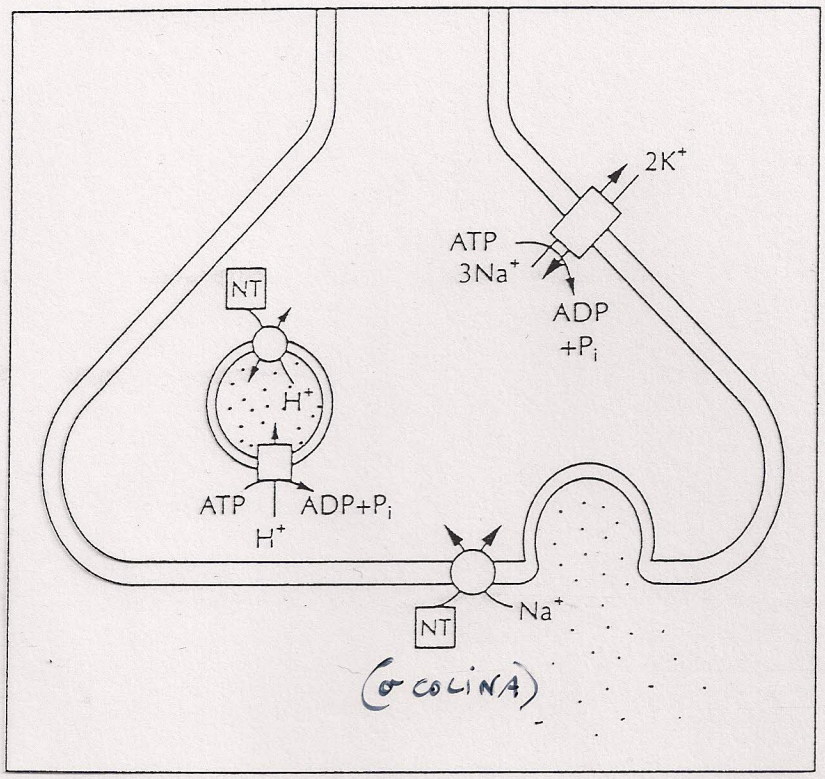
MECCANISMI PRESINAPTICI

Da: Aidley D.J., The Physiology of Excitable Cells, 3rd ed., Cambridge University Press.



Acetil CoA + COLINA ⇌ ACh + CoA
ChAT
(COLINA ACETIL TRANSFERASI)

VAChT: trasportatore vescicolare per captare ACh nelle vescicole

ChoT: per il riassorbimento della colina

SINAPSI GIGANTI

- GIUNZIONE NEUROMUSCOLARE (Rana)
- GANGLIO STELLATO DI CALAMARO
- CALICE DI HELD (vie uditive del tronco cerebrale dei Mammiferi)

a) Relazione depolarizzazione - rilascio
b) Relazione tra Ca^{2+} e rilascio del NT
c) Classi di canali del Ca^{2+}
d) Meccanismo dell'esocitosi.

