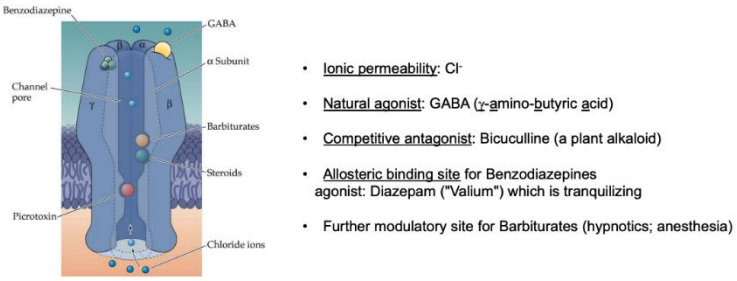
Neuroscience BIO-311 Ramdya
Solutions of exercises for
Unit 3: Synaptic Transmission: Principles and excitatory synapses

1) (i) What distinguishes an "excitatory" from an "inhibitory" transmitter? (ii) Name two receptors which can inhibit a neuron. (iii) Explain how their activation leads to the inhibition of a neuron (ion conductance?).

(i) Excitatory: non-selective cation channel (AMPAR, NMDAR), G_q or G_s. These tend to depolarize the cell membrane, or increase specific cellular processes (*phosphorylation*)
Inhibitory: Ligand-gated Cl- channel (GABAR), or $G_{i/o}$. These tend to hyperpolarize the cell membrane, or decrease specific cellular processes (*phosphorylation*)

(ii) GABA or Glycine receptor

The GABA receptor, some facts



- Ionic permeability: Cl^-
- Natural agonist: GABA (γ-amino-butyric acid)
- Competitive antagonist: Bicuculline (a plant alkaloid)
- Allosteric binding site for Benzodiazepines agonist: Diazepam ("Valium") which is tranquilizing
- Further modulatory site for Barbiturates (hypnotics; anesthesia)

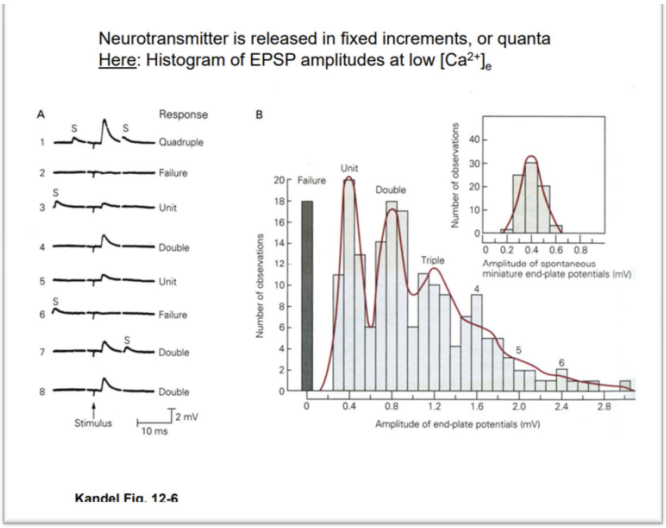
(iii) Both receptors are permeable to Cl^-. Under normal conditions, the equilibrium potential of Cl^- is around -80 mV, which will hyperpolarize the cell when the channels are open.

2) What is the "quantal theory" of synaptic transmission? Explain what is a "miniature EPSP" (at the neuromuscular synapse), and how the observation of such "minis" has given rise to the "quantal" theory of synaptic transmission.

(i) Quantal theory: neurotransmitters are released at synapses in pre-determined unit sizes called "quanta"
(later shown = content of 1 synaptic vesicle)

(ii) Miniature EPSP: spontaneous synaptic potentials that occurred in the absence of motor neuron stimulation (presynaptic stimulation).
A miniature EPSP is caused by spontaneous release of one vesicle.

(iii) The amplitude distribution of EPSPs is step-like. The amplitude of a miniature EPSP is comparable to the step unit (or "quantal") size of the EPSPs.

