Types of neurotransmitter receptors

Even though there are many (>100) neurotransmitters, there are often several distinct receptors for each - mediating different types of response. (e.g. >10 receptor sub-types for glutamate).

There are 2 basic mechanisms by which receptors control ion flow across the postsynaptic membrane:

① Ionotropic Receptors

Receptor site and ion channel are part of the same molecule (e.g. ACh-activated channel at end-plate)

These mediate fast synaptic responses - direct through-put of signals in the nervous system.

② Metabotropic Receptors

Receptor and channel are different proteins, physically separated in the cell membrane. The link between them is a diffusible intracellular second messenger.

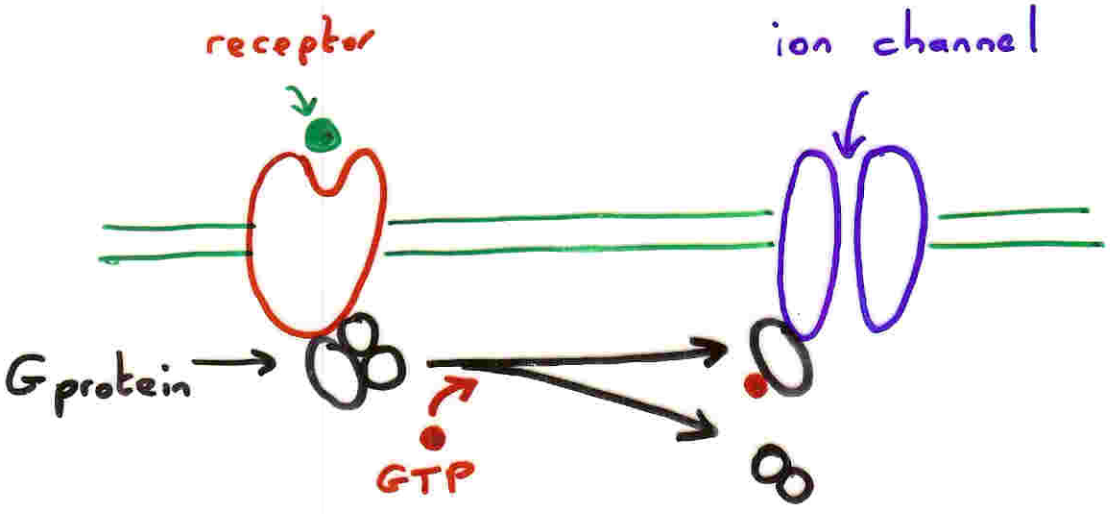


Fig. 7.4C

↑

Binding of neurotransmitter to receptor causes GTP to bind to G protein, which then dissociates into two subunit pieces (α and βγ). One of these may then control the opening of an ion channel, or ↓

A G protein subunit causes a separate effector protein (enzyme) to make a further second messenger, which in turn controls an ion channel.

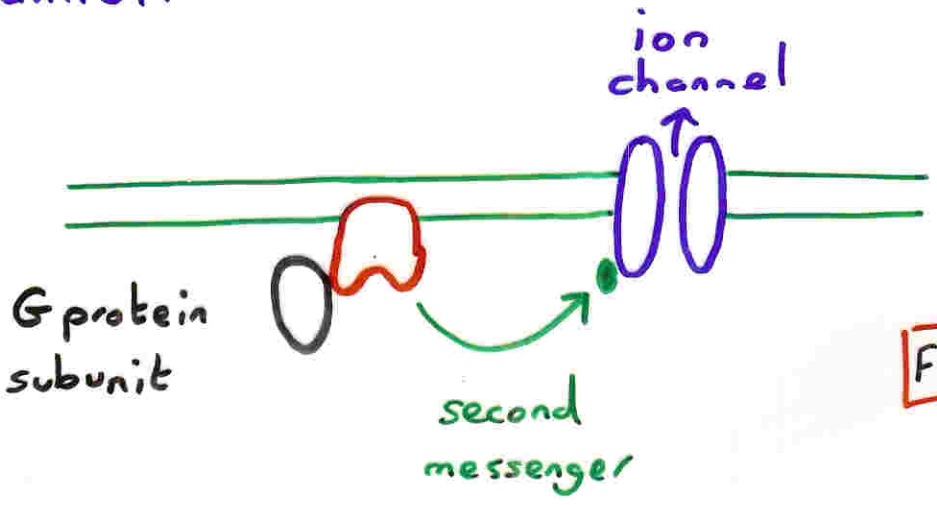


Fig. 7.5A

examples of second messengers:

- cyclic AMP
- cyclic GMP
- inositol trisphosphate
- diacylglycerol

Second-messenger-mediated responses are relatively slow and prolonged. Tend to serve to modulate the transmission of fast signals through the nervous system

Postsynaptic excitation and inhibition

Excitation – current flow through ion channels tends to depolarize cell toward threshold for triggering action potential

Inhibition – current through channels tends to stop action potentials from firing (but does not necessarily hyperpolarize the cell)

Whether a given synapse is excitatory or inhibitory depends on which ions go through the channels.

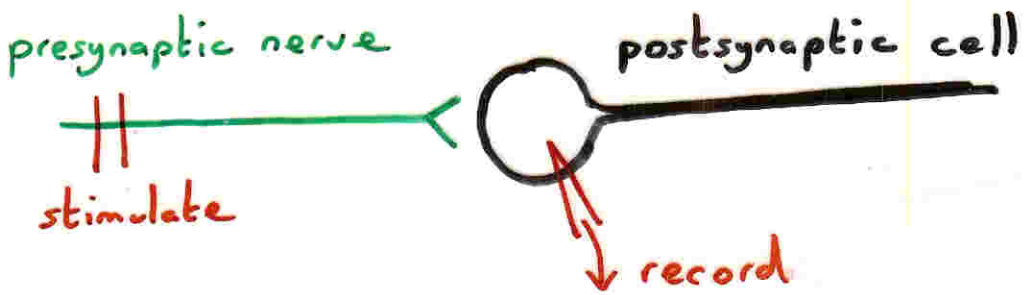
A particular neurotransmitter can be excitatory or inhibitory – depending on receptor sub-type: but some are most always excitatory (e.g. glutamate) or inhibitory (e.g. GABA)