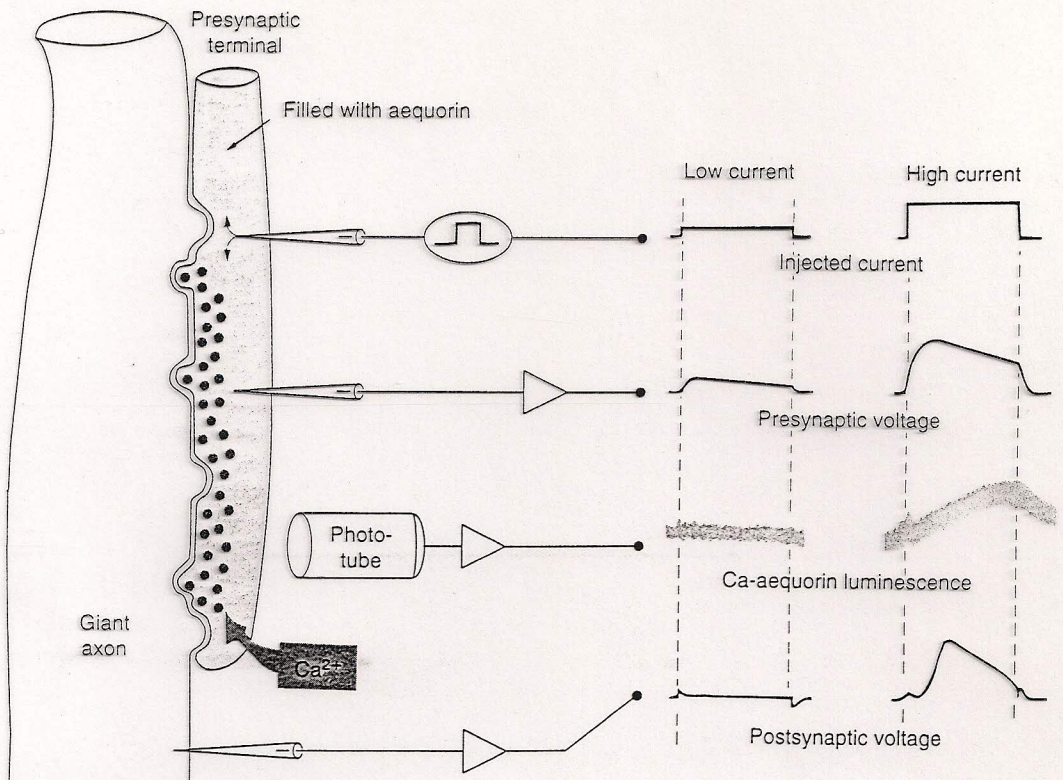


Figure 6-28 The light-emitting protein aequorin showed that transmitter is released only when calcium ions can enter the presynaptic terminal. In this experiment, Na^+ and K^+ currents at the squid giant synapse were blocked with TTX and TEA. The Ca^{2+}-indicator aequorin was injected into the presynaptic terminal (light red), and the terminal was stimulated with injected depolarizing current. Pre- and postsynaptic potentials were recorded with intracellular microelectrodes. The responses to weak and strong presynaptic stimulating currents are shown at the right. A postsynaptic potential was recorded only when aequorin produced light, indicating that Ca^{2+} had entered the presynaptic terminal. Synaptic vesicles in the terminal are shown as small red circles. [Adapted from Llinás and Nicholson, 1975.]

From: Eckert's Animal Physiology
4th edition Freeman and Co.

STRUMENTI PER LO STUDIO DEI PROCESSI CHE DIPENDONO DA $[Ca^{2+}]_i$:

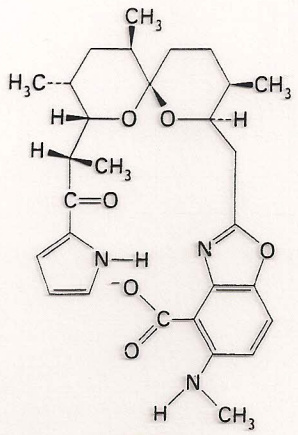
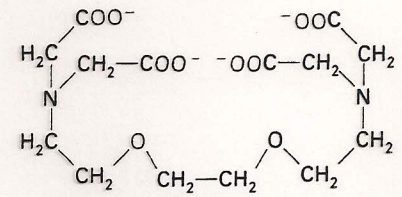


