Ion channels, membrane potential and synaptic transmission

离子通道 膜电势 突触传递

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Outlines

- 1. review of Hodgkin-Huxley model
- 2. synaptic transmission - presynaptic mechanism:

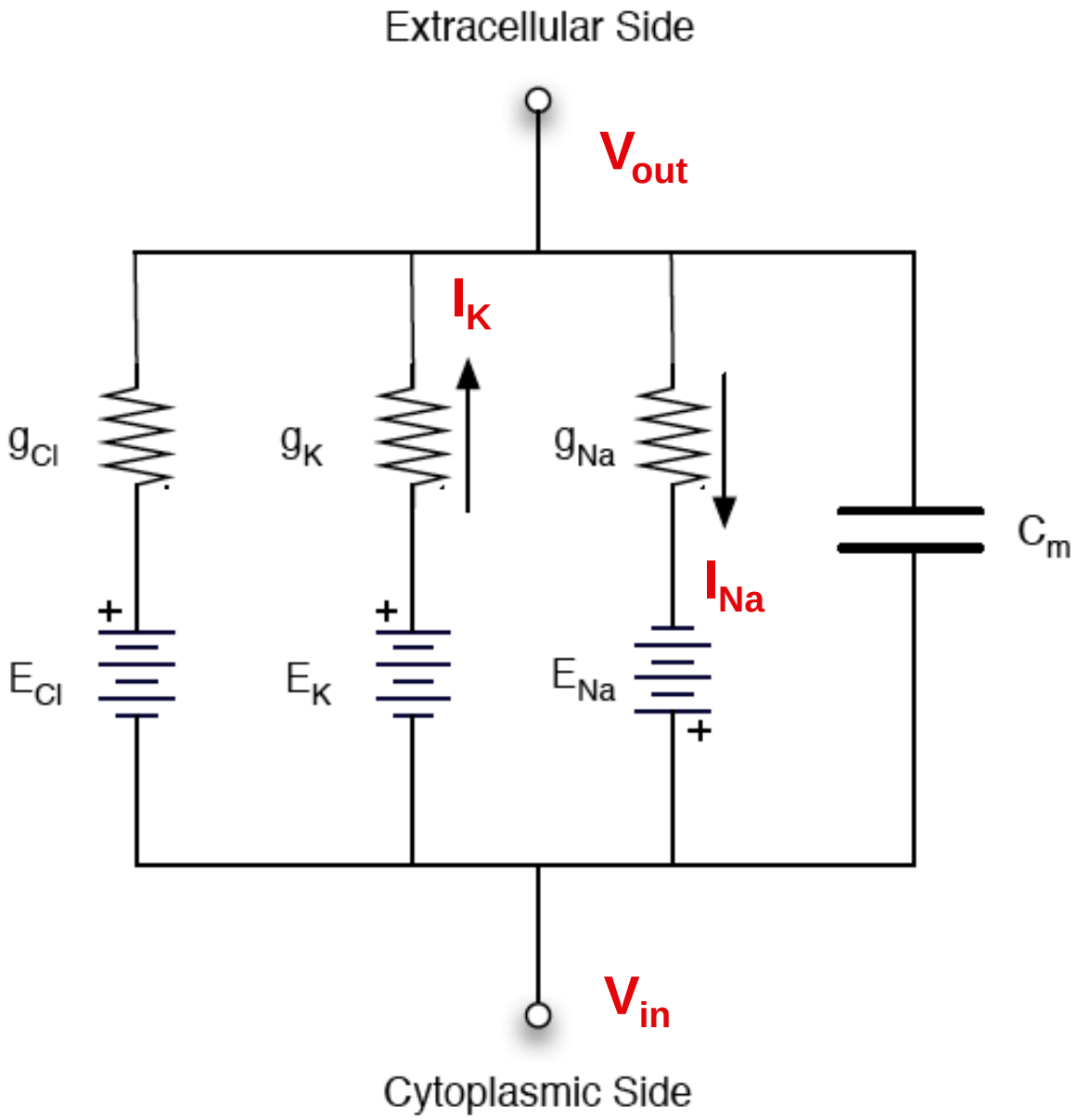
A) Calcium triggered transmitter release

