Synaptic Conductance Models

BENG/BGGN 260 Neurodynamics

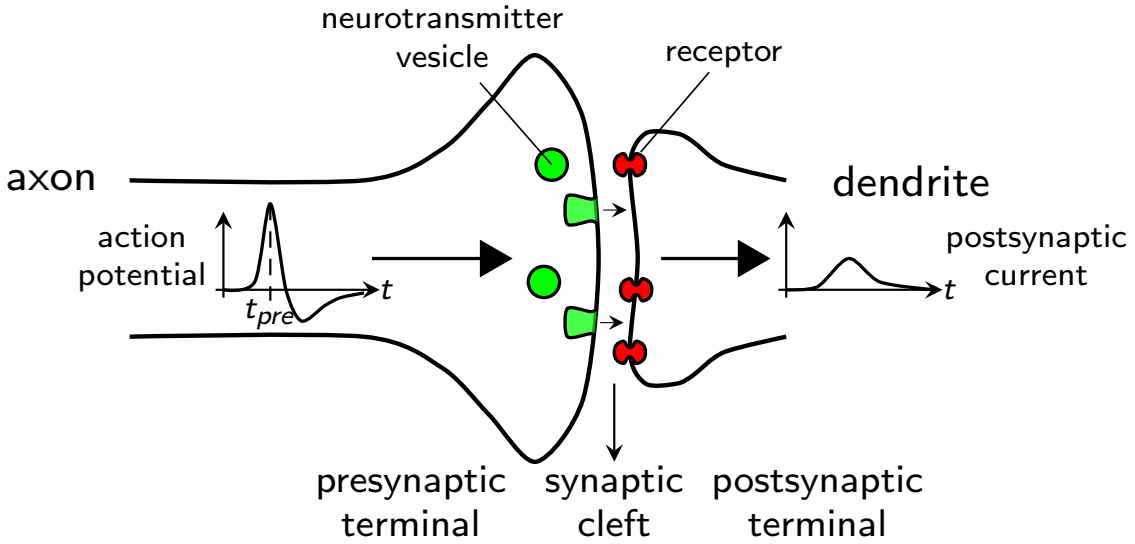
University of California, San Diego

Week 4

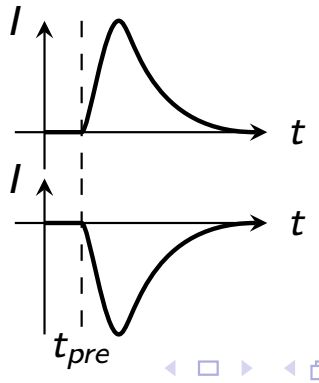
Reading Material

- C. Koch, *Biophysics of Computation*, Oxford Univ. Press, 1999, Ch. 1, pp. 14-23 and 85-115.
- B. Hille, *Ion Channels of Excitable Membranes*, Sinauer, 2001, Ch. 6, pp. 169-100.
- A. Destexhe, Z.F. Mainen and T.J. Sejnowski, "Synthesis of Models for Excitable Membranes, Synaptic Transmission and Neuromodulation Using a Common Kinetic Formalism", *J. Comp. Neuroscience*, vol. 1, pp. 195-230, 1994.
- P. Dayan and L. Abbott, *Theoretical Neuroscience*, MIT Press, 2001, Ch. 5.8, pp. 177-178.

Synaptic Transmission



- Presynaptic action potential triggers release of neurotransmitter (through Ca^{2+})
- Postsynaptic binding of neurotransmitter at receptor induces opening of a channel leading to a postsynaptic current
  - Excitatory (AMPA, NMDA, ...)
  - Inhibitory ($GABA_A$, ...)