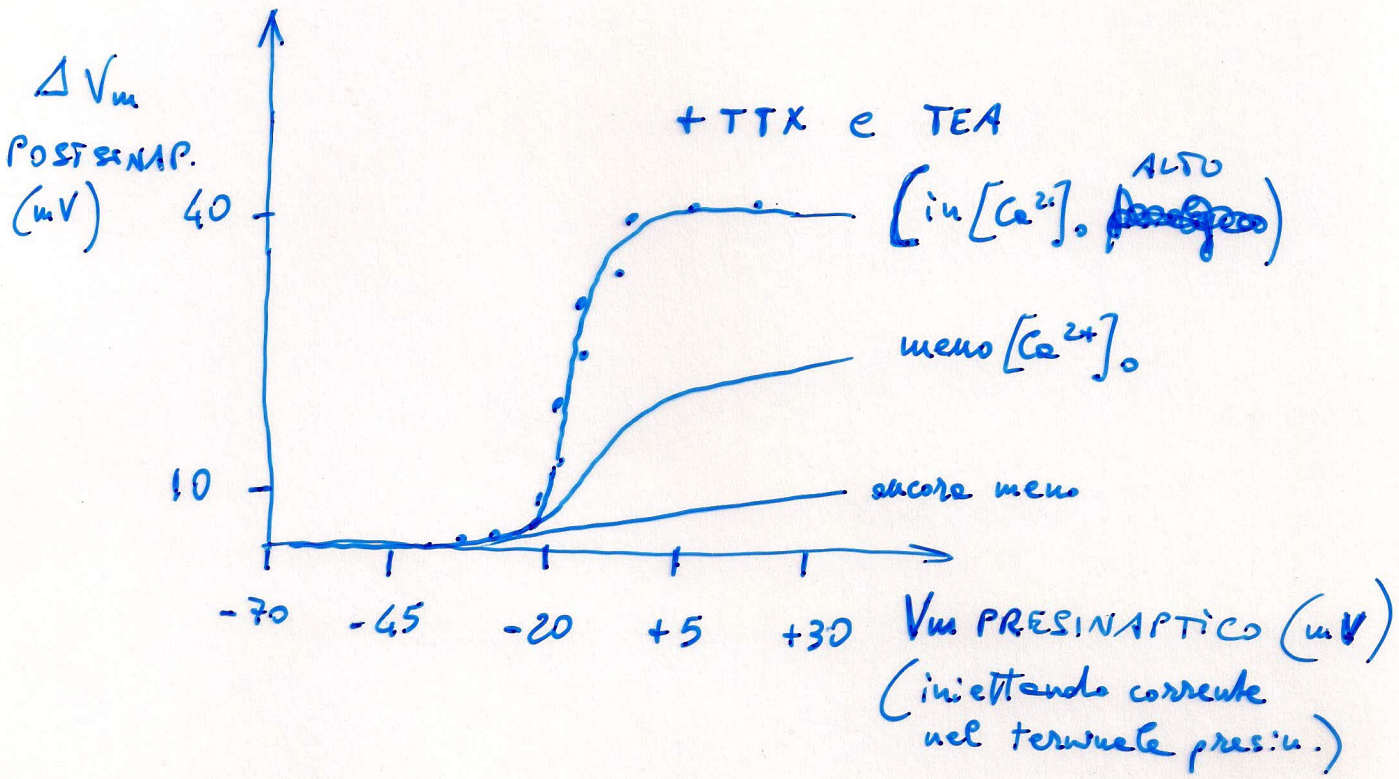
Figure 38-19
Structural formula of A23187, a calcium ionophore.



EGTA
(Ethylene glycol bis(β-aminoethyl ether)-*N,N,N′,N′*-tetraacetate)

From Stryer's Biochemistry
Freeman and Co.