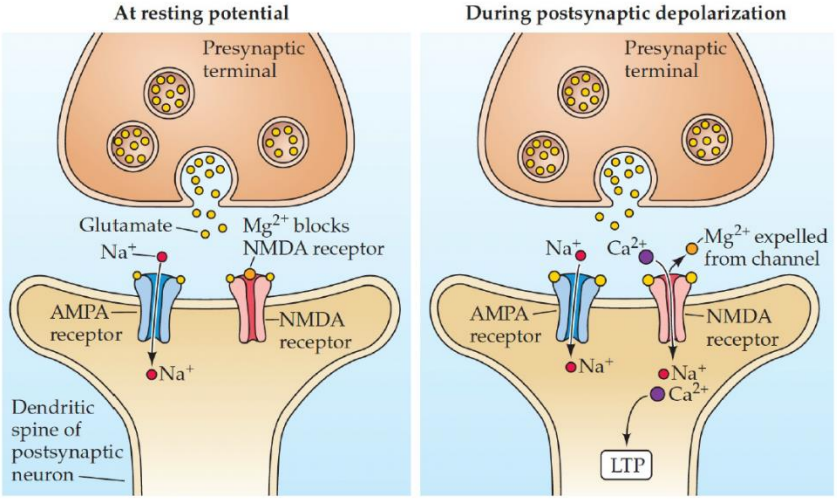


Kandel Fig. 12-6

3) (i) What are the respective effects of glutamate and GABA on a typical postsynaptic adult mammalian neuron? (ii) Specifically name the effects of either Glutamate and GABA binding to a downstream neuron (depolarization, or hyperpolarization). (iii) What might happen if a neuron receives equal amounts of both Glutamate and GABA at the same time?

(i) Glutamate – excitatory
GABA – inhibitory
(ii) Glutamate – depolarizing
GABA – hyperpolarizing
(iii) Nothing happens. The depolarization and hyperpolarization cancel one another. The exact effect can vary from a neuron to another, e.g. depending on the density of postsynaptic receptors.

4) One mechanism for learning is thought to be the strengthening of the synaptic connection between neurons that fire together frequently, called long-term potentiation (LTP).
Explain how AMPA and NMDA can mediate this learning.

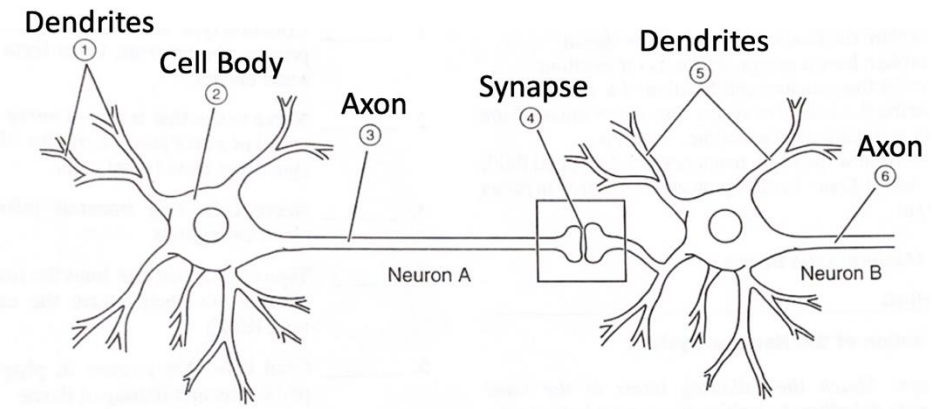


- Voltage-dependent Mg^{2+} ion block of NMDA channel means the channel can only function if
  (i) glutamate is bound (**pre**synaptic activity) **AND**
  (ii) the Mg^{2+} block is relieved (**post**synaptic depolarization)
- This serves as a means of **"coincidence detection"** for pre- and postsynaptic activity
- The resulting Ca^{2+} influx induces synaptic plasticity via long-term potentiation (LTP)