EPSC $\rightarrow$ EPSP

IPSC $\rightarrow$ IPSP

Synapses are Stochastic

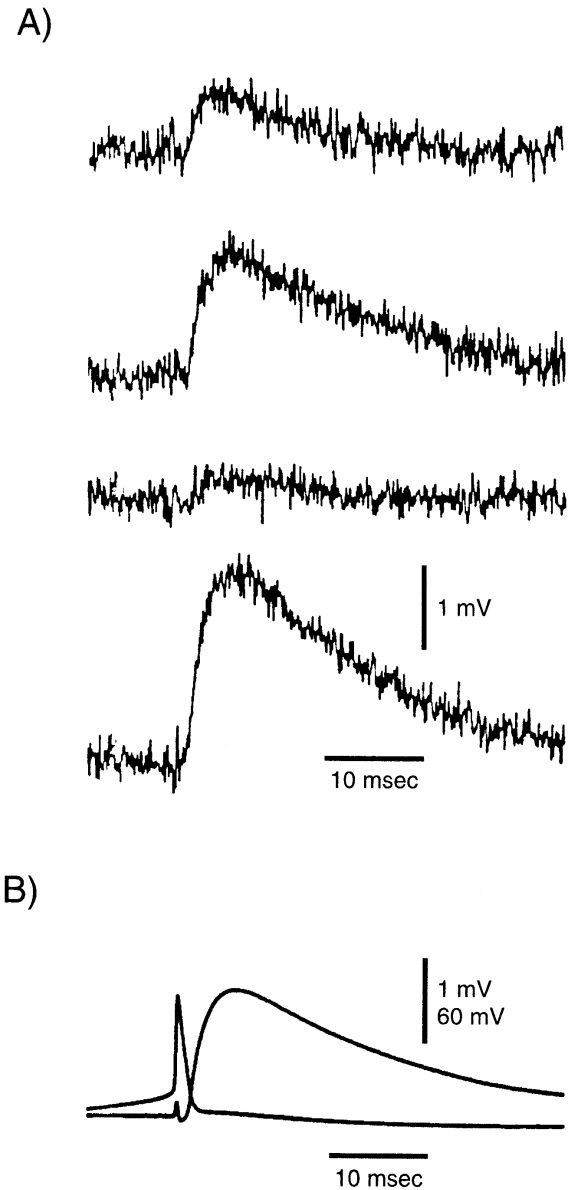


Fig. 4.4 Postsynaptic Amplitude Is Highly Variable

Fluctuations in the amplitude of EPSPs observed in a pyramidal cell by evoking an action potential in a nearby pyramidal cell. Both pairs of neurons are located in layer 2/3 of brain slices taken from rat visual cortex. **(A)** Four individual sweeps from the same synaptic connection. The EPSP amplitude over the entire population of cell pairs is 0.55 ± 0.49 mV. **(B)** Average of 2008 such sweeps, together with the presynaptic record, showing that the EPSP in the postsynaptic cell is caused by the presynaptic spike. Due to technical reasons, no events less than 0.03 mV — and, in particular, no failures as in Fig. 4.3 — can be recorded. Reprinted by permission from Mason, Nicoll, and Stratford (1991).