ACCOPPIAMENTO DEPOLARIZZAZIONE-RILASCIO



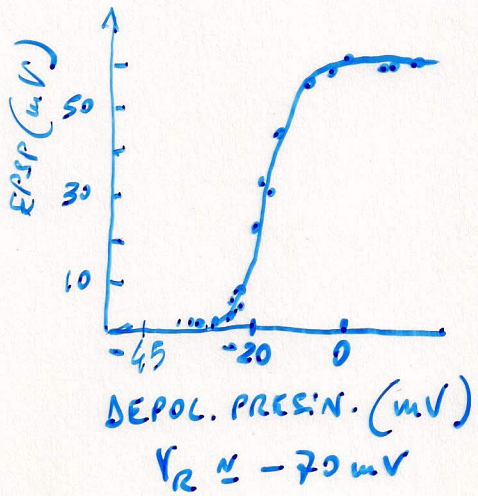
KATZ e MILEDI 1966

- IL Ca^{2+} EXTRACELLULARE REGOLA L'EFFETTO
- IL Mg^{2+} EXTRACELLULARE INIBISCE

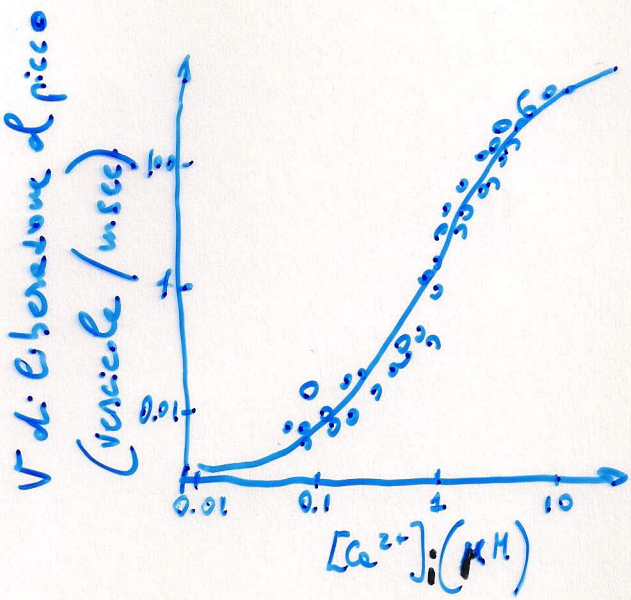
- SE IL V_m PRESINAPTICO $\bar{e} = E_{Ca}$, L'EFFETTO SI BLOCCA

SINAPSI GIGANTE NEL GANGLIO STELLATO DI CALAMARO

P.es. Katz e Miledi, Journal of Physiology 1967.



SINAPSI DI CALAMARO



CALICE DI HELD

Azione cooperativa del Ca^{2+}.

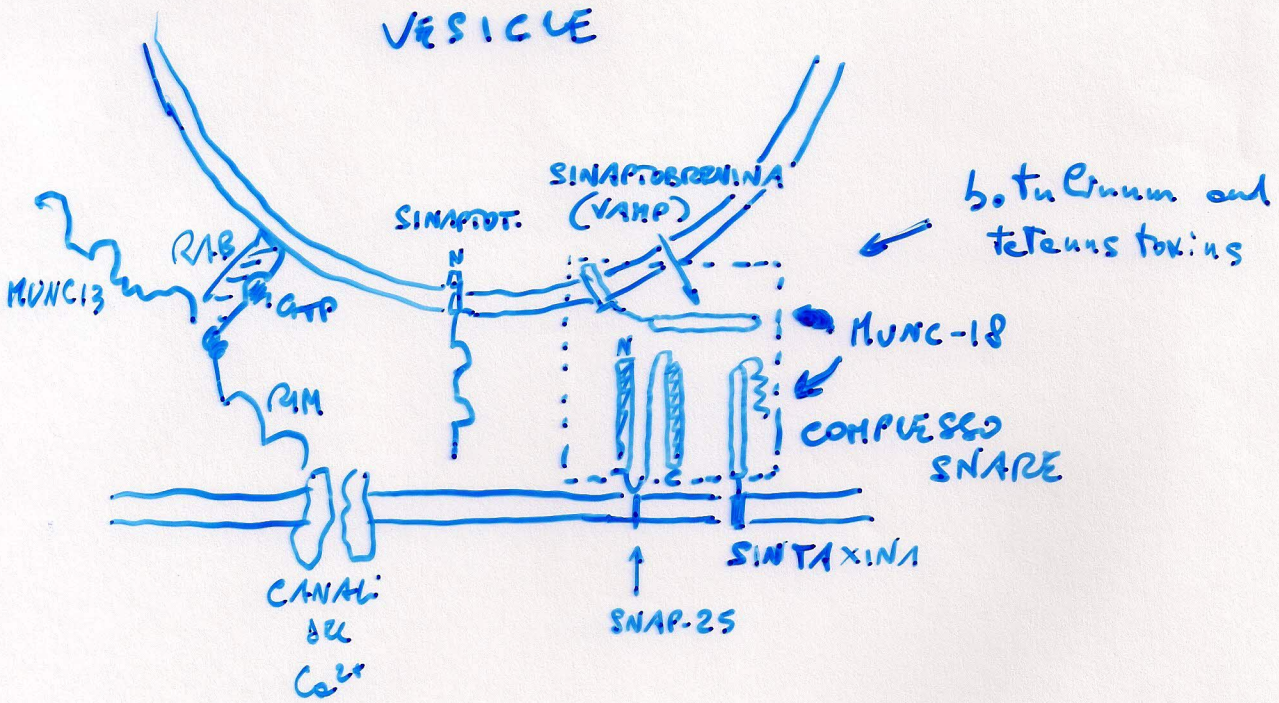
5 ioni Ca^{2+} devono legarsi ad una proteina della vescicola.

