excitable cells: nerve and muscle tissue cells, characterized by a RMP:
RMP: voltage difference (from -60 mV to -90 mV) across the plasma membrane (Vm)→ observed only in the vicinity of the plasma membrane (most of intracellular and extracellular space is electrically neutral)→ surplus of negative charge inside the cell and an accumulation of positive charge outside the cell → unequal distribution of ions → polarized cells
Vm is measured by a microelectrode in the cytosol
concentration of Na+ inside the cell is low (5-15 mM) and 145 mM outside → chemical gradient of Na+ concentration across the cell membrane
concentration of K+ inside the cell is high (140 mM) and low outside (5 mM)
RMP in a typical neuron → -65 mV → maintained when neurons don't generate APs
RMP can be calculated by Goldman equaton
sodium potassium pump: causes the unequal distribution of ions → ion channel → actively transports (ATP required) → 1 ATP for 1 cycle → 3 Na+ outside, 2 K+ inside
simple diffusion → from higher concentration to lower → no ATP → net influx of substances in the lower concentration region → depends on the coefficient of permeability and on concentrations → in case of ions coefficient is low → do not diffuse across the membrane → not like oxygen (hydrophobic molecule)
ion channels: increase movements of ions across the membrane facilitating the diffusion → IMP → selectively permeable by recognizing the ions → opening/closing the channel gate → 2 types:
voltage-gated channels: mechanism 4 closing/opening the channel → influenced by other factors normally closed
responsible for AP
have a pore → passage of ions
can be hetero-oligomeric
voltage-gated K+ channels → 4 polypeptide subunits → each with 6 transmembrane segments (p/b region) and 1 P loop/segment → the P loops together → are important 4 selectivity of the channel → influx or efflux of just one ion
voltage-gated Na+ channel → pore in the membrane highly selective to Na+ → pore opened/closed by changes in Vm → single long polypeptide → 4 domains (I-IV) → each consisting of 6 transmembrane α helices (S1-S6) and 1 P segment→ domains clump together to form a pore between them → pore closed at negative RMP → during depolarization the molecules twist into a configuration allowing passage of Na+ through the pore
have a selectivity filter → confer more permeability to Na+ rather than K+
passive channels: always open → not influenced by extrinsic factors → ex: the ones for K+ allow the passage of these ions and lead to the rise of a negative resting potential of the cell
electrical gradient brink K+ back inside the cell where negative charge has accumulated
at equilibrium → net flux of K+ = 0 → RMP is -80 mV → *potassium equilibrium potential* → calculated by the Nernst equation
stress-activated channels: activated by pressure
more K+ channels → membrane more permeable to K+ than Na+ → RMP close to the potassium equilibrium potential (negative) → RMP generated by electrochemical gradient caused by the large efflux of K+ and modest influx of Na+ → to maintain the gradient is needed ATP
membrane potential → sensitive to changes in the concentration of extracellular K+ → due to its high permeability to it
depolarization: increase of extracellular K+ → change from -65 mV (normal resting value) to less negative value
action potential: rapid change in RMP → for an instant membrane becomes positively charged relative to the outside (2-3 ms) → 4 characteristics:
rising phase: rapid depolarization of the membrane → change continues until Vm reaches a peak value → 40 mV
overshoot: the inside of the neuron is positively charged with respect of the outside

falling phase: rapid repolarization until the inside of the membrane is more negative than the RMP
undershoot/after-hyperpolarization: gradual restoration of the RMP
AP → triggered by influx of large amounts of Na+ → depolarization surface of the membrane less negative → if depolarization arrives at the threshold (critical level) → generation of AP
all-none event: whenever threshold is reached, if we increase stimulus the AP has same characteristics → AP doesn't get stronger with stronger stimuli (amplitude and direction)