$$\mathbf{R = npq}$$

R: mean rate synaptic response

n: number of quantal release sites

p: probability of release per site

q: response per quanta released

Koch 1999, p. 91-92

Synaptic Conductance

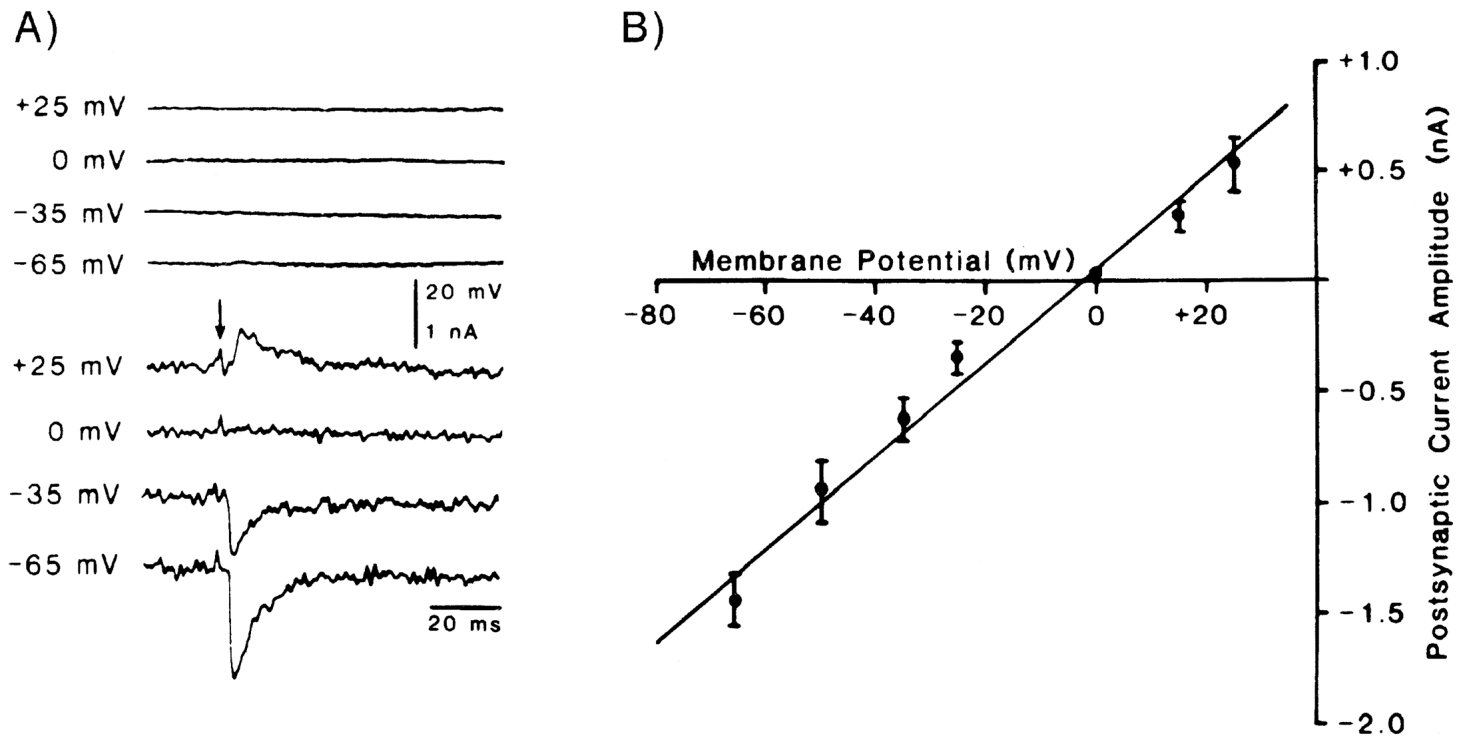


Fig. 1.6 A Fast Excitatory Synaptic Input

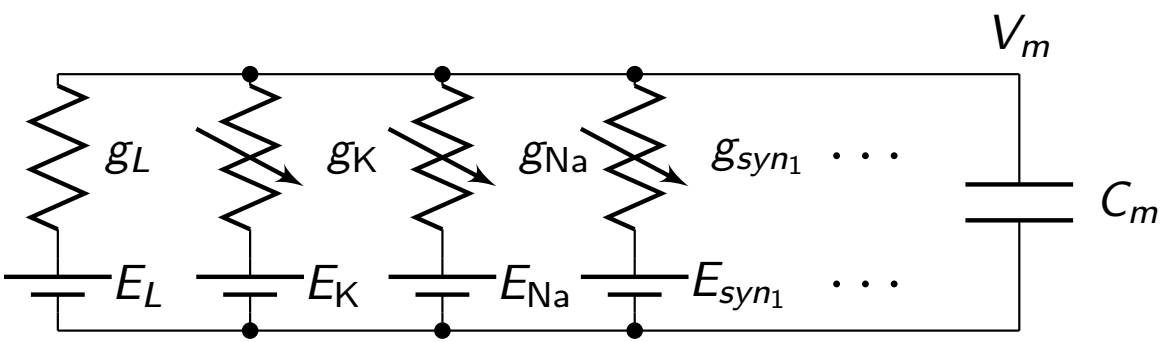
Excitatory postsynaptic current (EPSC) caused by the simultaneous activation of synapses (arrow) made by the mossy fibers onto CA3 pyramidal cells in the rodent hippocampus. This classical experiment showed how a central synapse can be successfully voltage clamped. **(A)** The voltage-clamp setup stabilizes—via electronic feedback control—the membrane potential at a fixed value. Here four experiments are shown, carried out at the holding potentials indicated at the left. The current that is drawn to keep the membrane potential constant, termed the clamp current, corresponds to the negative EPSC. It is maximal at negative potentials and reverses sign around zero. The synaptic current rises within 1 msec to its peak value, decaying to baseline over 20-30 msec. The experiments were carried out in the presence of pharmacological agents that blocked synaptic inhibition. **(B)** When the peak EPSC is plotted against the holding potential, an approximately linear relationship emerges; the regression line yields an x-axis intercept of -1.9 mV and a slope of 20.6 nS Thus, once the synaptic reversal potential is accounted for, Ohm's law appears to be reasonably well obeyed. We conclude that synaptic input is caused by a transient increase in the conductance of the membrane to certain ions. Reprinted by permission from Brown and Johnston (1983).

