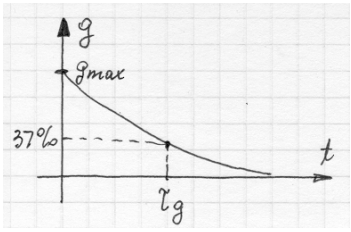
13.3 Chemical synapse modeling

- We previously utilized square wave (Fig. 11.8) and alpha function (Fig. 11.12) current injections as inputs to our models.
- The former was a realistic model of current injected through an electrode by an experimentalist.
- The latter was an intermediate model that had the approximate form of a synaptic current.
- Chemical synaptic responses are actually conductance changes rather than current injections.
- A synaptic conductance change will permit current flow.
- As I show, sometimes it is the synaptic conductance change, rather than the synaptic current, that affects postsynaptic activity.
- The Hodgkin-Huxley model describes membrane rheostats controlled by voltage.
- Chemical synapses are membrane rheostats controlled by neurotransmitters.
- When modeling a network, these neurotransmitters are not explicitly included.
- Instead, a spike in a presynaptic neuron is used to activate a rheostat in the postsynaptic neuron.
- The postsynaptic rheostat represents an ion channel triggered by a postsynaptic receptor.
- Depending on the polarity of the battery associated with that rheostat (inward positive or inward negative), that synapse could be, made excitatory or inhibitory (Fig. 13.2).

- As with most things in nature, chemical synaptic transmission is terribly complex.
- Synaptic simulation can be made terribly complex as well.
- A full synaptic model would have to consider chemical diffusion, reuptake, breakdown, and interaction with proteins before one even gets to a receptor.
- Then, at the receptor level, one would consider the fact that receptors are proteins that typically have multiple states (each of which could be included in a more complex model, e.g., a Markov model).
- This gives them properties such as activation, deactivation, inactivation, and deinactivation as well as desensitization (channel turns off if the chemical ligand has been sitting there too long),
  allosteric interactions (other chemicals binding at different sites can alter the response to the main neurotransmitter),
  and multiple binding sites (more than one molecule must bind for the channel to open).
- Then, there's the fact that the synapse can grow and change.
- This depends not only on classical learning effects but also on more low-level adaptation to the chemical environment.
- For example, receptors will typically upregulate (more receptors will be inserted into the membrane) if they do not see much neurotransmitter for a while and downregulate in the converse condition.
- They can also change shape and shift the location of receptors.

- Of course, we want to ignore all of that and focus on the basics: a chemical is released and binds, the associated channel opens (activates) and then closes (deactivates).
- For simplicity, we will have the channel open instantly.
- This means that the conductance will go instantly from 0 to g_{mx} and the current will also shoot up instantly.
- However, the voltage will not shoot up since the membrane capacitance provides a brake.
- We will then use an exponential decay for conductance inactivation.
- This corresponds to the simple differential equation for conductance:

$$\tau_s \frac{dg_s}{dt} = -g_s + g_{mx}\delta(t) \tag{13.1}$$



- Assuming that at $t = 0$ the conductance is $g(0) = g_{mx}$, as described in eqn (13.1) by Dirac's delta function $\delta(t)$, the solution of the above equation is a decaying exponential:

$$g_s(t) = g_{mx} e^{-\frac{t}{\tau_s}} \tag{13.2}$$

- To get a more realistic model of the synaptic conductance we can assume that an instantaneous release of neurotransmitters c_m at time $t = 0$ binds them according to a first order differential equation

$$\tau_s \frac{dc}{dt} = -c + c_m\delta(t) \tag{13.3}$$

  where $\delta(t)$ (Dirac's delta) represents an initial instantaneous release of neurotransmitters.
- The chemical c now drives the synaptic conductance through a appropriately modified eqn (13.1):

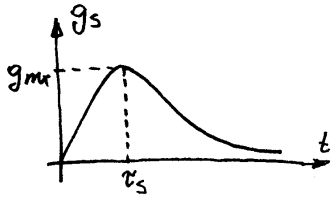
$$\tau_s \frac{dg_s}{dt} = -g_s + c \tag{13.4}$$

- It can be shown that the solution to the pair of first order differential equations (13.3) and (13.4) is given by the following alpha function:

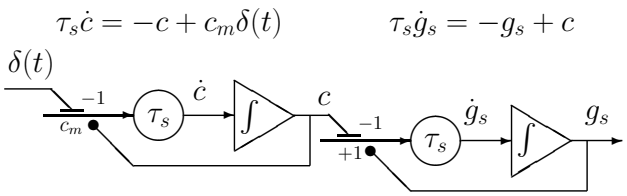
$$g_s(t) = \frac{c_m}{\tau_s} t e^{-\frac{t}{\tau_s}} \tag{13.5}$$

