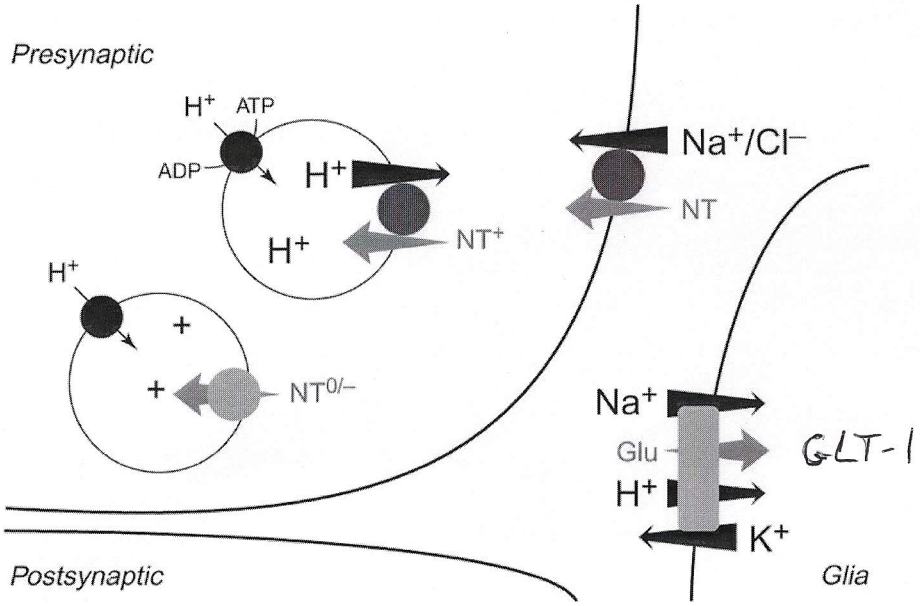


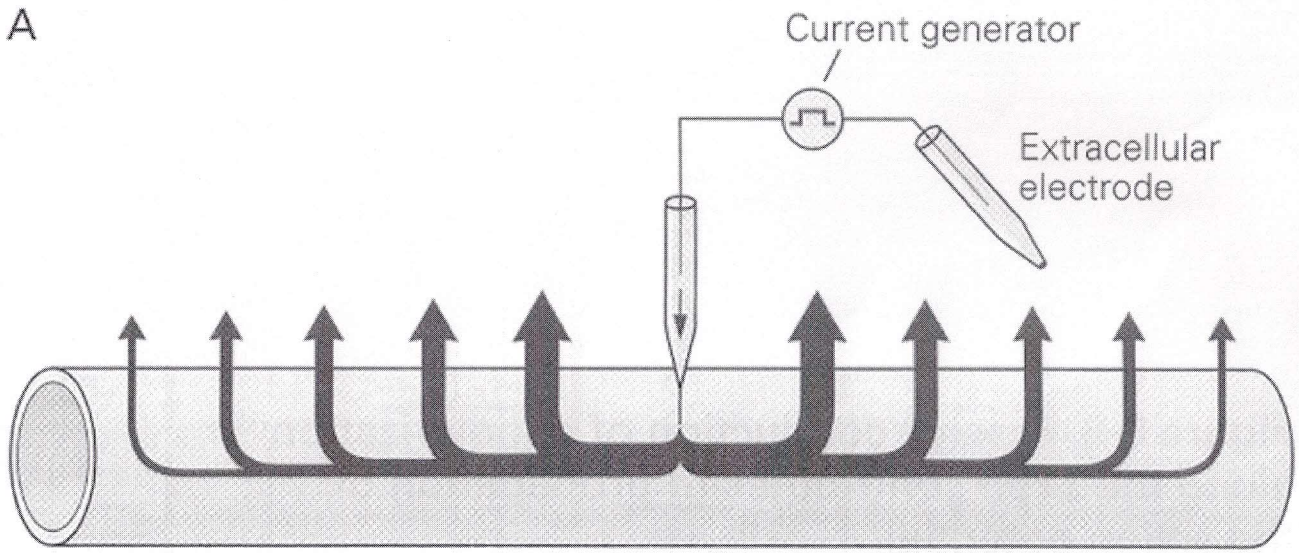
FIGURE 1

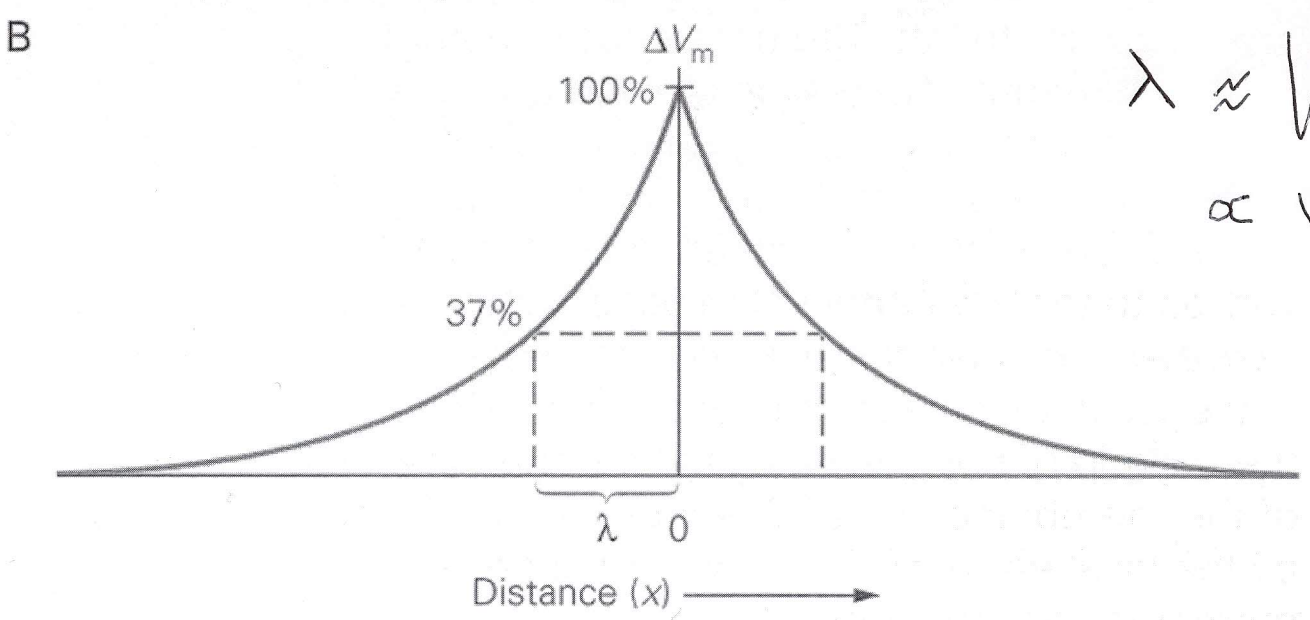
Four classes of activity mediate neurotransmitter transport. The transport of neurotransmitters across biological membranes is mediated by four distinct classes of transport proteins with no sequence similarity to each other. Plasma membrane transport (blue and purple) uses the movement of Na^+ down its electrochemical gradient to drive the reuptake of neurotransmitter against a concentration gradient. However, one class of plasma membrane transport activity (blue) requires Cl^- in addition to Na^+ and includes the GABA, monoamine, glycine and proline transporters. Although shown only in the presynaptic neuron (above left), some of these transporters are expressed predominantly if not exclusively by glia. The excitatory amino acid transporters (purple) do not require cotransport of Cl^- but do involve the cotransport of H^+ and exchange for K^+. Shown in glia here (lower right), different members of this family are also expressed by neurons, but usually in the post- rather than the presynaptic cell. Vesicular transport (red, orange) involves the exchange of lumenal protons for the cytoplasmic transmitter and hence relies on a proton electrochemical gradient made by the vacuolar H^+-ATPase (black). However, the vesicular monoamine and acetylcholine transporters (red) rely predominantly on the chemical component of this gradient (ΔpH), whereas the vesicular amino acid transporters (orange) depend principally on the electrical component ($\Delta\psi$).