Block it → Measure it → See it → Move it

B) Molecular mechanism of transmitter release

1. Hodgkin-Huxley模型
2. 突触传递-突触前机制：

The passive equivalent circuit



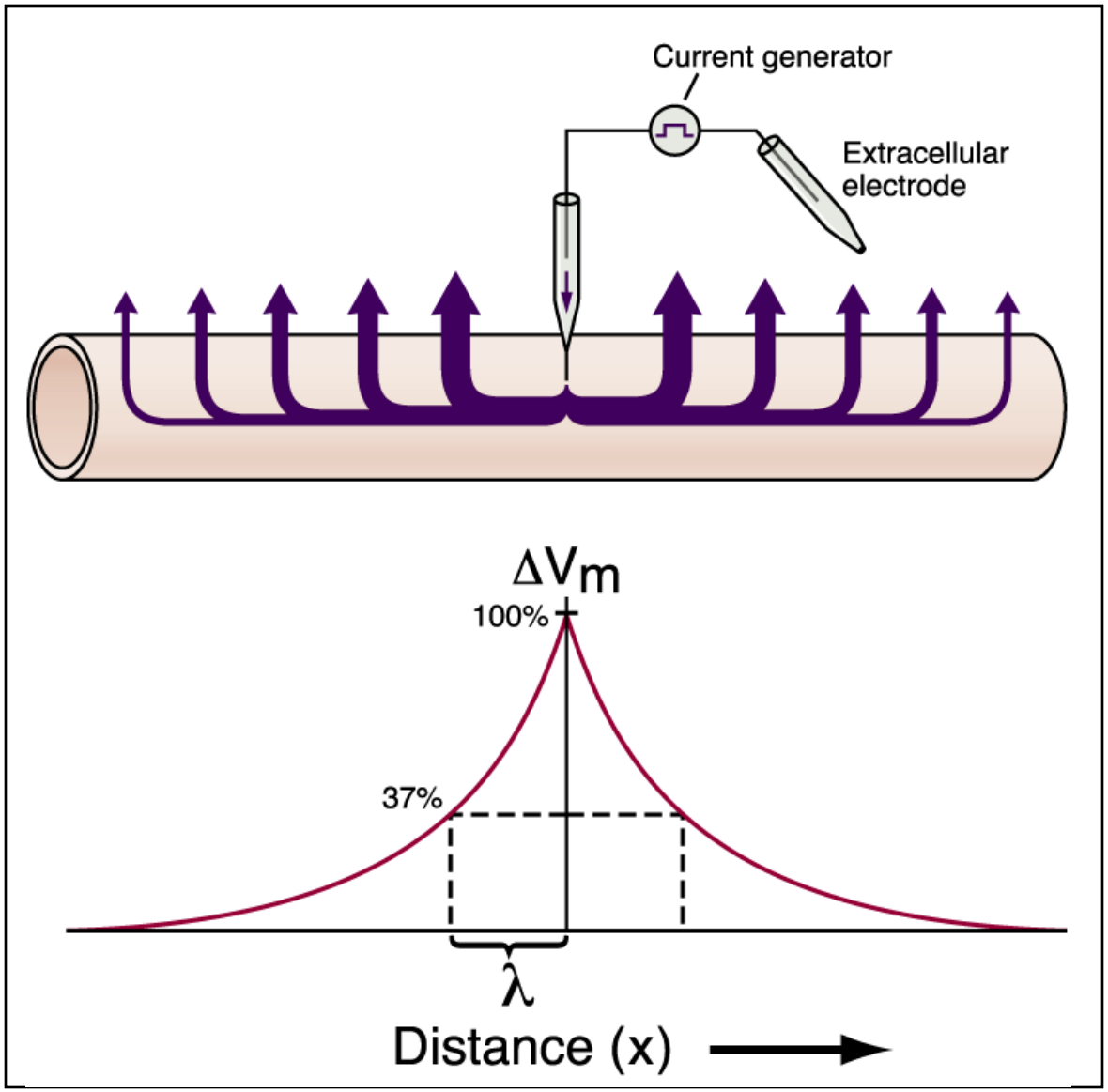
Solving for V_{rest}

1. $I_{Na} + I_K = 0$
2. $V_{in} - V_{out} = E_K + I_K / g_K$
3. $V_{in} - V_{out} = E_{Na} + I_{Na} / g_{Na}$
4. **$I_K = g_K(V_m - E_K)$**
5. **$I_{Na} = g_{Na}(V_m - E_{Na})$**