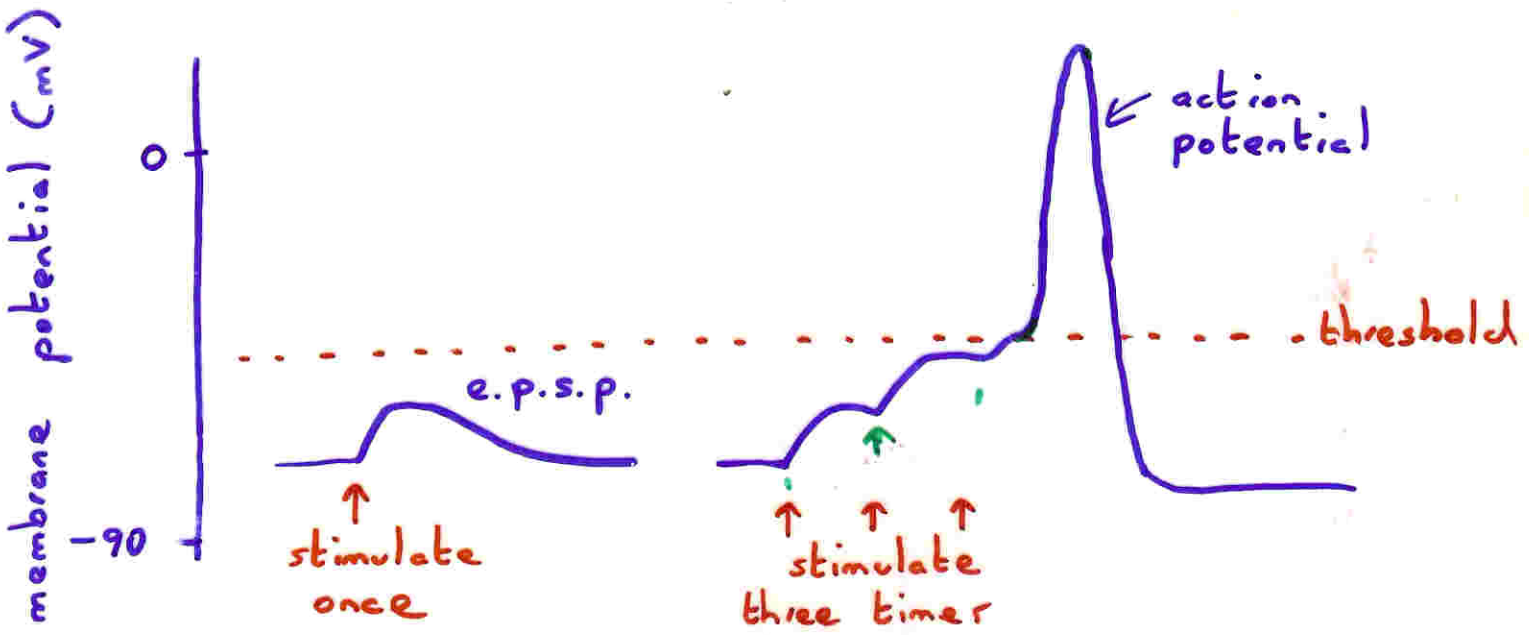
Integration of excitatory signals

① Temporal Summation

The e.p.s.p. (excitatory post-synaptic potential) produced by a single presynaptic action potential may not be enough to depolarize a postsynaptic cell to the threshold for an action potential.

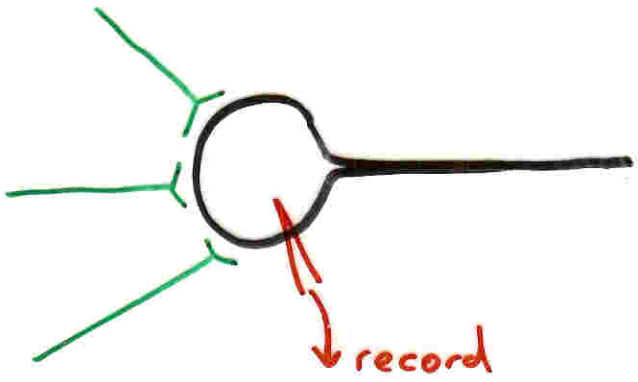
But – if there are several action potentials in quick succession, e.p.s.p.s summate to depolarize abobe the action potential threshold.