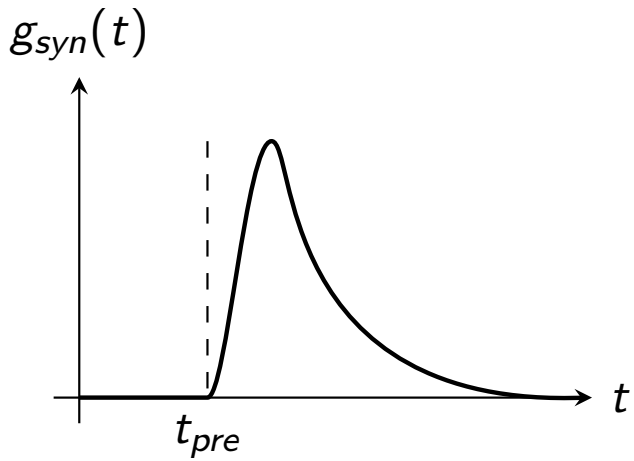
Koch 1999, p. 16

Postsynaptic membrane current and voltage:

$$C_m \frac{dV_m}{dt} = I_{ext} - I_{\mathrm{K}} - I_{\mathrm{Na}} - I_L - \sum_i I_{syn_i}$$

$$I_{syn_i} = g_{syn_i}(t) \cdot (V_m - E_{syn_i})$$





Nonlinear Synaptic Interaction

Shunting Inhibition:

$$C\frac{dV}{dt} = \cancel{g_e}(E_e - V) - \cancel{g_i}V - \frac{V}{R}$$

$\downarrow$ excitation $\quad$ $\downarrow$ shunting inhibition

$$\Downarrow$$

$$\frac{dV}{dt} = -\frac{V - \cancel{V_\infty}}{\cancel{\tau}}$$

$$\text{with} \begin{cases} V_\infty = \dfrac{R\cancel{g_e}E_e}{1 + R(\cancel{g_e} + \cancel{g_i})} & g_i \text{ “shunts” } g_e \\ \tau = \dfrac{RC}{1 + R(\cancel{g_e} + \cancel{g_i})} & g_i \text{ also speeds } g_e \end{cases}$$