BOX 1 – FOUR CLASSES OF NEUROTRANSMITTER TRANSPORTERS

Transporter type	Substrate
Plasma membrane transporter	
Na^+/Cl^- dependent transporters	
GAT 1–4	GABA
DAT, NET, SERT	Dopamine, norepinephrine, serotonin
GLYT1, 2	Glycine
PROT	Proline
Na^+ dependent, excitatory amino acid transporters (EAATs)	
GLAST (EAAT1), GLT-1 (EAAT2)	Glutamate, aspartate (glial)
EAAT3–5	Glutamate, aspartate (neuronal)
Vesicular transporters	
ΔpH-driven (>$\Delta\Psi$)	
VMAT1,2	Monoamines (all)
VAChT	ACh
$\Delta\Psi$-driven (>Δph)	
VGAT	GABA, glycine

Da: Kandel et al., Principles of Neural Science, IV ed., McGraw-Hill





$$\lambda \approx \sqrt{\frac{r_m}{r_i}} \propto \sqrt{a} \quad (a = \text{raggio})$$

Da: Kandel et al., Principles of Neural Science, IV ed., McGraw-Hill

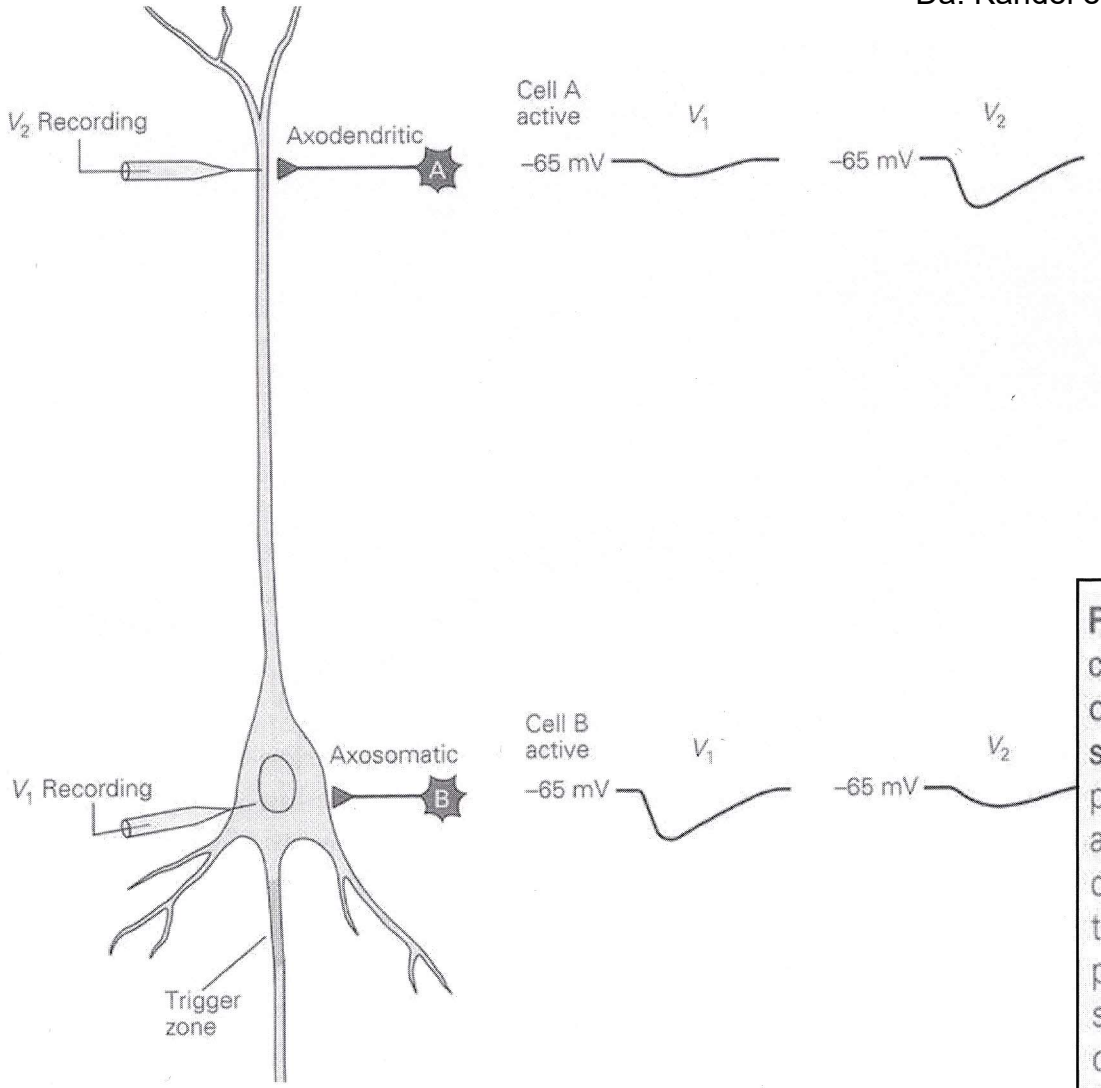
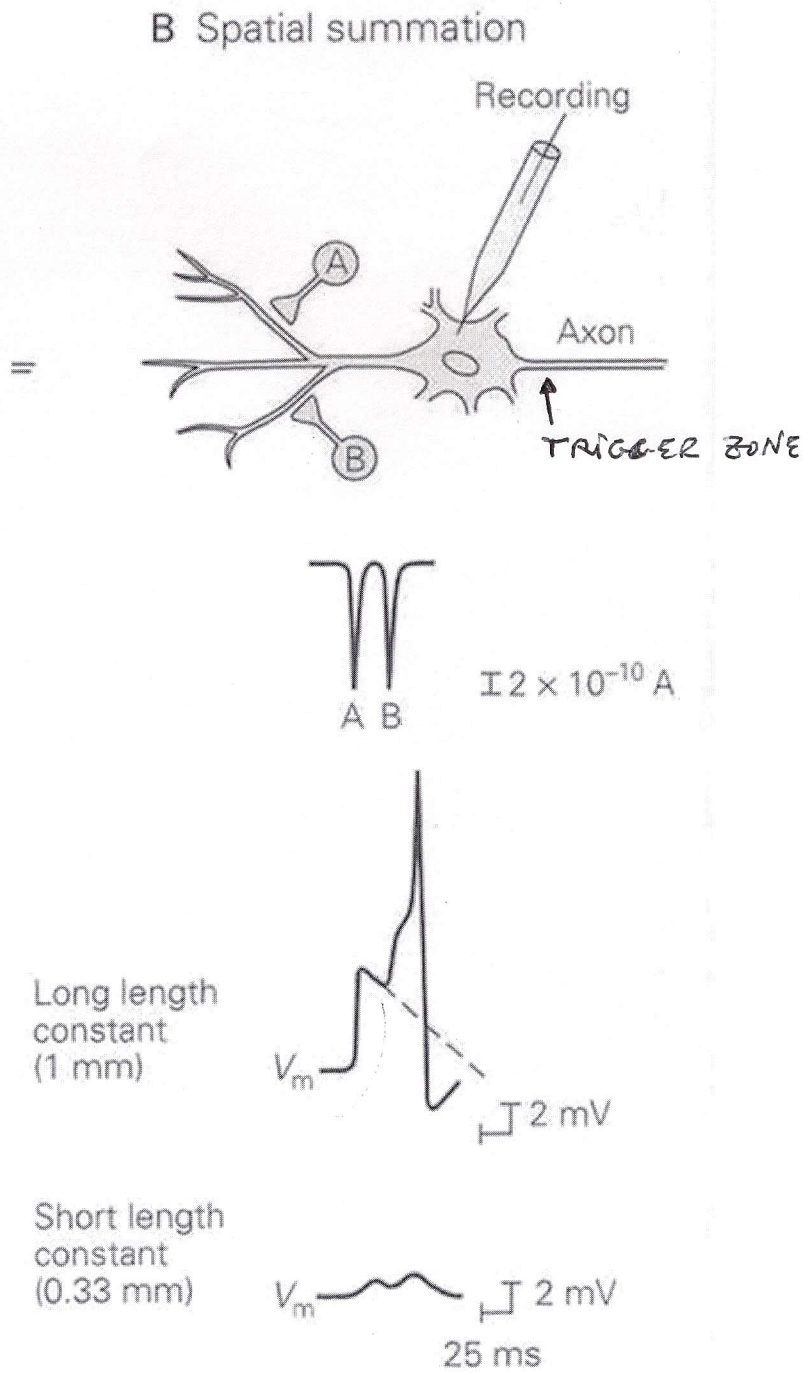