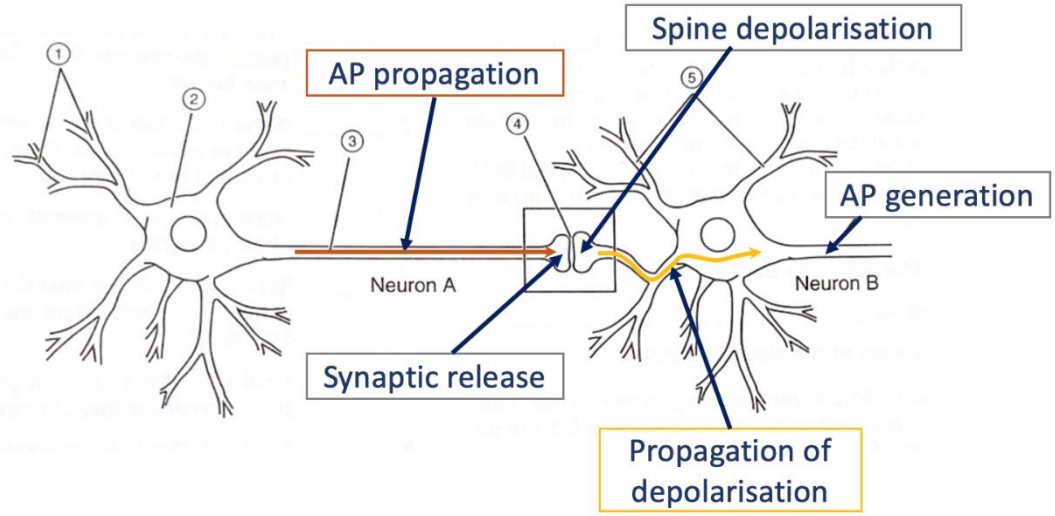
5) Suppose that an excitatory neuron A synapses onto a neuron B, such that when neuron A fires, it is followed by neuron B.

i. Draw a schematic of their connection, indicating the dendrites, synapses, cell body, and axon.
ii. Indicate the following on the drawing: action potential propagation, synaptic release, depolarisation of the spines, propagation of depolarisation current, action potential generation.
iii. Draw the membrane potential at a dendritic spine and at the axon hillock of neuron B from the moment that an AP appears in neuron A to the moment an AP appears in neuron B.
iv. Given that firing of neuron A results in firing of neuron B (in this exercise, not in general!), what can we hypothesise on the number of synapses between both?

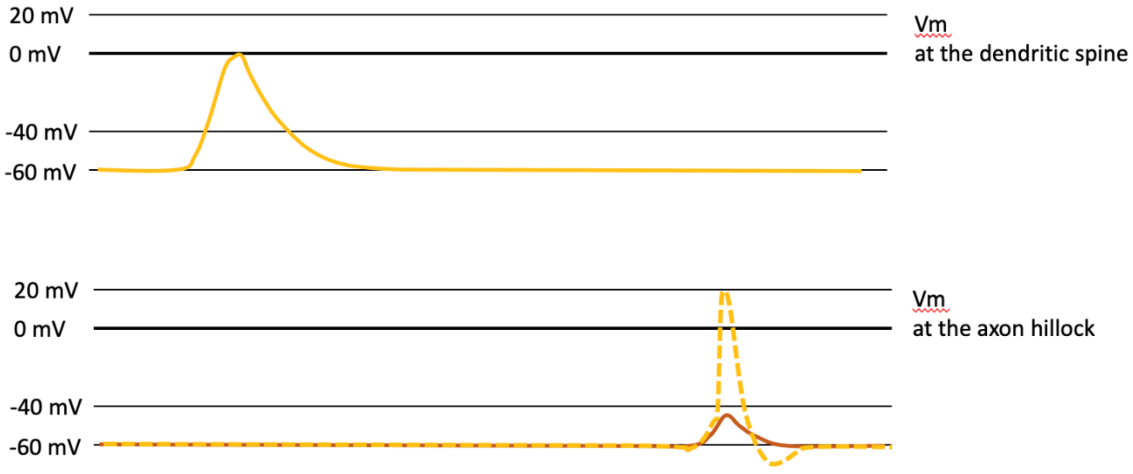
i)



ii)



iii)



In general, the depolarization is damped as it propagates along the dendrites due to the passive properties of the cell membrane. The generation of an AP depends on the resulting depolarisation at the axon hillock.

iv) It is likely that neurons A & B are connected through many synapses in parallel (sometimes thousands).