Shunting Inhibition

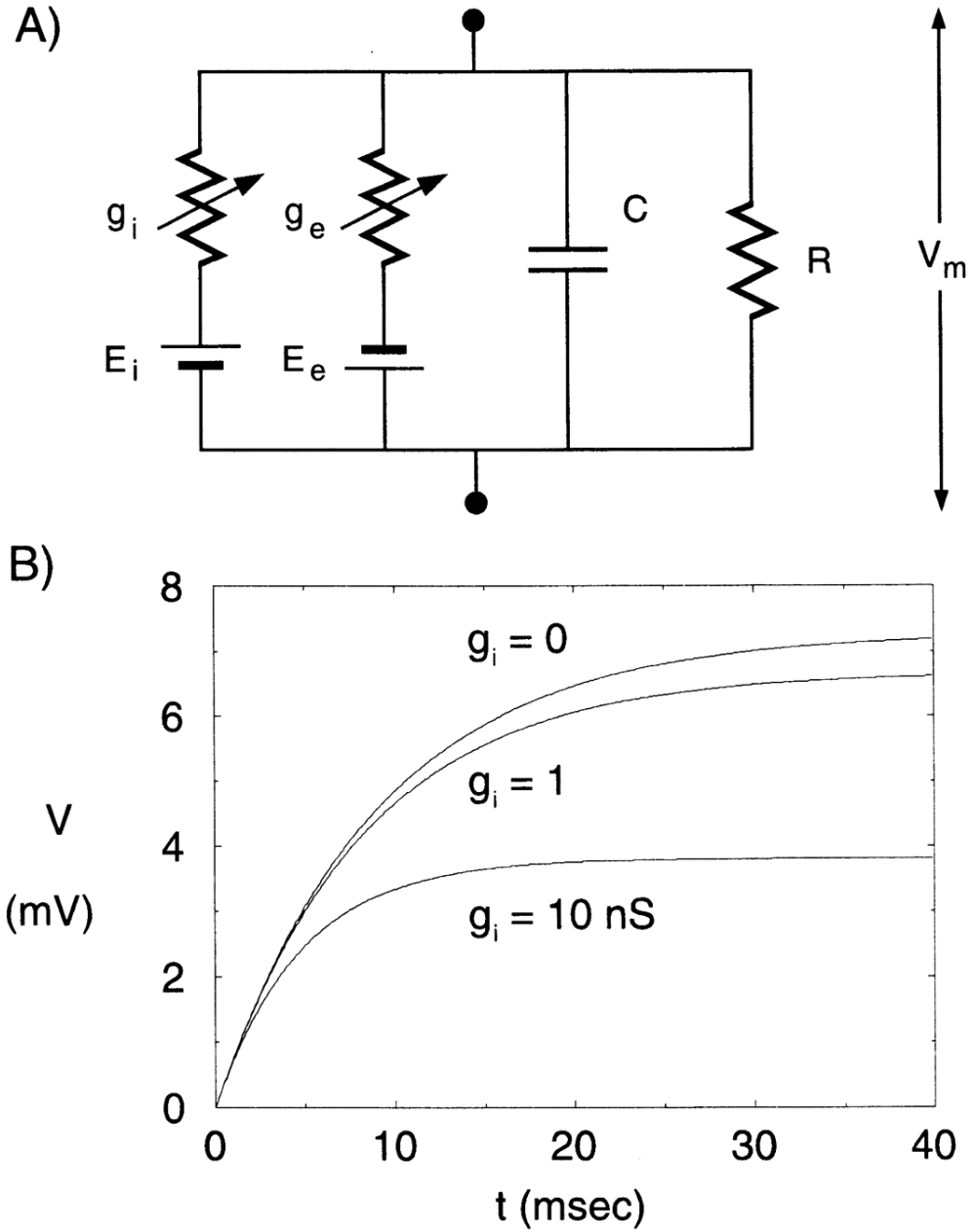


Fig. 1.10 Nonlinear Interaction between Excitation and Shunting Inhibition

Inhibitory synaptic input of the shunting type, that is, whose reversal potential is close to the cell's resting potential, can implement a form of division. **(A)** This is demonstrated for an RC circuit ($R = 100\text{M}\Omega$, $C = 100\text{pF}$) in the presence of both excitation (with battery $E_e = 80\text{mV}$) and shunting inhibition (with $E_i = 0$). We are here only considering the change in membrane potential relative to V_{rest}. **(B)** Time course of the membrane depolarization in response to a step onset of both excitation (of amplitude $g_e = 1\text{nS}$) and shunting inhibition (for three values of $g_i = 0, 1, \text{and} 10\text{nS}$). One effect of increasing g_i is an almost proportional reduction in EPSP amplitude. A further consequence of increasing the amount of shunting inhibition is to decrease the time constant τ', from its original 10 msec in the absence of any synaptic input to 9 msec in the presence of only excitation to 4.8 msec in the presence of excitation and the 10 times larger shunting inhibition.

Koch 1999, p. 22

Synaptic Receptor Types

TABLE 4.2 Synaptic Receptor Types

Neurotransmitter	Receptor	E_{syn}	Type	Comments	Ion Types
Glutamate	"AMPA"	0	I	Very fast	Na^+ K^+ ...
Glutamate	NMDA	0	I	Voltage dependent	Na^+ K^+ Ca^{2+} Mg^{2+} (block)
GABA	$GABA_A$	−70	I	Fast inhibition	Cl^-
GABA	$GABA_B$	−100	M	Slow inhibition	K^+
ACh	Nicotinic	−5	I	Neuromuscular junction	Na^+ K^+ Ca^{2+}
ACh	Muscarinic	−90	M	Decreases K conductance	K^+
Noradrenaline	α_2	−100	M	Increases K conductance	K^+
Noradrenaline	β_1	−100	M	Decreases K conductance	K^+

List of major types of synaptic receptors and the associated neurotransmitters. The four top listings are the dominant transmitters used for fast communication in the vertebrate central nervous system. The synaptic reversal potential E_{syn} is specified in millivolts absolute potential. The type corresponds to either ionotropic (I) or metabotropic (M) receptors.