refractory period: time following an AP → neurons cannot trigger another AP:
absolute refractory period: Na+ channels inactivate when membrane depolarizes → cannot be activated again → second stimulus applied won't generate a second AP → until membrane becomes negative again
relative refractory applied: membrane potential stays hyperpolarized until the voltage-gated K+ channel close → more depolarizing current is required to bring the Vm to the threshold → second stimulus applied generate a less strong AP
threshold: membrane potential at which enough volted-gated sodium channels open → relative ionic permeability of the membrane favours Na+ over K+
rising phase: rushing of Na+ inside the cell → depolarization
overshoot: membrane potential greater than 0 mV (closer to sodium equilibrium potential)
falling phase: inactivation of Na+ voltage-gated channels → voltage-gated K+ channels open (triggered 1 ms before depolarization occur) → K+ rushes out of the cell → repolarization (negative again)
The RMP is negative because the neuron is full of negative charged molecules (e.g., proteins)
voltage gated channels (Focus) → opened when voltage change (as in AP) → permeability regulated by activation gate→ can have 3 conformational states:
closed
opened
inactive
voltage-gated sodium channels: 9 subtypes → open at -55 mV → have rapid activation and inactivation kinetics → blocked by tetrodotoxin obtained from pufferfish
voltage-gated potassium channels: 12 families → slow activation kinetics → more time to switch between different conformations → blocked by tetraethylammonium
when the membrane is brought to -55 mV the voltage-gated sodium channels open, the open probability increase and a huge influx of sodium change the Vm to +30 mV (polarization), resulting in the switching off of the voltage-gated sodium channels. after a short delay, the voltage-gated potassium channels open, we have a potassium efflux thanks to a chemical and electrical gradient, repolarizing the membrane.
If both of the channels are open at the same time, there is no net change in the voltage as the charge on both K+ and Na+ is the same. This short delay between Na+ influx and K+ efflux is needed
patch clump techinque: electrophysiological technique allowing the recording of the current flow through the channels → a micropipette is used on a neuron → we can record the activity of a single channel or the whole cell:
single channel: record the influx or efflux of ions through a single channel → we have a rapid change in the conformation of the channel from the closed to the open state → opens or closes in all-or-nothing manner → during depolarization the possibility of the channel to be open is high → open probability is the time fraction for which the channel is in an open state → ranges from 0 to 1.0 when closed and is 1.0 if is alway open → we record current of few pA
whole cell: we apply a strong suction → rupture of the membrane till a point we can record the activity of all the channels in the cell → recording of hundreds of pA or few nA
the techinque also allows the analyzation of the inactive state of these voltage-gated channels: changing of the membrane potential from -80 mV to +20 mV let us record a deflection corresponding to the influx of Na+ → in fraction of ms the current reaches its peak value → soon after the current decreases even if the membrane is still depolarized because the channel undergoes

inactivation → the open probability (Po) reduces → channel is not permeable to Na+ anymore → at rest the activation gate is closed and the inactivation one is open → depolarizing the membrane let the activation gate open and the inactivation gate open as well → after some time the membrane is still depolarized and the inactivation gate closes → sodium influx doesn't occur anymore → channel remain open for a short duration of time → goes to inactivation state quickly after it has opened → to reopen the channel for this cycle the RMP needs to be established again
how the voltage gated channels change the conformation state of the channel?