Figure 12-15 The impact of an inhibitory current in the postsynaptic neuron depends on the distance the current travels from the synapse to the cell's trigger zone. In this hypothetical experiment the inputs from inhibitory axosomatic and axodendritic synapses are compared by means of recordings from both the cell body (V_1) and the dendrite (V_2) of the postsynaptic cell. Stimulating cell B at the axosomatic synapse produces a large IPSP in the cell body. Because the synaptic potential is initiated in the cell body it will not decay before arriving at the trigger zone in the initial segment of the axon. Stimulating cell A at the axodendritic synapse produces only a small IPSP in the cell body because the potential is initiated so far from the axon hillock; it decays as it spreads to the cell body.

Lenght constant = costante di spazio

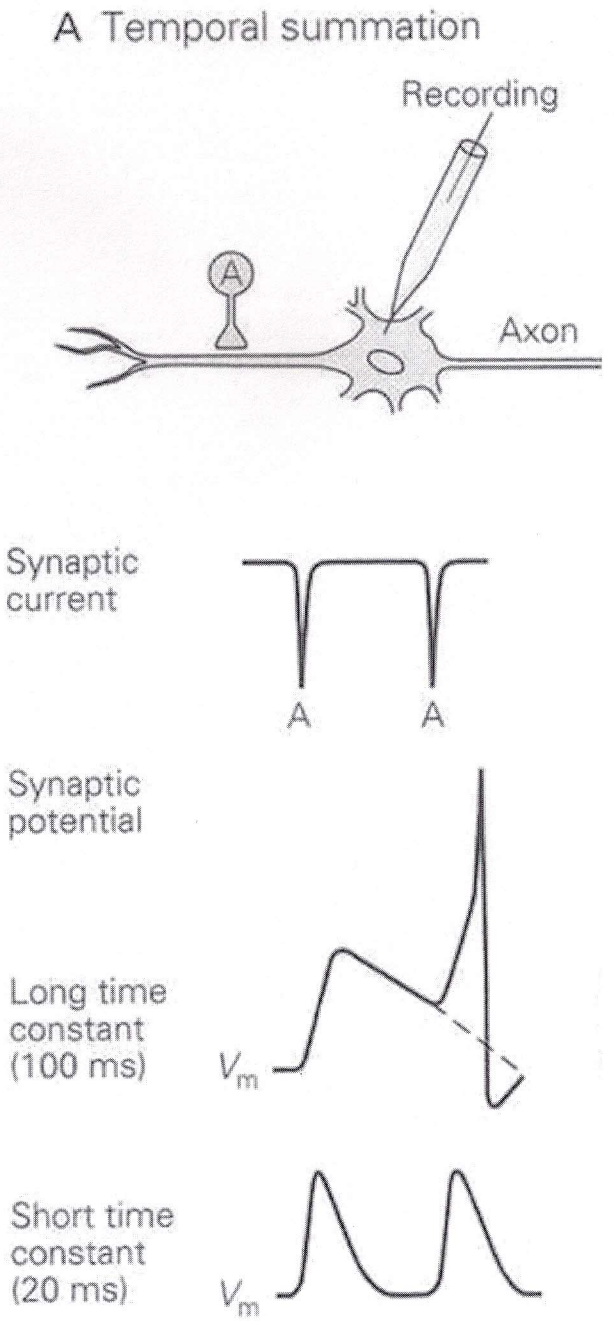
B. The length constant of a postsynaptic cell (see Figure 8-5) affects the amplitudes of two excitatory postsynaptic potentials produced by two presynaptic neurons (A and B). For illustrative purposes, both synapses are the same distance from the postsynaptic cell's trigger zone in the initial axon segment, and the current produced by each synaptic contact is the same. If the distance between the site of synaptic input and the trigger zone in the postsynaptic cell is only one length constant (the postsynaptic cell has a *long* length constant of 1 mm), the synaptic potentials produced by each of the two presynaptic neurons will decrease to 37% of their original amplitude by the time they reach the trigger zone. Summation of the two potentials results in enough depolarization to exceed threshold, triggering an action potential. If the distance between the synapse and the trigger zone is equal to three length constants (the postsynaptic cell has a *short* length constant of 0.33 mm), each synaptic potential will be barely detectable when it arrives at the trigger zone, and even the summation of two potentials is not sufficient to trigger an action potential.