Koch 1999, p. 95

Synaptic Receptors and Channels

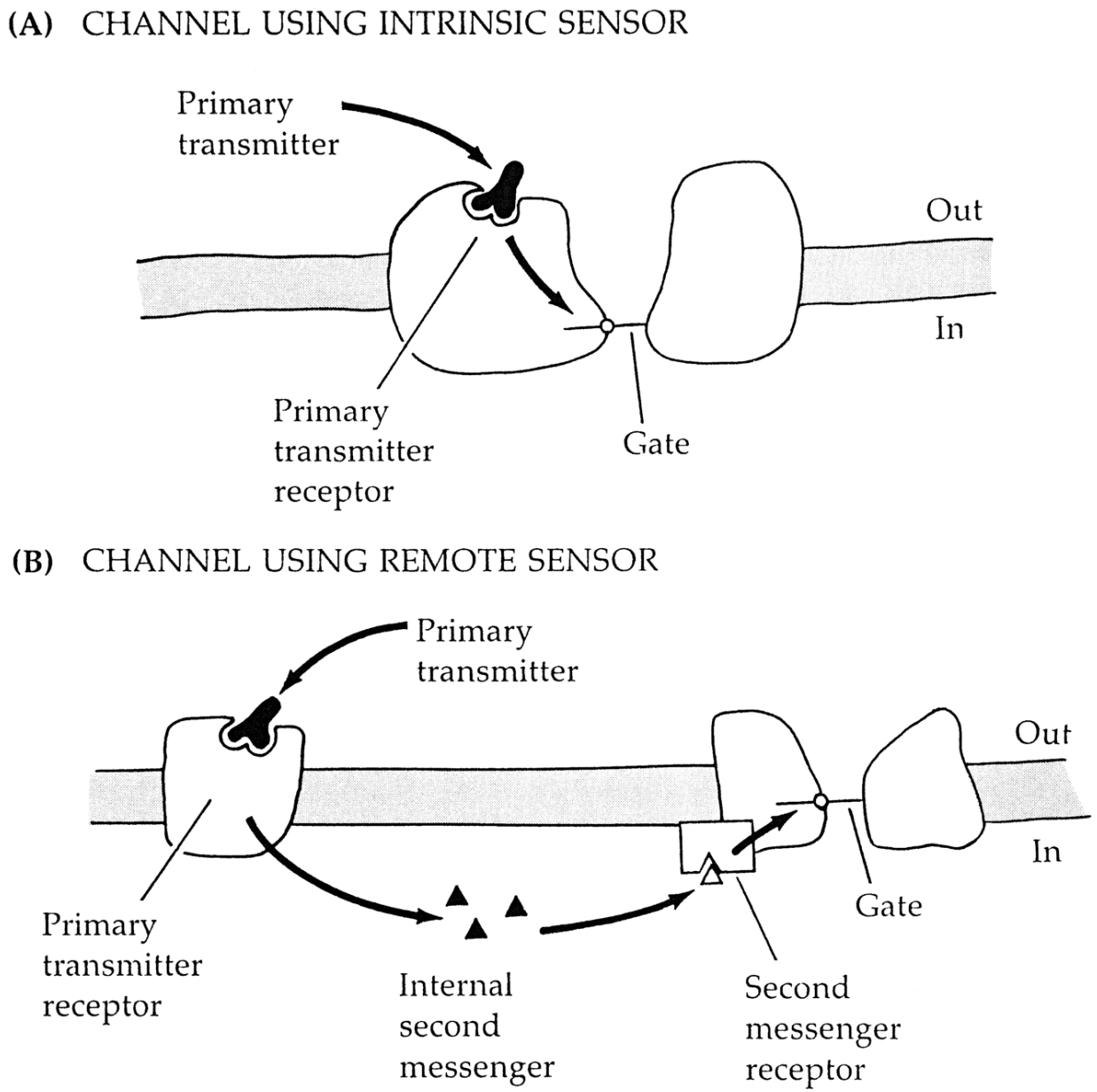
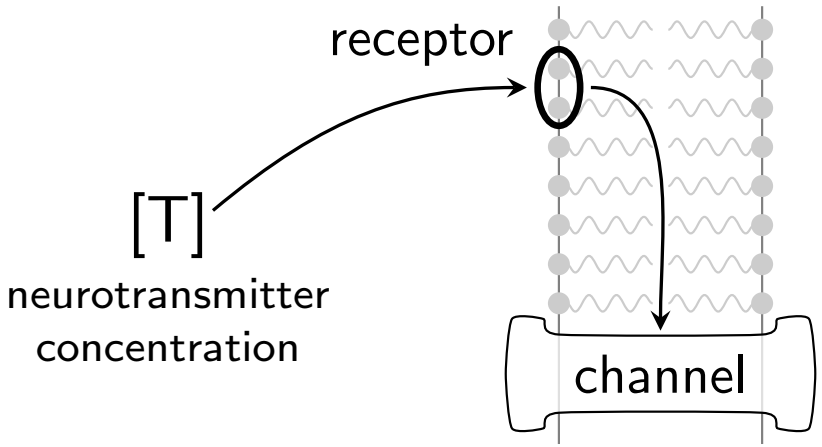


Fig. 4.5 Ionotropic and Metabotropic Synaptic Action

(A) Fast excitatory and inhibitory input mediated by a tightly linked ionotropic receptor-channel complex. Binding of the neurotransmitter leads to a rapid opening of the associated ionic channel. **(B)** In the case of a *metabotropic* receptor, binding of the neurotransmitter leads to activation of a second messenger substance (such as Ca^{2+} ions). This messenger molecule, possibly after diffusing to its site of action, binds to a particular ionic channel and will modulate its properties. While the action of the ionotropic receptor is point to point and rapid, both the onset and the duration of the metabotropic mediated synaptic input are usually slow and its action can extend over larger distances. Both receptor types can be colocalized. Reprinted by permission from Hille (1992).

