+++ title = 'Chapter 2 - Principles of Neural Science' date = 2024-01-14T09:32:56+05:30 tags = "Neurobiology" draft = false +++

Chapter 2 (Chapter%202.md) Principles of Neural Science (Principles%20of%20Neural%20Science.md) Synaptic Plasticity and localisation of mRNA translation in axons (Synaptic%20Plasticity%20and%20localisation%20of%20mRNA%20translation%20in%20axons.pdf) Nuerobiology (Nuerobiology.md)

Glial Cells

Functions:

- Nourishment to neurons
- Structure
- Dev --- migration cues by radial glia
- Myelin Sheath
- Blood Brain Barrier
- Scavengers
- Signalling
- Pre-synaptic terminal control

Types:

Microglia

- Immune cells arising from macrophages, embryologically and physiologically diff from other merve cells
- Unknown rest conditions, stouter process when activated after injury
- Produce antigens, active in MS and AIDS-related dementia

Macroglia

- Oligodendrocytes and Schwann cells
    - Provide insulation through myelin sheath
    - not very branched, myelin by each differes in chemical composition
- Astrocytes
    - Not very processed
    - Has end feet
    - Brings nutrients
    - Blood-brain barrier
    - Maintains K-ion conc. in ECM

Neurons

Ramon y Cajal

- Silver Staining method of staoining neurons
- Established that neurons are distinct and do not for synctium
- Principle of dynamic polarisation Unidirectional transmission of nerve signals from soma to axon
- Principle of connectional specificity Connections between neurons arew not random but specific
- Shape-based classification into unipolar, bipolar and multipolar

Specific signaling network --- control specific behaviour

- Four types of connections - sensory, motor, inhibitory (to opposing muscles for example) and conveyance to brain
- in knee-jerk reflex Stretching of extensor muscle | (Sensory info) Dorsal root ganglion |(Interneuron helps) Motor neuron for extensor (activated) & Flexor (opposing) inhibited | Contraction of extensor
- Feedback and feed-forward inhibition

Components of signal in neuron and uniformity in all of them

- Four types of signals in all cells - input, trigger, signalling, output
- Action potential, Na+-K+ pump
- Neuronal convergence(integration of instructions by motor neurons) and divergence(affecting diverse cells at once)

Amplitude of signals decrease along distance (graded receptor and synaptic potential)

- Receptor potential generated locally--- strength depends solely on amplitude and duration of triggering muscle stretch
- Also synaptic potential - graded --- depends on amount and duration of neurotransmitters released
- Both decay with distance

Trigger component starts action potential

- Trigger zone --- impulse initiation zone
- sums up activity of all receptor potentials
- Highest density of Na+ channels (voltage sensitive ones) -- lowest threshold
- once input potential crosses threshold, action potential generated, whose frequency is decided by duration of input potential

All-or-none principle

- All action potentials are the same in amlitude and duration - does not decay as periodically regenerated
- Only frequency changes with input duration --- produces stronger sensation or speed of movement
- Must cross threshold to be generated

Neurotransmitter

- Graded output signal
- No. of neurotransmitters depends on no. and freq. of action potential
- Generates synaptic potential in post-synaptic cell
- Whether excitatory or inhibitory effect determined by receptor on the postsynaptic cell and not on the neurotransmitter itself

Molecular difference b/w Neurons

- differ in whether they produce action potential
- what ion channels they use (leads to diff. signals and thresholds)
- differ in what neurotransmitters they use and can recept

Specific Networks --- Unique info. transmission

- Localisation of brain func.
- Two kinds of neural maps - sensory and motor
- Parallel processing single behaviour --- different groups of neurons work simultaneously to convey similar info --- increases speed and reliability of CNS
- complexity of connection and not complexity of neurons themselves --- responsible for unique messages

How the specific conn. change --- Adaptability of behaviour

- Plasticity Hypothesis Changes in chemical synapses
    - Short term - Physiological changes like alteration of strength of synapse connection (day long)
    - Long term - Anatomical changes like pruning of pre-existing connection and development of new connections (learning and memory formation or dev)
- potential for plasticity responsible for individuality

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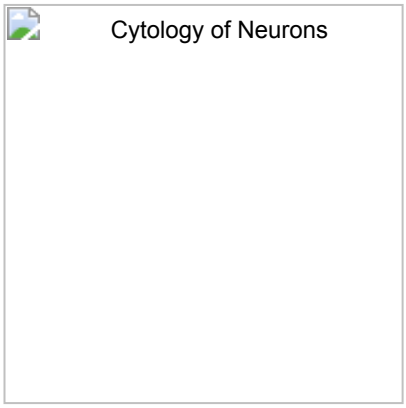

- deals with degree of localisation in brain

- explanaing behaviour as properties of specific nerve cells and interconnections in particular regions of brain
- Talks about how neurons are different because of polarisation, excitability, and molecules they produce, along with compartmentalisation which helps in effective and quick conduction of signals

Neurons similar to epithelial cells

- neurons develop from epithelium
- basolateral surface – cyton part with dendrite & apical surface - part from which axon arises
- plasmalemma with asymmetric bilayer, same cytosolic housekeeping proteins; extra is some special ones, like ones used to degrade neurotransmitters

Selective distribution of organelles and molecules throughout cell

- 
- Vesicular pathways - exocytic (membrane proteins secreted by RER - Golgi incorporated into plasmalemma, secretory pathway) & endocytic (membrane taken in from plasmalemma shuttled back by vesicular recycling, or taken to lysosomes for degradation by endosomes)