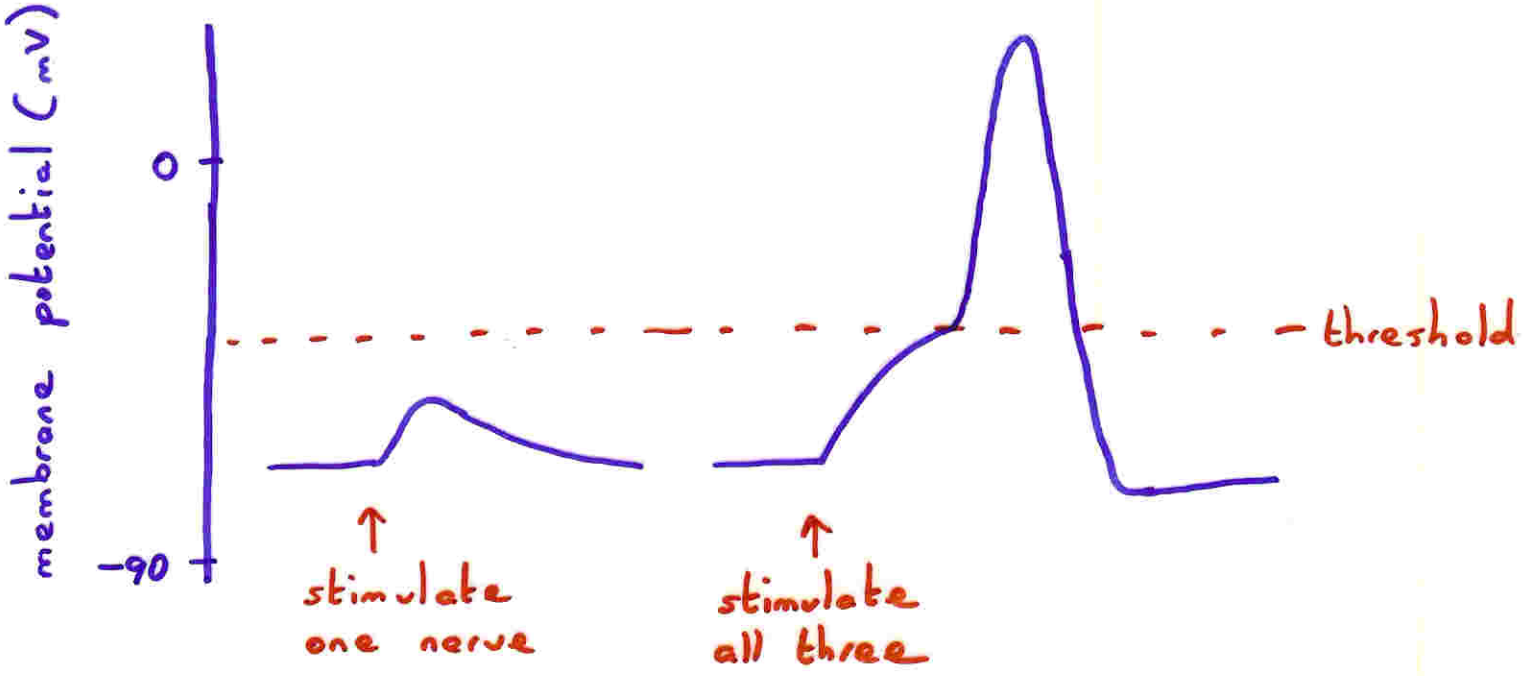




② Spatial summation

Action potentials in several presynaptic nerves may give e.p.s.ps that summate to reach threshold, even if e.p.s.p. from a single nerve is too small.





Inhibitory conductance changes

e.g. receptors to GABA.

GABA opens channels permeable to Cl^- ions.

Equilibrium (Nernst) potential for Cl^- in neurons is about −80mV. So action of GABA is to make cell's potential go toward −80mV.

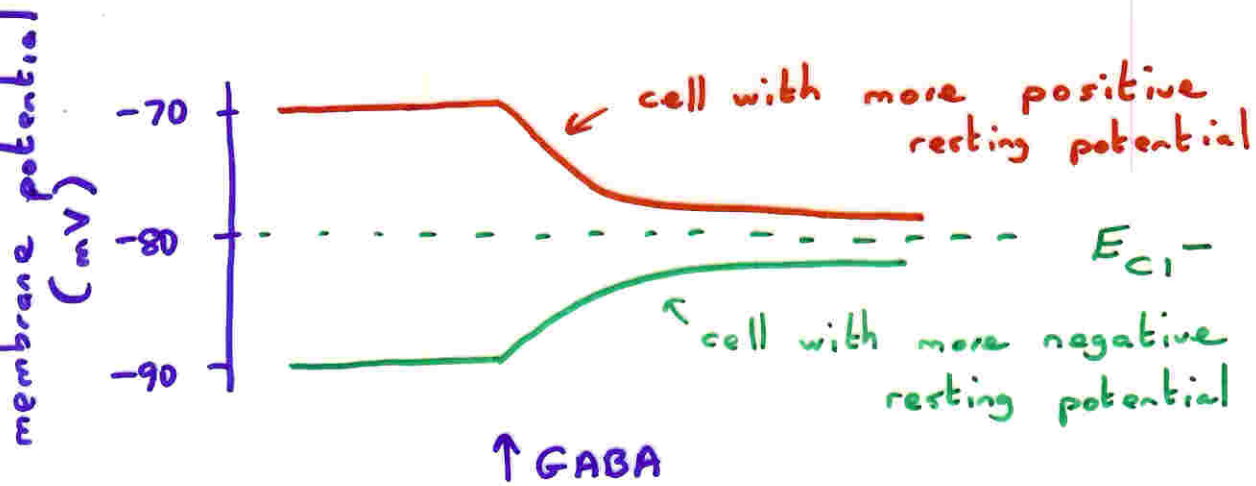


Fig. 5.19

If GABA can cause a depolarization, why is it inhibitory?

① Potential change evoked by GABA cannot go more positive than −80mV : this is well below threshold for action potential.

② Cl^- current through GABA-activated channels tends to hold cell at −80mV, opposing depolarization by excitatory synapses.