- The alpha function attains the maximum

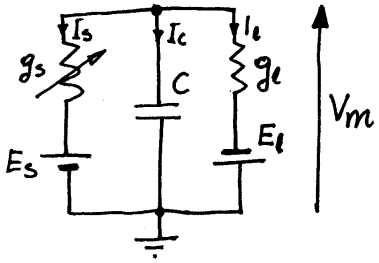
$$g_{mx} = \frac{c_m}{e\tau_s} \ , \text{ for } \ t = \tau_s$$



- The pair of differential equations (13.3) and (13.4) can be also represented by the following diagram



- The resulting conductance pulse is the input to a patch (a compartment) of the neuronal membrane in which the synapse is embedded.
- We will now consider details of an electrical model of the "fast voltage-independent" chemical synapse embedded into a patch of neuronal membrane.
- Voltage-independent means that the parameters of the electrical model are independent of the membrane voltage.
- As explained above the synaptic input is modelled by the increase in the membrane conductance.



g_s — synaptic conductance
E_s — Synaptic reversal potential (battery)
C, g_l, E_l — parameters of the membrane patch (compartment)
V_m — membrane patch voltage

- The currents through three branches are calculated as for the Hodgkin-Huxley membrane model:

$$I_s = g_s(V_m - E_s)\ ; \quad I_C = C\frac{dV_m}{dt}\ ; \quad I_l = g_l(V_m - E_l)$$

- On the basis of Kirchhoff's law the sum of all currents must be zero, which gives the following differential equation:

$$C\frac{dV_m}{dt} = -g_s(V_m - E_s) - g_l(V_m - E_l)$$

- Dividing by g_l and denoting the passive membrane time constant $\tau_m = \dfrac{C}{g_l}$ we can re-write the above equation into the following standard form:

$$\tau_m\frac{dV_m}{dt} = -(1 + \frac{g_s}{g_l})V_m + \frac{g_s}{g_l}E_s + E_l \tag{13.6}$$

where g_s is given by eqn (13.5).

- Now we will compare the excitatory and inhibitory synaptic responses assuming for simplicity the exponentially decaying channel conductance.

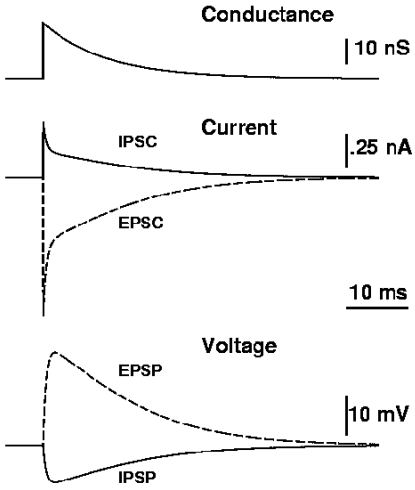


Fig. 13.3: Behaviour of a chemical synapse:

- Excitatory and inhibitory synaptic responses are compared.
- The same conductance is used in both cases.
- However, the synaptic reversal potentials (E_s) differ.
- For this reason the excitatory postsynaptic current (EPSC) is negative (inward and depolarizing — dashed line)
- while the inhibitory postsynaptic current (IPSC) is positive (outward and hyperpolarizing —solid line).
- This is the result of the expression for current: $I_s = g_s(V_m - E_s)$

- In the case of the excitatory synapse, the reversal potential (E_s) is more positive than resting potential.
- For the inhibitory synapse, the reversal potential is more negative than the resting membrane potential (RMP).
- Although the conductances in Fig. 13.3 are the same in both the excitatory and inhibitory cases, the magnitudes of both postsynaptic currents and postsynaptic potentials differ.
- The differing size of EPSC and IPSC reflects the difference between membrane voltage and E_s in each case: $V_m - E_s$

- E_{excit}, is far from rest, while E_{inhib} is close to rest.
- This potential difference is called the driving force for the current.
- In Fig. 13.3, the initial driving force ($RMP - E_s$) is $-70 + 20 = -50$ mV for the excitatory case, and $-70 + 90 = 20$ mV for the inhibitory case.
- As membrane voltage moves toward E_s, driving force gradually decreases.
- A very large synaptic conductance can drag membrane voltage all the way to E_s.