the conformation depends on positively charged regions in the channel like the S4 segment which have many positively charged aa. when Vm difference across the membrane changes, the S4 segment moves. An upward movement of S4 leads to an increase of the open probability. At rest the S4 is positioned closer to the cytoplasm. So, during depolarization the S4 segment moves upward, causing the gate to open because the inner layer of the plasma membrane becomes positively charged and repels the S4 segment
phases of AP
depolarization → -70 to +30 mV : due to the opening of voltage gated Na+ channels → influx of Na+ due to an electrochemical gradient
repolarization phase: inactivation of Na+ channel and delayed opening of K+ channels → K+ efflux down to its electrochemical gradient
Threshold: voltage at which the opening probability of the voltage gated Na+ channels start to increase (high Po) → usually -55 mV
refractory period: the absolute starts immediately after the initiation of the AP and lasts until after the peak of AP due to an inactivation of sodium channels which remain inactivated until the membrane potential goes back to its RMP. The absolute one lasts from 2 to 4 ms, the sodium channels can be activated again with a strong enough stimulus
propagation of AP
AP is propagated along the axon of the neuron → neurons have a soma with dendrites and an axon → carry messages over long distances → from the brain to the spinal cord → the ones that carry messages to the muscles are motor neurons → each of its endings is close to a muscle fiber
axon → long structure → allows communication between motor neurons and muscle cells; in CNS are short (few millimeters), in PNS are longer (even one meter)
in most of the cells the AP is initiated in the initial portion of the axon (axon potential initial segment)
AP is generated in the region with the lowest threshold → in soma -35 mV; initial portion of the axon -55 mV (high density of voltage-gated Na+ channels) → so AP usually generated in the initial portion of the axon
amplitude and direction of the AP is without decrement
the propagation along an unmyelinated axon involved the regeneration of AP point by point requiring the activation of voltage-gated Na+ channels along the entire length of the axon → Na+ enters the trigger zone, creates a local current depolarizing the membrane and triggers adjacent voltage gated Na+ channels to open
propagation along a myelinated axon → in PNS axons are myelinated by Schwann cells forming a spiral of multiple layers of myelin around the axon by wrapping around it → at the end of each myelin segment there is a bare portion of the axon → nodes of Ranvier (internode) → continuous propagation; propagation along myelinated axons require the activation of voltage gated Na+ channels only in the nodal spaces so the AP can jump from one node of Ranvier to another → saltatory conduction → no need to regenerate AP continuously along the axon → speed impulse conduction
velocity of conduction increase by increasing the diameter of the axon (and decreasing the internal resistance) → local current flow is more efficient
synapse: specialized zone of contact at which one neuron transmits electrical signals to another neuron or to a muscle cell

neuromuscular junction: synapse between a peripheral motor nerve terminal and a skeletal muscle fiber
In every synapse we have:
presynaptic element → axon terminal
postsynaptic element → dendrite or soma
synaptic cleft → separate pre and post synaptic elements and through it the information is transferred
each neuron established around 1000 synaptic contacts and receives even more, in the human brain we have at least 10^14 synapses
most synapses are axodendritic while axoaxonic ones are less frequent
electrical synaptic transmission: direct passage of information without the involvement of neurotransmitters → characterized by presence of gap junctions channels allowing continuity of the cytoplasm in the pre and post synaptic neurons → AP reached the terminal end of the presynaptic neuron and continues through the gap junction to the postsynaptic neuron → direct and instantaneous transfer→ all the ions can flow through the gap junctions with a conductance of 100 pS → prevalent in invertebrates; in mammals are found in the mesencephalic nucleus of the trigeminal nerve; retina, inferior olivary nucleus, during prenatal development, hypothalamic neurons, brainstem areas → the transmission is operated by the ionic current
