Repolarization returns the membrane potential to the -70 mV value that indicates the resting potential, but it actually overshoots that value. Potassium ions reach equilibrium when the membrane voltage is below -70 mV, so a period of hyperpolarization occurs while the K+ channels are open. Those K+ channels are slightly delayed in closing, accounting for this short overshoot.

The Refractory Period

Refractory periods are a short phase in time following an action potential where another action potential cannot be generated. There are two types of refractory periods:

Absolute refractory period:

Where it is impossible for another action potential to be activated, regardless of the size of the trigger (stimulus). This is because the sodium channels are inactivated and remain that way until hyperpolarisation occurs. In the cardiovascular mechanism, this refractory period is sometimes called effective refractory period (ERP)

Relative refractory period:

The period that occurs during the undershoot phase; where an action potential can be activated but only if the trigger (stimulus) is large enough. (Higher than normal threshold). This is because some of the sodium channels have been reactivated and have recovered but it is a difficult process due to the counter-acting potassium flow as some potassium ion channels are still open.

A fibre first enters the absolute refractory period directly after an action potential has been fired, then the relative refractory period. The absolute refractory period of a human muscle fibre is typically between 2.2 and 4.6 ms.

The refractory period causes 3 things to occur:

The brain will be able to perceive nerve impulses as separated events since there is a time lag between them.

The number of generated impulses or repetitive firing rate of a neuron will be limited in a given period of time[4].

The nerve impulses will only travel in one direction. This is because, as the action potential is moving forwards along axons, the resting potential will be re-established behind it. However, not until this happens can a new action potential occur.

Glial Cells

Glia, also called glial cells or neuroglia, are non-neuronal cells in the central nervous system and the peripheral nervous system. They maintain homeostasis, form myelin, and provide support and protection for neurons.

Note: A **Schwann cell** is a type of glial cells found in the peripheral nervous system (PNS) of higher vertebrates.

End Plate potential

What is an End – Plate Potential?

End plate potentials (EPPs) are the voltages which cause depolarization of skeletal muscle fibers caused by neurotransmitters binding to the postsynaptic membrane in the neuromuscular junction. They are called "end plates" because the postsynaptic terminals of muscle fibers have a large, saucer-like appearance. When an action potential reaches the axon terminal of a motor neuron, vesicles carrying neurotransmitters (mostly acetylcholine) are exocytosed and the contents are released into the neuromuscular junction. These neurotransmitters bind to receptors on the postsynaptic membrane and lead to its depolarization.

- If the EPP exceeds the threshold value an action potential is generated – by the opening of voltage gated Na channels – (i.e. two different electrical events)
- EPP decays as it moves away from end-plate – (nAChRs absent away from synapse)
- Action potential travels through the muscle cell

Properties of EPP

• Timing: Pre-synaptic AP to EPP ~ 1 msec

• EPP generated by ligand-gated channels opening voltage-gated channels (i.e. an action potential)

• EPP is very large (compared to most synaptic potentials) – Many ACh vesicles released; high density of nAChRs

• Threshold for AP generation easily passed – high density of voltage-gated Na+ channels at end-plate)

Fate of ACh

- binds to its receptors
- released into the synaptic bouton where it is hydrolysed by acetylcholinesterase

- An AP invades the t-tubule system to transfer the electrical impulse to the contractile proteins in the msucle fibres
- Sarcoplasmic Reticulum (SR) – is a Ca2+ store and it initiates the contraction of a muscle.
- When the excited the t-tubule membrane depolarises = a change in the t-tubule voltage sensor.
- = Changes conformation of the SR Ca2+ channel
- =Ca enters the space around the contractile protein.
- Higher the frequency of motor neurone activity – the muscle stays contracted

Myesthenia Gravis

- Muscle weakness during sustained activity
- Autoimmune disease of the nicotinic acetylcholine receptors – generates antibodies that work against the receptors. – reduced number of receptors at NMJ

5. Synapses and the Roles of N.T.S

Glial Cells Functions:

- guiding connections
- physical support –
- metabolic support –
- electrical insulation
- signaling

Gap Junctions/ Electrical Synapses

- bi-directional
- Cell-cell communication
- Very fast
- = synchronous activity between cells
- Rare between neurons in adult CNS, common in developing CNS
- Common between neurones and glia
- Connections that allow depolarization of cardiac muscle (and coordinated contraction)

Chemical Synapse

- Uni – directional transfer of info.
- What happens:
  1. Vesicle containing NT in pre-synaptic knob
  2. A.P. when membrane depolarizes due to Na^+ ion influx through V.G Na channels
  3. AP reaches nerve ending
  4. Causes V.G. Ca^{2+} ion channels to open and Ca^{2+} enters cell
  5. Triggers exocytosis (vesicle moves towards and fuses with pre-synaptic membrane)
  6. N.T. diffuses into and across synaptic cleft
  7. N.T. binds to specific receptor (exogenous substances can also do this)
  8. Signalling occurs

How does the signal terminate?