Shape of neuron determined by cytoskeleton

- cytoskeleton - microtubules, neuronal filaments, actin
- microtubules - made of tubulin (GTPase); poylmerisation happens due to binding of GTP bound tubulin dimers. After polymerisation, GTP is hydrolysed to GDP and depolymerisation happens. Normally this would be very unstable and would lead to catastrophic depolarisation , but des not happen due to MAP Microtubule Associated Proteins that stabilise it - these are different in cyton and axon
- neuronal filaments - interfilaments made of neuronal proteins called cytokeratins that are responsible for producing in interfilaments in other cell types as well and very stable and fully polymerised

> *[!note] neurofibrillary tangle in Alzheimer's and other neurodegenerative disorders #ReadLater*

- Actins- short polymers near the plasmalemma; controls dynamical processes, responsible for growth cone mediation, development of pre- and post- synaptic morphological specialisation

SNS and motor neuron systems

nothing very new

- homonymous and synergistic muscles
- central neurons - intensive dendritic branching because of regulation by input from many neurons; spines in dendrites to increase area for reception
- mRNA localisation at dendritic spinces, dendrons more of an extension of the cell body, more closely related than to axon --- conc. of proteins and mRNA essential for synaptic plasticity
- recurrent collateral branches in axons - responsible for going back to motor neuron and modifying activity, or may go back to Renshaw cell in spine and inhibit firing in motor neuron

One motor neurons -- several muscle cells

- Many synapses in cell body and dendrons(more) - inhibitory ones closely in cell body and excitatory ones on dendrons
- Sensory - motor info flow both convergent (100 sensory to one motor) & divergent (1 sensory to 500-1000 motor)
- Low innervation ratio (no. of muscles by an axon) - more precision
- acetylcholine transmitter - essential molecules reqd. to be present

Defects in Myelin

Demyelinating diseases

> *[!Note] #ReadLater*

- *shiverer* (recessive mutation for MBP gene exon deletion)& *trembler* mutants of mice
- three classes of myelin proteins -
    - Myelin Basic Proteins(MBP) - 7 related proteins formed from a single MB gene, elicits strong immune response when injected(demyelination) & scanty myelination
    - Myelin Associated Glycoproteins(MAG) - homophilic adhesion molecule helping in myelin compaction in axon, belongs to superfamily related to immunoglobulin; again, isoforms of same MAG generated from a single gene by alternative RNA splicing

    > *[!Note] Alternative RNA Splicing (?)*

    - PLP - jimpy mice, Merzbacher disease due to PLP mutations, resulting in demyelination
    - Myelin Protein 0 - membrane spanning domain of Schwann cell, extracellular domain affected by mutation, also helps in compaction and adhesion, deletion leads to *trembler* mutants

- PMP22 - compaction of myelin

Hippocampus Pyramidal Neurons

- CA1 and CA3 regions
- CA3 regions have axons comprising the Schafer-collateral pathway, that runs through the stratum radiatum, forming connections to the dendritic spines (excitatory) of CA1 regions -- intensive branching (pyramidal cells have two dendritic trees) and excitatory connection
- all dendritic spines of CA1 very compartmentalised, useful in memory formation and learning

+++ title = 'Chapter 5 - Neural Science' date = 2023-01-14 tags = "Neurobiology" draft = false +++

Synthesis and Transport of Neuronal Protein (Principles%20of%20Neural%20Science.md#%5Ej2d1346dabs)

Protein Synthesis in the Cell Body

- mostly in cell body and dendrite beginnings
- different sequences in N-terminal or inside mark it for different processes, for example, modification, secretion, or say degradation(Ubiquitinylation)
- chaperons(Hsp70) help in protein folding (energy dependent)

Protein Modification

- changes - cotranslational/ posttranslational
- permanent/transient
- N-acylation (Myristoylation) - addition of lipid chain to acylated N-terminus(Gly) allow it to associate with membrane through chain
- Thioacylation - allow protein to associate with cytosolic leaflet of membrane (e.g., helps GABA-secreting GAD to associate with membrane)
- Isoprenylation - also similar to thioacylation, by farnesyl, or geranyl-geranyl
- Reversible - (de)phosphorylation, which also controls enzyme kinetics
- ATP-ubiquitin-proteasome pathway - selective and regulated proteolysis of cytosolic proteins, important in many neuronal processes, including synaptogenesis and long-term memory storage

Cytosolic protein uptake by other organelles

- Nuclear import of large proteins through pores - requires energy, marked with nuclear localisation signals and export signals for opposite
- Mitochondrial and peroxisomal transport- signal sequence is amphipathic helix so that it can cross bilayer

Protein synthesis and modification in ER

- Signal recognition particle & stop-transfer sequences mediating transport during cotranslation
- glycosylation

- intramolecular disulfide linkages

Modification and processing by Golgi bodies

- clathrin-coated vesicles
- mechanism of transfer

Endocytosis

- reuse of used synaptic vesicles
- very selective transport by clathrin mediated vesicles, termed receptor mediated endocytosis

Axonal transport

- used by scientists to visualise neurons and neuronal networks
- labelled material carried by the axon helps visualise the entire network
- e.g., Herpes Simplex virus has been used to trace cortical pathways in monkeys
- **Anteretrogade** - towards axon terminal, **Retrograde** - towards terminal ^7b597c
- Moderate slow movement of axoplasm from cell body to terminal over time (axoplasmic transport) visualised by Paul Weiss in the sciatic nerve
- membranous proteins - both anteretrograde (Chapter%205.md#%5E7b597c) & retrograde (Chapter%205.md#%5E7b597c) (*fast axonal transport*)||| cytoplasmic skeletons and proteins - only retrograde (Chapter%205.md#%5E7b597c) (*slow axonal transport*)
- used by scientists to visualise axonal transport and neural network

Anteretrograde transport

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