chemical synaptic transmission: transfer of information is mediated by neurotransmitters molecules; pre and postsynaptic terminals are separated by a synaptic cleft → synaptic delay from 0.3 to 0.5 ms → in mammals they are prevalent → double transduction of the signal → the arriving electrical signal of the AP to the presynaptic terminal is transduced into chemical signals (neurotransmitters; NT) and from here it is transduced in electrical signals by interactions between receptors located across the synaptic cleft and NTS → depolarization or hyperpolarization at postsynaptic level
Chemical transmission
presynaptic level: close to the ending of the axon
synaptic vesicles containing NTs
neurotransmitters aren't present in the cytoplasm but in vesicles → soma are located close to the presynaptic membrane ready to be fused into the synaptic cleft → high numbers of mitochondria → synaptic transmission requires ATP
ER
active zone → specialized regions where vesicles cluster → site of exocytosis and release of NTs at synaptic level
ECM maintains presynaptic and postsynaptic elements
postsynaptic element:
high density of receptors for NTs
ion channels and other receptors
Rapidity of signal transmission→ ET: instant characterized by synchronous AP generation in all of the interconnected neurons, connected by electrical synapses (neuronal syncitium); CT: delay of 0.3-5 ms
differences bw ET and CT

	ET	CT
agent of transmission	ionic current	chemical transmitter
cytoplasmic continuity	yes	no
ultrastructural components	gap junctions	active zone, vesicles and receptors
synaptic delay	absent	0.3-5 ms
direction of transmission	bidirectional	unidirectional (NTs required are only in presynaptic neurons)
action	excitatory	excitatory or inhibitory

CT requires sequential events → AP is propagated along the axon → reaches the presynaptic terminal which depolarizes → triggering of opening voltage gated calcium channels in the active zone→ influx of Ca2+ in presynaptic terminal → Ca2+ cause vesicles filled with NTs to fuse with the presynaptic membrane → NTs are released into the synaptic cleft → in postsynaptic level receptors cause depolarization or hyperpolarization of the postsynaptic compartment → change in the RMP at postsynaptic neuron
note that the rise of Ca2+ is local (at level of active zone) and transient (not permanent)
NTs → 2 classes:
small molecule transmitter substance: low molecular weight → stored in small vesicles; examples:
amino acids:
glutamergic postsynaptic transmission is the most common (80%) excitatory synaptic transmission among the CNS → neurons utilize glutamate/glutamic acid
inhibitory neurotransmitter → GABA → GABAergic neurons
glycine
monoamines
synaptic transmission at muscular junctions utilize acetylcholine (Ach)
serotonin
histamine
catecholamine:
dopamine
norepinephrine/noradrenaline
epinephrine/adrenaline
each neuron utilizes only one NT → specialized names
neuropeptides: small peptides → 2-40 AA → 10 families → >50 neuropeptides → stored in big vesicles
synthesized in the soma (ribosomes)
transported at presynaptic level with rapid axonal transport → requires microtubules
no reuptake system
glutamate synthesis
glutamatergic synaptic transmission → 80% of synaptic transmissions → biosynthesized at the presynaptic terminal (cause is a small molecule) → glutaminase (present at the presynaptic) catalyze glutamine to give glutamate; neurons are not able to synthesize glutamine → reuptake system → the source of glutamine is Glial cells → synthesize glutamate back to glutamine with glutamine synthetase
During the reuptake of glutamate, most of the molecules are transported inside the astrocytes (selective glutamate transport) and other are directly reuptaken by the presynaptic membrane. Glutamine inside the glial cells is then transported through extracellular space by transporters
Astrocytes enwrap neuronal processes → they are located surrounding synapses to better reuptake NTs → glutamate synthesis depends on astrocytes activity
GABA synthesis
20% of synaptic transmission in the cellular cortex are made by GABAenergic synaptic transmissions → the precursors of GABA is glutamate and the enzyme used is glutamic acid decarboxylase (at presynaptic)
vesicles contain small NT molecules
small molecule NTs are synthesized in the cytoplasm and stored in vesicles with constant numbers of NTs in them (103-104) → the transport of NTs in vesicles is against their chemical gradient with an active mechanism that involves vesicular transporters → the energy needed originates from an antiport → the exchange between Nts and hydrogen ions → V-ATPase → also responsible for pH gradient (cytosol 7.2, vesicles 5.5); V stands for vesicular

V-ATPase use the energy generated by hydrolysis of cytoplasmic ATP → influx of protons into the vesicle → creation of a pH gradient → transporters use the proton gradient to drive the NTs into the vesicles agains the concentration gradient