Da: Kandel et al., Principles of Neural Science, IV ed., McGraw-Hill

Figure 12-13 Central neurons are able to integrate a variety of synaptic inputs through temporal and spatial summation of synaptic potentials.

A. The time constant of a postsynaptic cell (see Figure 8-3) affects the amplitude of the depolarization caused by consecutive EPSPs produced by a single presynaptic neuron (A). Here the synaptic current generated by the presynaptic neuron is nearly the same for both EPSPs. In a cell with a *long* time constant the first EPSP does not decay totally by the time the second EPSP is triggered. Therefore the depolarizing effects of both potentials are additive, bringing the membrane potential above the threshold and triggering an action potential. In a cell with a *short* time constant the first EPSP decays to the resting potential before the second EPSP is triggered. The second EPSP alone does not cause enough depolarization to trigger an action potential.

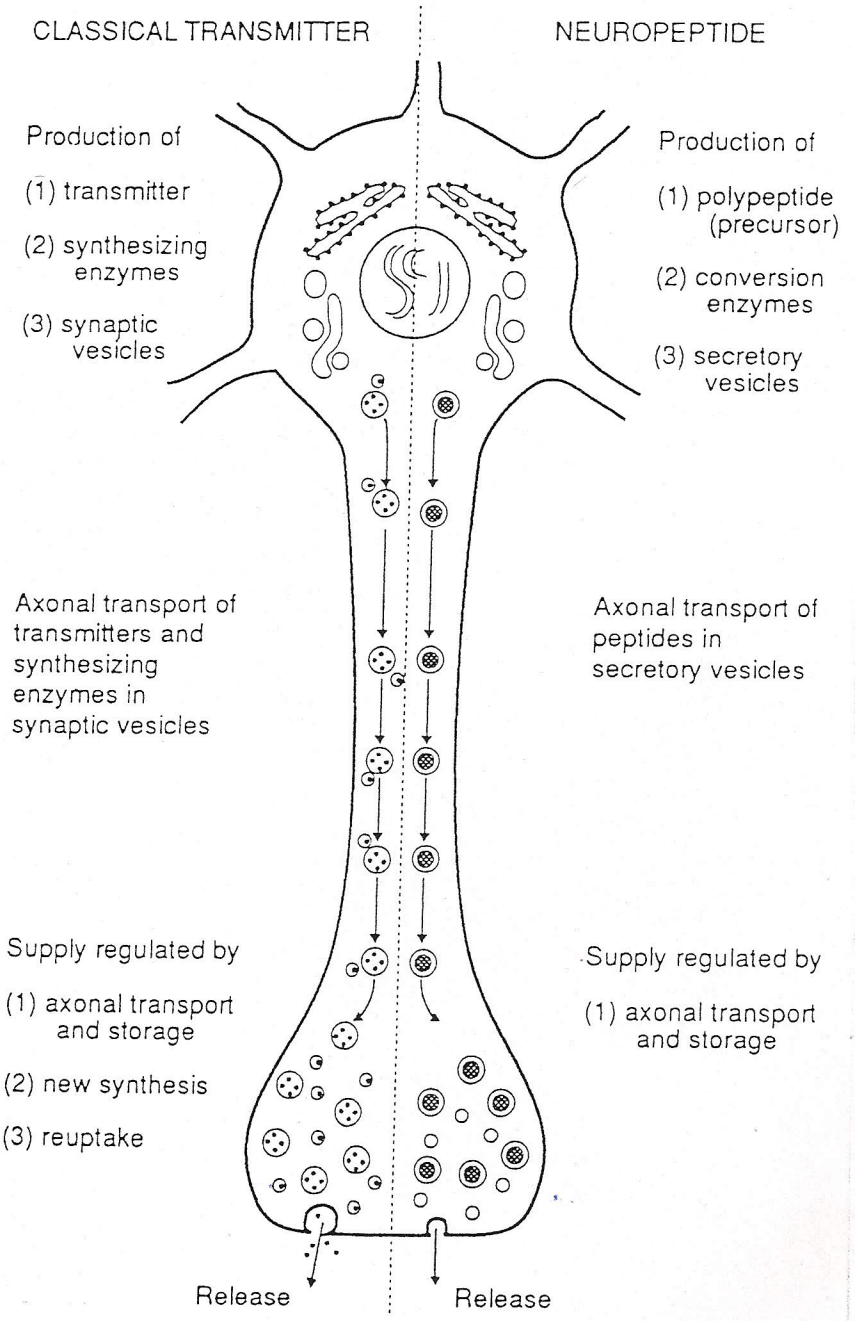


τ_m = COSTANTE DI TEMPO DELLA MEMBRANA = $R_m C_m$

Da: Kandel et al., Principles of Neural Science, IV ed., McGraw-Hill

I neuropeptidi modulano l'azione del trasmettitore veloce