Koch 1999, p. 94

Receptor Channel Kinetics



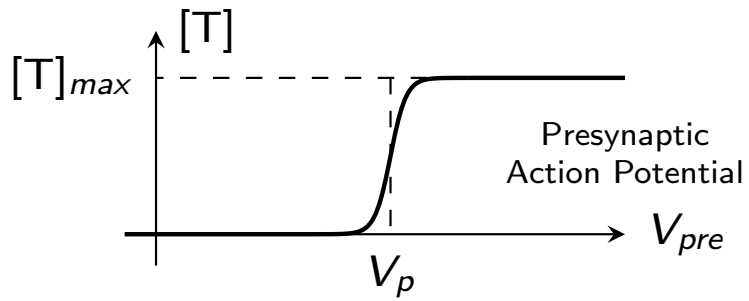
$$1 - r \underset{\beta}{\overset{\alpha \cdot [\mathrm{T}]}{\rightleftharpoons}} r$$

fraction of gates closed — fraction of gates open

- Opening rate proportional to concentration [T], $\alpha[\mathrm{T}]$
- Closing rate constant, and small, $\beta < \alpha[\mathrm{T}]_{max}$

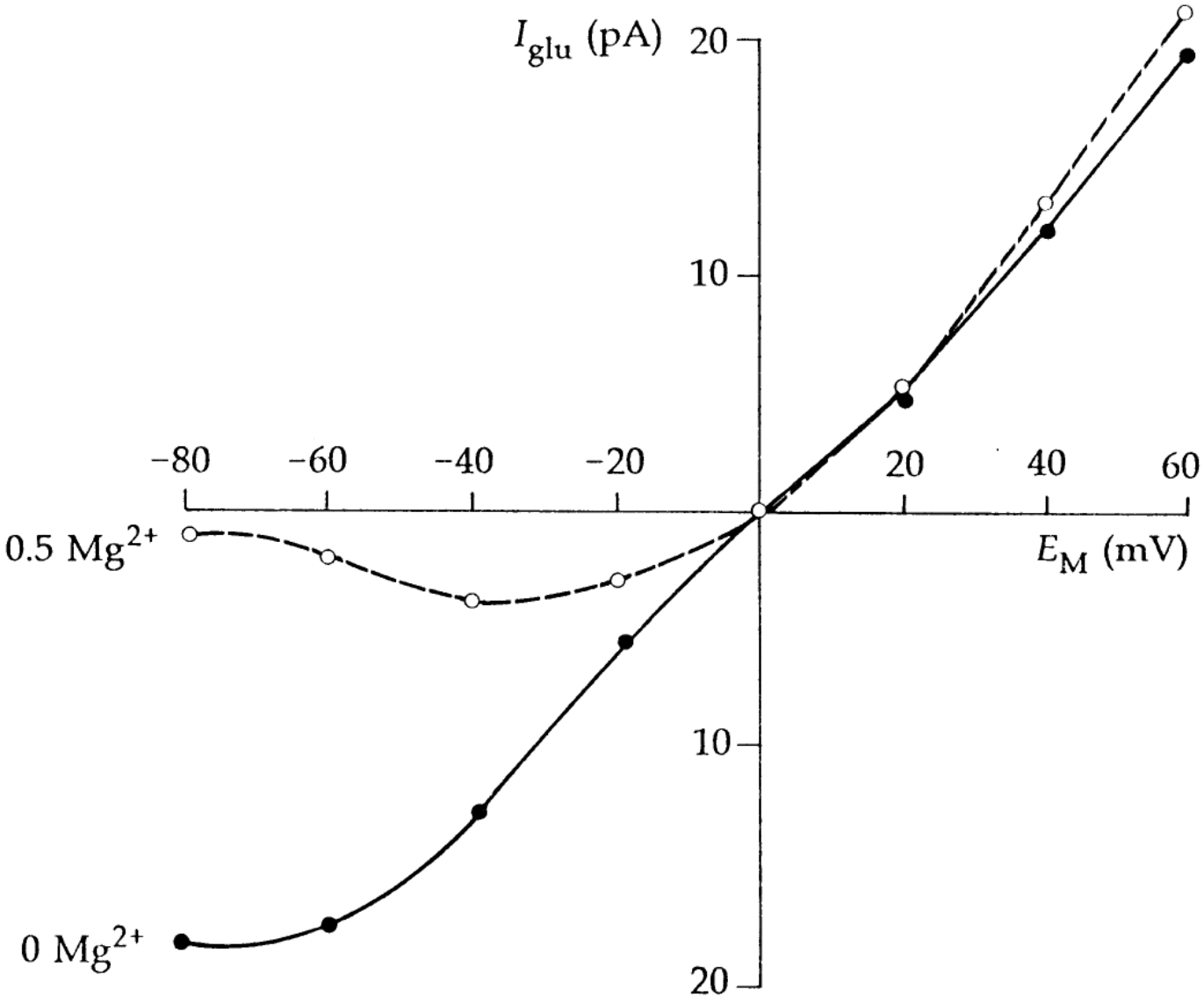
$$\Rightarrow \frac{dr}{dt} = \alpha[\mathrm{T}](1 - r) - \beta r$$