the uptake of transmitters into vesicles is energy-dependent
we have 4 vesicles transporters:
vGLUT: glutamate
vGAT: GABA
vMAT: monoamine
vAChT: acetylcholine
All of them span the vesicle membrane 12 times
Talking again about volted-gated channels, we have 2 families:
high voltage activated: require a stronger depolarization of LVA to open
low voltage activated: increase their opening probability at -40 mV
examples: P/Q (in CNS), N (in PNS and CNS) and R (CNS, PNS, kidney) are HVA channels in the presynaptic level → when AP reaches the presynaptic level the channels open during depolarization → massive influx of Ca2+
reserve pool: contains vesicles (80-95% of them) outside the active zone → cannot move freely → anchored to cytoskeletal filaments by synapsin
readily-releasable pool: docked vesicles (5-10%) at the active zone and close to the presynaptic cleft → ready to be fused → docked by SNARE proteins → form a macromolecular complex that spans the 2 membranes (presynaptic and vesicle) → close apposition
SNARE proteins → each with a lipid-loving end embedding itself within the membrane and a long tail projecting into the cytosol → specific IMP in vesicle membrane (vesicle-SNARES/v-SNARES) bind to specific receptor proteins in the target membrane (t-SNARES)
examples of t-SNARES: SNAP-25 and syntaxin (in the brain)
examples of v-SNARES: synaptotagmin and synaptobrevin
at presynaptic level synaptobrevin binds to the 2 t-SNARES forming a stable complex. The coiled structure is parallel to the plane of the membrane → vesicle and target membrane in close apposition → promotion of fusion → probability of fusion is 0 even if the vesicle is ready to do it probability of fusion increase with Ca2+ increase; synaptotagmin binds to Ca2+ as it is the Ca2+ sensor for exocytosis → it contains 2 domains that bind to phospholipids in a calcium-dependent manner → vesicle fusion with plasma membrane → release of NT by simple diffusion in the synaptic cleft
types of vesicle fusion mechanisms
kiss-and-run fusion: vesicle doesn't completely integrate itself into the plasma membrane → involvement of a fusion pore
complete fusion: vesicle completely collapses with the membrane
recycling of vesicles
when the nerve terminal is depolarized and Ca2+ enters, synapsins become phosphorylated by *calmodulin-dependent protein kinase (CaMK)* → detachment of vesicles from the cytoskeleton → movement of them into the active zone
Rab3A bound to GTP binds to synaptic vesicles → during mobilization of vesicles to the active zone → Rab3A hydrolyzes the GTP into GDP → may serve to make a reversible reaction irreversible preventing vesicles from leaving the active zone once they arrive
during fusion and exocytosis → Rab3A-GDP complex dissociates from the vesicle → exchange of GTP for GDP → association of Rab3A-GTP with a new synaptic vesicle → completion of cycle
for recycling vesicles it is necessary that the SNARE complex assemble → vesicle is free to move → after fusion, two cytoplasmic proteins NSF and SNAP bind to the SNARE complex and disassemble it
the retrieval of vesicles after exocytosis occurs with a clathrin-coated pits mechanism → clathrin-coated vesicles transport cargo from the TGN, plasma membrane or endosomal network → clathrin

is involved in the endocytotic recovery of vesicles from the plasma membrane → namely surrounds the vesicle at the region where they are fused to the plasma membrane; clathrin proteins aid invagination and constriction of the structure, and fission of the clathrin net and then uncoating of the vesicle → vesicle is free to be used again and stay in the active zone or migrate to the reserve pool → all of this happen at the presynaptic terminal
postsynaptic level have an high density of receptors to which NTs biind to → opening/closing of channels; 2 types of receptors:
ionotropic receptors: 2 functional domains → one on the extracellular side binds to NT; the other on the intracellular side forms an ion channel → binding to the NT increase the open probability of the channel; 3 classes:
Class I: 5 subunits → 2 α, 1 β, 1 γ 1 delta → each made of 4 transmembrane segments → M segments generates the pores and form the selectivity filter of the channel; examples:
Acetylcholine receptors (AChR) or Nicotinic receptors: ACh is a NT playing a role in muscle contraction → α subunit is responsible for binding ACh → the open probability increase when both α subunits bind ACh → required to open the channel:
in case of Na+ ions: channels are permeable to Na+, K+ and Ca2+ → opening of the channel lead to sodium influx of increased rate
in case of K+ ions: chemical gradient of K+ leading an efflux of them → there is also electrical gradient keeping K+ inside → opening of the channel doesn't cause a difference in K+ concentration across the membrane
