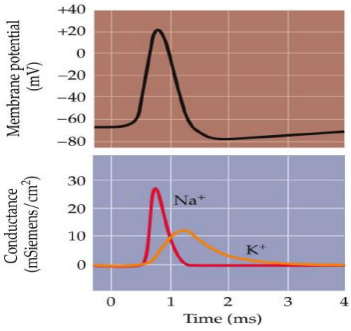


Electrochemical Equilibrium-

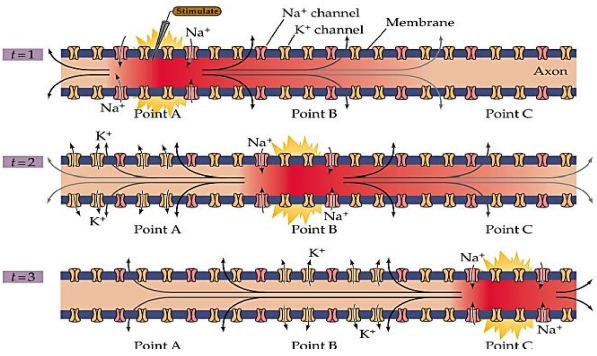
With even [K] on either side, and permeability to K, there is no mV generated

With a change in [K], a concentration gradient is establish (K moves from [high] to [low]) and as this occurs, an electrical gradient also establishes which prevents full equilibrium of K between spaces → -58mV established

Action Potentials



- Nerve impulses are dependent on the voltage of the ion channels
- Na+ moves in to depolarise and K+ out to repolarise
- Only really a small amount of concentration change needed to change potential enough
- Myelination in vertebrates allows APs to skip along nodes



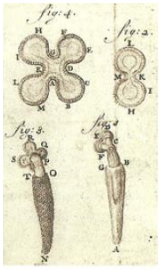
Neuron stimulated and depolarises until threshold is reach → Na+ channels flow in to further depolarise (make more positive) – positive feed forward effect.

K+ channels also open at time of stimulant, but open with greater latency –once opened, K+ flows out and Na+ channels become inactive → repolarise the neuron

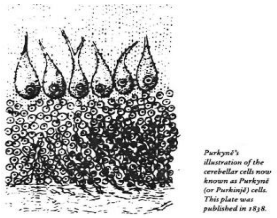
•So, was established that neural tissue was excitable –generate electrical impulses

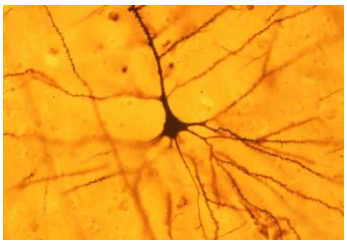
- now need to figure out how nerve cells communicate
- Progress of neuroscience for next 100 years now focused on brain function
- **Broca** and others corroborated by experiments showing cortical localisation and the discipline of neurology was established → mainly from **Jean-Martin Charcott**

- Until the end of the 19th century words describing the NS weren't around (neuron, dendrite etc.)
  - cell theory by **Schwann** and others in mid-19th century was controversial initially → even when broadly accepted, thought not to apply to the NS
  - end of 19th century –microscopes and new histological methods and a willingness to refute established doctrine → Nervous system seen as organised tissue
- A century before, cells within were being revealed
  - **Leeuwenhoeks** animalcules (1665) → saw 'little eels' in vinegar
  - also published a drawing of a piece of nerve



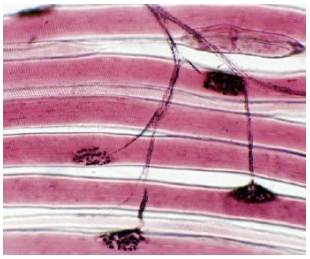
- **Jan Purkinje** was a pioneer in neuro-histology –preserved, sectioned and viewed parts of the brain; he described a large cell in the cerebellum
  - at this time (1838) → Cell Theory was proposed but neural tissue was considered not to comprise individual cells but rather reticular network
  - Purkinje was one of the first to suggest the NS (like other tissues) composed of discrete cells





- **Camilo Golgi's** silver stain → able to view fine nerve cells
- Improved silver stain by **Sabtiago Ramon-y-Cajal** → 'Black reaction'
  - MAJOR FIGURE; precipitate silver stain to be able to view neurons in great detail → able to see distinct cells

➢ By end of 19th century –reticular theory (brain as a mesh network) had given way to neuron doctrine
  - **Wilhelm Von Waldeyer** in 1891 conclude that the nerve cell is the anatomical and functional unit of the NS
  - Neuron, dendrite and axon introduced
  - Microscopy was key to supporting the neuron doctrine
  - Discrete neurons…then connectivity?



- The established electrical nature of the nerve impulse –spark could jump between neurons

- Argument against fusion being necessary for signal transmission → Neuromuscular junction
  - motor nerve terminates at muscle fibre in branches → fuse there or not?

Examining Peripheral Innervation

- Knowledge about neural interactions came from examining peripheral innervation → innervation of skeletal muscle and the autonomic nervous system
- Recognised different divisions innervated the same organ –effects of stimulation were opposite
  - Parasympathetic stimulation by vagus nerve slowed the heart whilst sympathetic nerves increased HR
  - How could a spark from a nerve that was supposedly 'fused' to the heart do both opposing actions?

➢ **Cajal's** recognition of superior staining in developing tissues led him to discover growth cones and the evidence of dynamic morphology of growing neurons
  - How 'fixed' is the structure of neurons in the mature brain?
  - Embryonic staining proved to be better to view as less myelin so stain took to the neuron better; ends of axons were dynamic and growing

Lecture 3 –*Neural Communication and Plasticity*

➢ British physiologist –Charles Sherrington supported the neuron doctrine even before Cajal; he showed:
  - studies of degeneration of the NS always resulted in discrete pattern of loss (not diffuse)
  - reflex responses he was studying were much slower than was explicable by the speed of nerve conduction (a delay somewhere → a process between = synapse)
  - unidirectional reflex conduction

➢ Up until end of 19th century –thought transmission between neurons was electrical (jumped over)
➢ George Oliver and Hendry Dale conducted experiments with natural substances that causes effects similar to nerve stimulation (chemicals causing vasoconstriction of blood vessels → same chemical for neurons…ACh)