$$\text{with } [\mathrm{T}] = \frac{[\mathrm{T}]_{max}}{1 + e^{-(V_{pre} - V_p)/K_p}}$$



- For NMDA, β is voltage dependent and very small (Mg^{2+} blocker)

NMDA Voltage Dependence



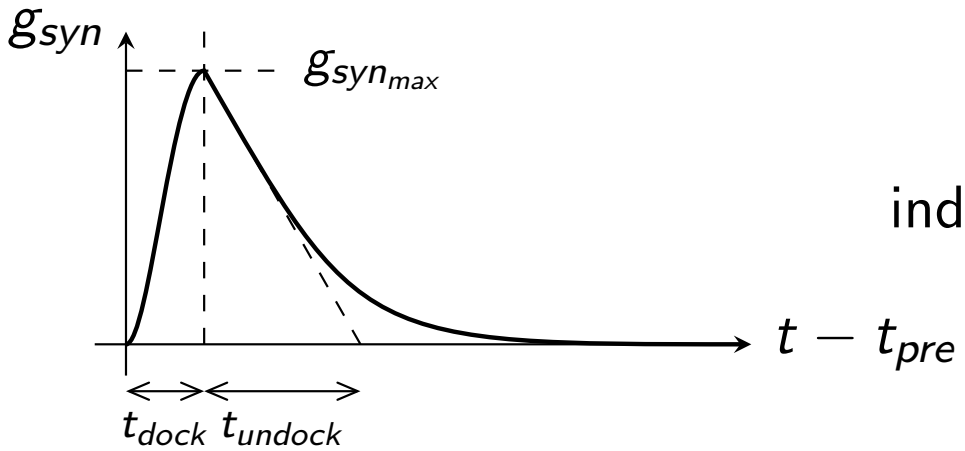
6.15 Mg^{2+} Block of NMDA Receptor Channels

Current-voltage relation of whole-cell current induced by 10 μM glutamate in a cultured mouse mesencephalic neuron bathed in a saline solution with or without 0.5 mM Mg^{2+}. [From Nowak et al. 1984.]

Hille 2001, p. 198

Synaptic Dynamics Simplified

$$I_{syn} = g_{syn}(t - t_{pre}, V_m) \cdot (V_m - E_{syn})$$



independent of V_{pre} profile

Receptor	**Neurotransmitter**		$\mathbf{E_{syn}}$	$\mathbf{t_{dock}}$	$\mathbf{t_{undock}}$
AMPA (non-NMDA)	excitatory	glutamate	0mV	1ms	2ms
NMDA*	excitatory	glutamate	0mV	1ms	120ms
$GABA_A$	inhibitory	GABA	-80mV	2ms	4ms

* NMDA: $g_{syn_{max}} \propto \frac{1}{1 + \frac{[Mg^{2+}]}{3.6mM} \cdot e^{-V_m/16mV}}$ voltage dependence

Coupling Between Neurons

$$C_i \frac{dV_i}{dt} = I_{ext_i} + (K, Na)... + \sum_j I_{ij}$$

Gap junctions: $I_{ij} = g_{ij}(V_j - V_i)$

Chemical synapses: $I_{ij} = g_{syn_{ij}}(t - t_j, V_i) \cdot (E_{syn_{ij}} - V_i)$

- **Synchronization** (Phase Locking)
- **Phase Modulation**

Ch. 10 of Izhikevich (on-line)