binding of NT to the receptor cause rapid depolarization of the membrane → RMP of skeletal muscle goes from -90 mV to -20 mV → the difference of 70 mV is called end-plate potential → due o the intensity of depolarization one single synaptic transmission can generate the AP → cause skeletal muscle cells to contract
note that the synapse in this case has numerous active zones not like in the central synaptic transmission where the number of active zones is few → indeed in the CNS one synaptic transmission causes a change of about 0.1 to 0.4 mV
GABA receptors (GABAa): neurotropic receptor → mediates inhibitory synaptic transmission → responsible for the hyperpolarization of the membrane → they are permeable to Cl- ions → 5 subunits → M2 segment of each subunit forms the channel pore → when binds GABA it becomes selective and let the passage of only Cl- → Cl- is more concentrated outside the membrane than inside → chemical gradient for Cl- to enter → hyperpolarization of the membrane; there is also electrical gradient counteracting the chemical gradient and allow efflux of Cl- → however chemical gradient is stronger → influx of Cl-
during development of CNS, some GABAergic synaptic transmitters inhibitors because chemical gradient is inverted → electrical gradient is stronger → Cl- efflux → depolarization of the membrane → inhibitory synaptic transmission
Class II: 4 subunit → each made of 4 transmembrane segments → 3 of the M segments span the bilayer, the M2 doesn't and is located towards the intracellular side only partially spanning the membrane:
glutamate receptors → M2 segment forms a loop that lines the channel pore → the receptor can be divided into 3 subtypes on their selective exogenous agonists:
AMPA and keinate: highly permeable to Na+ and K+, low permeability for Ca2+ → rapid kinetics → their generated AP peaks in a couple of ms
NMDA: equal permeability to Na+, K+ and Ca2+ → slow kinetics → require few seconds for their AP to peak → their action can be blocked by magnesium ions → one ion is sufficient to block one NMDA channel → the block is removed only upon the depolarization of the membrane ; when NMDA opens → influx of ions, mostly Ca2+ that play fundamental role in synaptic transmission
Class III: 3 subunits → trimeric complex → activated by ATP
metabotropic receptors: not channels → just receptors binding NTs and gating ion channels indirectly → binding of NT activates an intracellular cascade → change in function of a channel →

channels can be G-protein activated channels in this case; second messengers activated by G-protein affect both influx and efflux of ions via the channel → the second messenger can result in the opening or closing of an ion gated channel; these receptors are made of a single polypeptide chain with 7 helical transmembrane segments; we have metabotropic receptors for each NT → for glutamate there are 3 classes, for GABA 2 and dopamin 5. Domaine, histamine, serotonin and adrenaline all act on these receptors
enzymatic cycle for G-protein
G-proteins bind and hydrolyze the GTP → family of 20 types of proteins → heterotrimeric → 3 subunits: α, β and γ → there are many subunits of them → many combinations; after NT binds to a metabotropic receptor it interacts with G-protein → conformational change in the G-protein → exchange of GDP to GTP → after G-protein dissociated 2 things can occur: Galfa subunit activate an enzyme leading to the formation of a second messenger activating downstream enzymes and altering ion channel functions so increasing the open probability of the channel (second messenger cascade); or the Gbetagamma subunit interact with ion channels directly without requiring the second messenger leading to an increase in the open probability of the channel (shortcut pathway, used in muscarinic receptors in the heart)
G- protein classes are defined based on the sequence and function of their α-subunits into 3 categories:
GalfaS and Galfaq: stimulatory (increase of cAMP and/or protein phosphorylation → stimulate adenyly cyclase)
Galfai: inhibitory (decrease of cAMP and/or protein phosphorylation → inhibits adenylyl cyclase)
Galfa subunit activates adenylyl cyclase leading to an increase of cAMP which activates protein kinase A which phosphorylated protein channels → increase of open probability
G-protein-coupled receptors signaling characteristics:
long delay in comparison to ionotropic receptors (fast) → the cascade is complex and slow
amplify signals (activation of one G-protein-coupled receptor lead to the activation of many ion channels)
the use of small messengers that can diffuse quickly (like cAMP) allows signaling at distance