Either: (dep. On the neurone and the NT used)

1. Reuptake:
- Transporter protein takes NT back up into presynaptic knob
- Can be metabolized (hence mitochondria needed for enzyme activity)
2. Presence of Enzymes

Enzymes breakdown NT (outside the presynaptic knob)

The major neurotransmitters

Amino acids: glutamate (**major excitatory**) gamma -aminobutyric acid (GABA; **major inhibitory**) glycine

Monoamines: noradrenaline, dopamine, 5-hydroxytryptamine (5-HT; serotonin)

Acetylcholine (ACh)

Neuroactive peptides: >100 different kinds e.g. opioid peptides (endorphin, enkephalin) tachykinins (Substance P, neurokinin A)

REMEMBER ADRENALINE = HORMONE, NORADRENALINE = NEUROTRANSMITTER

Receptors

- Transmembrane proteins
- recognition site for a neurotransmitter - initiates the intracellular signal
- transmitter binding causes structural change = signal
- receptors are specific for a neurotransmitter
- one neurotransmitter - several receptor subtypes

Receptor Signalling Mechanisms

1. Ionotropic (receptor operated/ligand gated channels)

- transmitter binding = conformational change = channel opening = ion movement
- fast transmission
- Excitatory ionotropic receptor e.g. glutamate AMPA, NMDA, kainate receptor subtypes ACh nicotinic receptor subtype (exogenous)
- How: Excitatory
  1. (as before)
  2. NT interacts with postsynaptic receptors = conformational change of receptors
  3. Receptors open = Na+ ion influx (diff. from high to low concentration and move from +ve to -ve charge)
  3. = depolarization of post synaptic membrane (ES????

  Inhibitory
- As before
- CL- ion influx (due to moving down conc. Gradient) =hyperpolarization of membrane (m.p. more ve)

2. Metabotropic (G -protein coupled)

- transmitter binding =conformational change =activates G-protein = activates 'effector systems' = indirect effects on excitability
- slower transmission longer lasting effects

Synaptic Integration of Information

Spatial Summation

-from excitatory synapse
- (EPSC) far from threshold
-if 2 synaptic inputs (spatially separate) occur at same time can be 'added' together = twice as much excitation

10. The Enteric Nervous System

What is it?

- 3rd div. of ANS – sometimes classed as parasymp.
- Intrinsically innervates viscera inc:
    - GI tract (oesophagus to rectum)
    - Pancreas
    - Biliary system
- Interchangeable w/ intramular plexus -> contained entirely within the walls of the GIT
- Network of 80-100 million neurons (AKA 'second brain'

Where is it?

- 2 major plexuses of ganglion cells and their fibre bundles:
    - Submucosal (Meissner's) Plexus: stomach and intestines only
    - Myenteric (Auerbach's) Plexus: full length of GIT
    - *The 2 are extensively connected*
- Longitudinal muscle contracts = shortens length of GIT
- Circular muscle contracts = decrease lumen diameter

Types of Neurons:

1. Afferent (sensory) neurons:
    - Mechano and chemosensitive -> detects via mechano- & chemoreceptors
2. Interneurons – coordinate input and output
    - excitatory (ACh) & inhibitory (many) NTs
3. Efferent (secretomotor) neurons:
    - Excitatory or inhibitory
    - Many NTs
    - Innervate motor and secretory effectors
4. Effectors:
    - Motor (smooth muscle):
        NTs include:
        - excitatory: ACh, substance P, 5-HT (investigated in disorders)
        - inhibitory: nitric oxide (NO), vasoactive intestinal peptide, ATP, nitrous oxide gas
    - Secretory:
        NTs Include:
        a. excitatory: ACh or VIP (excitatory not inhibitory -> receptors have different effects in different tissues)
        b. tonic activation

Function:

1. Controls motility, secretion and blood flow to gut

2. Motor reflex

- via myenteric plexus
- sensory fibres from wall of lumen carry impulse to m. plexus -> mucosal stimulation of bolus of food (bolus exerts distension on lumen)