ESEMPI:	TRASMETTITORE	PEPTIDE (nello stesso neurone)
	ACh	CGRP Encefaline Somatostatine ....
	GABA	CCK encefaline VIP SostanzaP ....
POTENZA	N 10^{-5} M	N 10^{-9}
	SINTESI ANCHE NEI BOTTONI SINAPTICI	SINTESI NEL SOMA E TRASPORTO ASSONICO ATTIVANO SEMPRE CASCATE SEGNALATORIE INTRACELL. EFFETTI LENTI DEGRADAZIONE LENTA E DIFFUSIONE IN UN VOLUME DI TESSUTO



FROM: AIDLEY - THE PHYSIOLOGY OF EXCITABLE CELLS, 1998. CAMB. UNIV. PRESS

PHYSIOLOGICAL FEATURES OF NEUROPEPTIDE TRANSMISSION

- stored in LARGE DENSE CORE VESICLES and released at a final concentration much lower than that of classical neurotransmitters.

- most postsynaptic (or presynaptic) receptors for neuropeptides are G-PROTEIN coupled 7-TM domains proteins.

- no reuptake, nor quick degradation. Slow effects because of long-term permanence in the extracellular space E.g. different (wider range, longer) pattern of pres. control compared to the classical transmitters.

- generally released by higher presynaptic activity, compared to the classical transmitters. They require a more intense stimulus, probably because the release site is far from the region of Ca^{2+} entry.