signal cascades generate very long-lasting chemical changes in cells
focus on the types of channels:
voltage-gated: controlled by membrane potential
ligand-gated: controlled by binding of a ligand involved in AP propagation → form the extracellular side of the ionotropic receptors
stress-activated: controlled by mechanical force exerted on the cell
at the end of the postsynaptic transmission, an electrical signal represented by an AP is transmitted to another neuron; we have:
EPSP: excitatory postsynaptic potential leading to a small depolarization (less negative)
IPSP: inhibitory postsynaptic potential leading to an hyperpolarization (more negative)
we have 2 types of electrical signals that can be generated in excitable cells:
graded potentials (postsynaptic potentials):
can be depolarizing or hyperpolarizing
amplitude is proportional to the strength of the stimulus and is generally small
may last a few ms to seconds
generated by ion channels which can be ligand-gated (extracellular ligands like NTs) or mechanosensitive
ions involved are Na+, K+, or Cl-
temporal summation and spatial summation
travel by passive (electrotonic) spread to neighboring membrane regions
amplitude diminishes as graded potentials travel away form the initial site (decremental) → electrotonic conduction
APs:

always lead to depolarization and reversal of the membrane potential
all-or-none amplitude (no matter the strength of the stimulus, amplitude will always be the same)
large amplitude of about 100 mV
duration of 3-5 ms
generated by voltage gated Na+ and K+ channels
ions involved are Na+ and K+
summation is not possible due to the all-or-none nature and the presence of refractory periods
the propagation to neighboring membrane regions is characterized by the regeneration of a new AP at every point along the way
amplitude doesn't diminishes cause AP propagate along neuronal projections (non-decremental)
a single synaptic transmission cannot trigger an AP in a neuron in CNS because the RMP is -65 mV. After a single excitatory synaptic transmission the RMP can increase to -64 mV, but the threshold of a neuron is -55 mV, so a single synaptic transmission is unable to generate an AP. For preventing this we have the neuronal integration → neurons receive thousands of synaptic impulses constantly and many of these are excitatory while others inhibitory → neuronal integration causes a summation of all the signals that a neuron receives → resulting in a combination effect determining whether the threshold is reached or not; in case of equal number of excitatory and inhibitory signals, the combined effect is cancelled and the neuron remains in its initial polarized state
threshold in axon → -55 mV; in soma → -35 mV (we need a stronger depolarization to generate an AP due to the higher density of Na+ and K+ channels in the soma)
2 types of integration methods:
temporal integration: multiple signals act at the same site of the neuron and get added up if the signals are received in a short time interval → if there is a large time interval between the signals they are not added up → the high frequency stimulation in the synapse generates an AP
spatial integration: multiple signals received at various sites of the neuron are integrated or added up; when signals are received at multiple synapses the signal is received by the membrane and it propagates along the membrane with a decrement → the propagated signal reach the synapse, get summed up and generate an AP
neurotransmitter recovery and degradation
during a synaptic transmission the vesicles fuse with the membrane and release the NTs in the synaptic cleft → high concentration of NTs in the cleft → concentration needs to be reduced for another synaptic transmission to take place in the synapse and is reduced by:
diffusion: simple diffusion of NTs through the extracellular fluid away from the synapse → are diffused to where their concentration is lower
reuptake of NTs: aid the diffusion by the presynaptic axon terminal; it occurs by the action of specific NTs transporter proteins located in the presynaptic membrane → once in the cytosol of the terminal, the transmitters may be reloaded into synaptic vesicles or enzymatically degraded → their breakdown products are recycled
enzymatic degradation: this is how ACh is removed at the neuromuscolar junction → the enzyme acetylcholinesterase (AChE) is deposited in the cleft by muscle cells → AChE cleaves the ACh molecule rendering it inactive at the ACh receptors
when we consider neuropeptides there is no reuptake of them by the presynaptic axon terminal, and there is a slow reduction in their concentration → this occurs mainly by diffusion to the extra-synaptic space or by breaking of peptides thanks to peptidases