P.es. Kochubey et al. Trends Neurosci. 2011.

SNARE : SOLUBLE N-ETHYLMALEIMIDE-SENSITIVE FACTOR ATTACHMENT RECEPTORS

(trafficking in general, not only of syn. vesicles)

Must overcome the large unfavourable activation energy for vesicle fusion with the plasma memb.



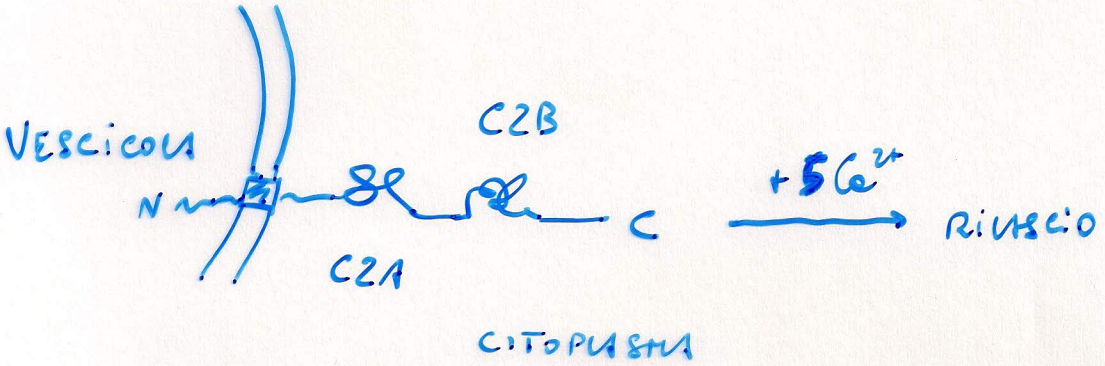
V-SNARE : vesicle

t-SNARE : plasma membrane ("target")

VAMP = vesicle associated membr. protein

PRINCIPALI SENSORI DEL Ca^{2+} NEL TERMINALE SINAPTICO

SINAPTOTAGMINE



C2A lega 3 Ca^{2+}
C2B ne lega 2

] DOMINI CHE LEGANO Ca^{2+} E FOSFOLIPIDI omologhi a quelli p.es. delle PKC

È nota la struttura cristallina di questi domini

- Il rilascio veloce e sincronizzato di neurotrasmettitore è causato da la SINAPTOTAGMINA 1 delta.
- I domini C2 interagiscono anche con il complesso di ancoraggio SNARE.

Canali del Ca^{2+} V-dipendenti

			blocco	
Ca_V 1.1 - 1.4	L	Muscolo Neuroni	DHP	ALTA SOGLIA (da -40 in su)
Ca_V 2.1	P/Q	neuroni	AGK (sperm.)	" "
Ca_V 2.2	N	"	CTX (Conus)	" "
Ca_V 2.3	R	"	SNX-482 (tarantola)	" "
Ca_V 3.1 - 3.3	T	muscolo neuroni		BASSA SOGLIA

Rilascio rapido del NT: P/Q ed N (siti attivi presinaptici)

Contrazione e rilascio lenti: L (p. es. neuropeptidi)

Controllo eccitabilità / pacemaker: T