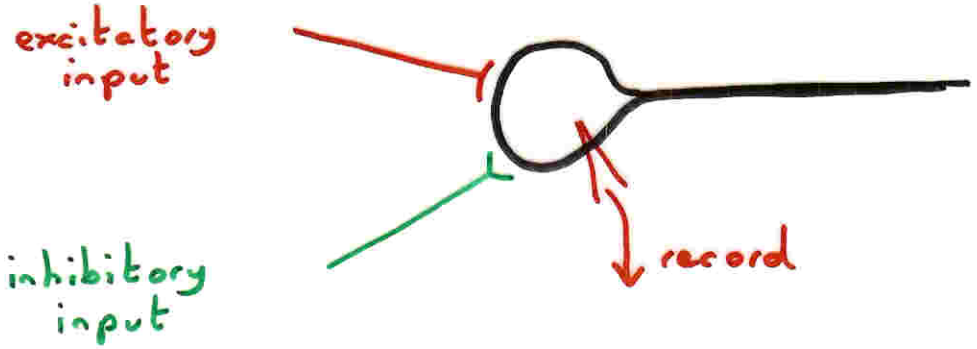
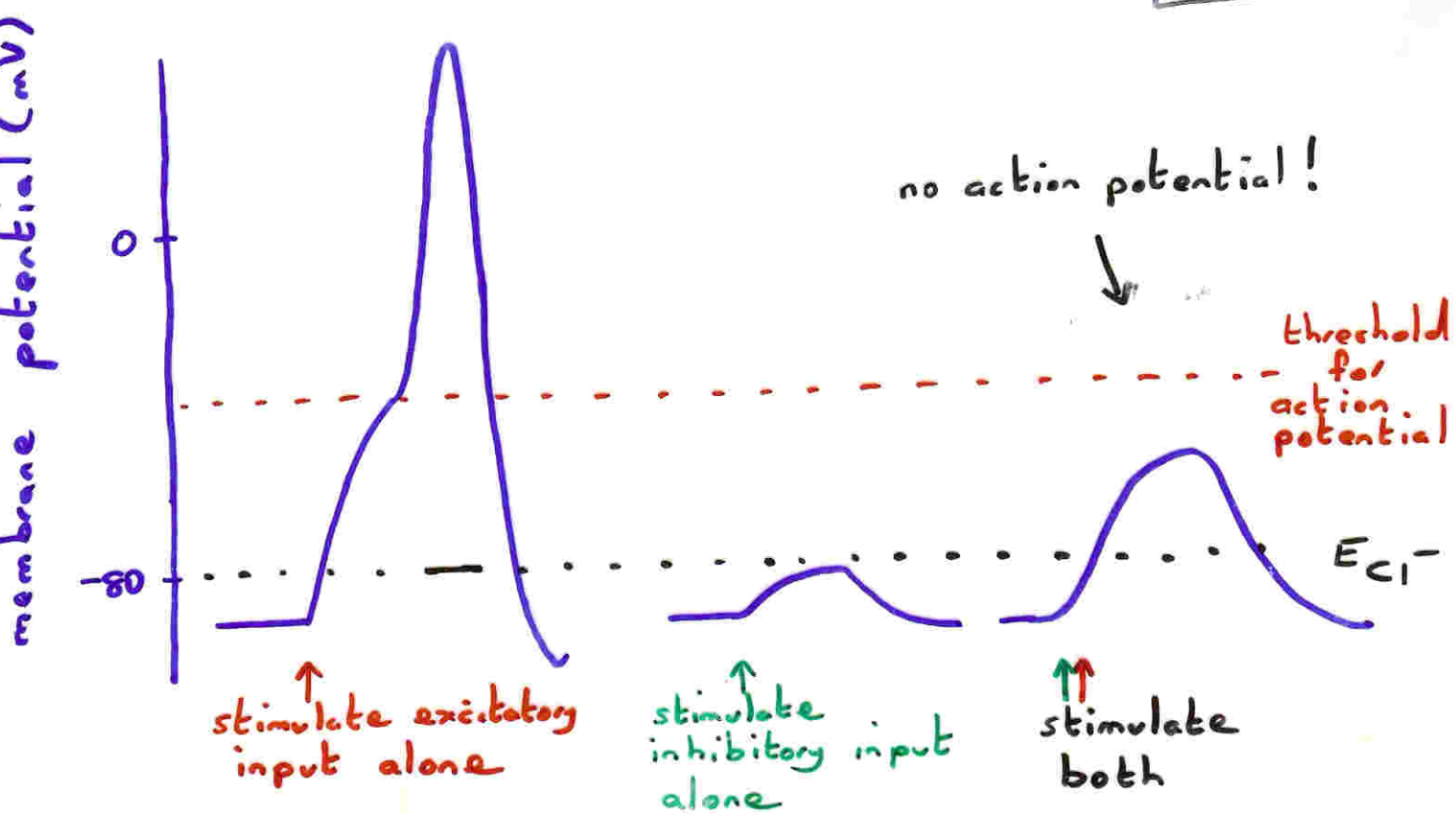
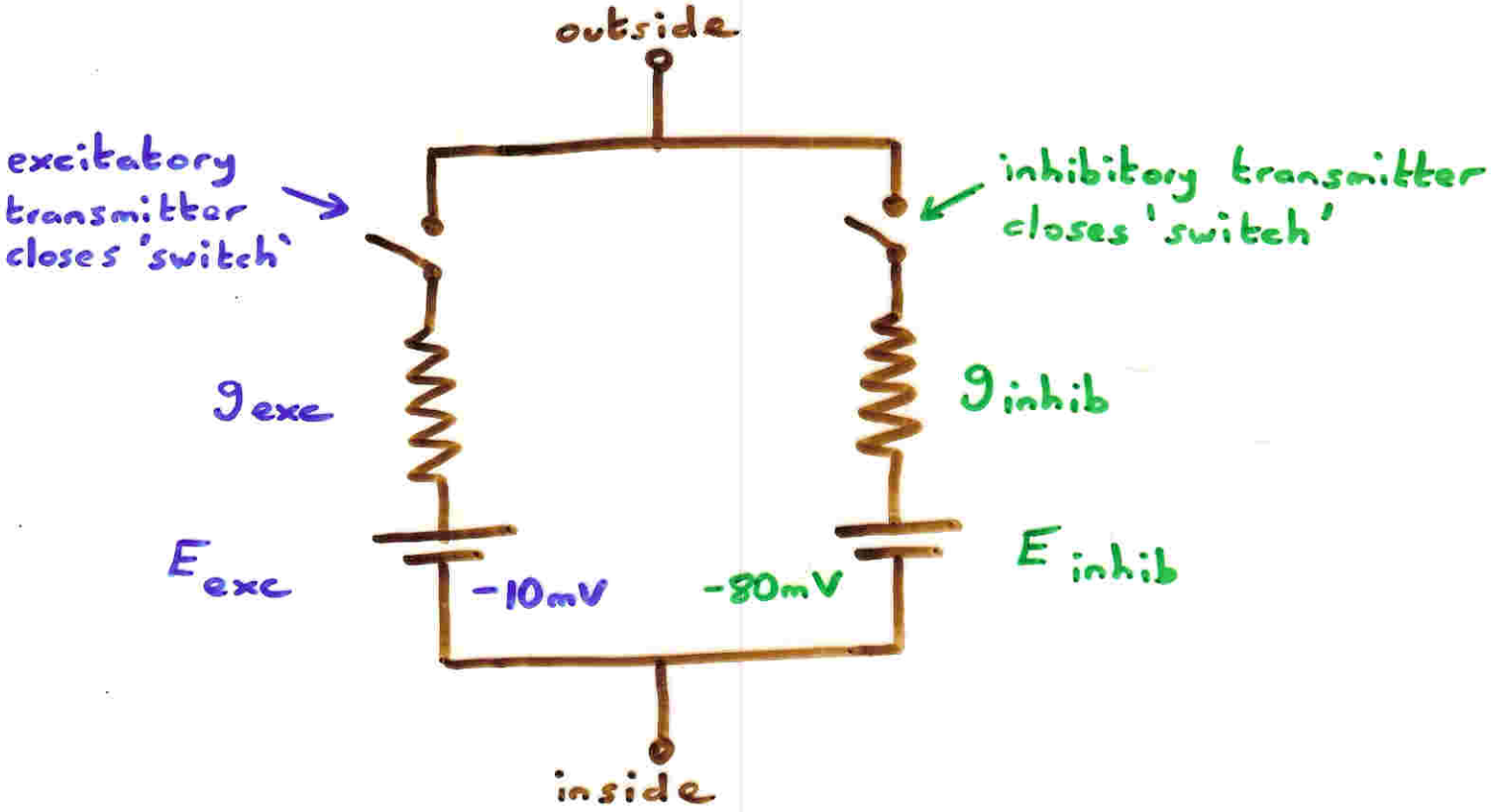


Fig. 5.20



If have both excitatory and inhibitory inputs, the potential toward which the cell polarizes depends on the relative sizes of the excitatory (g_{exc}) and inhibitory (g_{inhib}) conductance changes.



e.g. if $g_{exc} = g_{inhib}$, cell would depolarize toward potential midway between E_{exc} and E_{inhib}: about -45 mV.