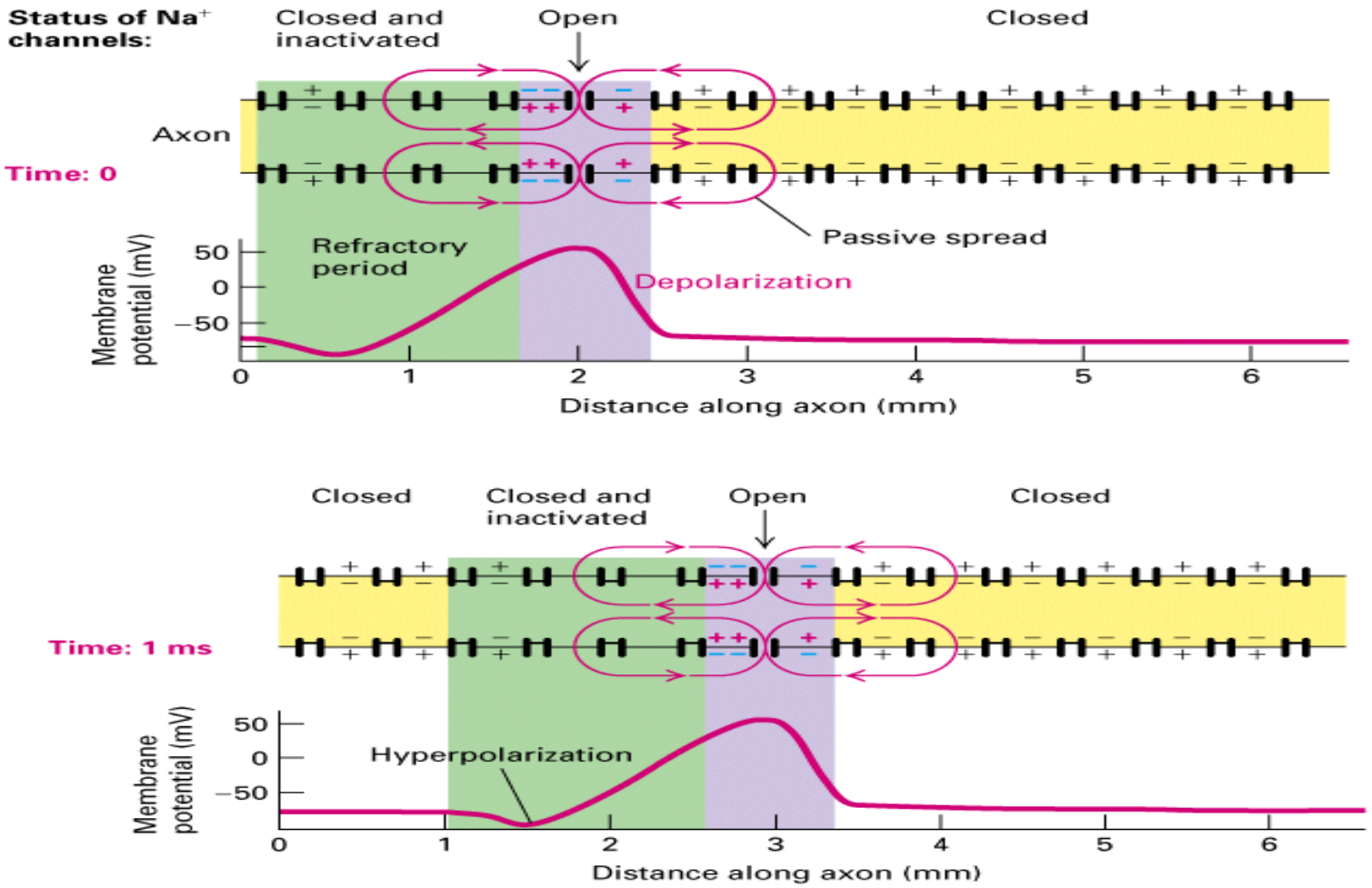
Finally,

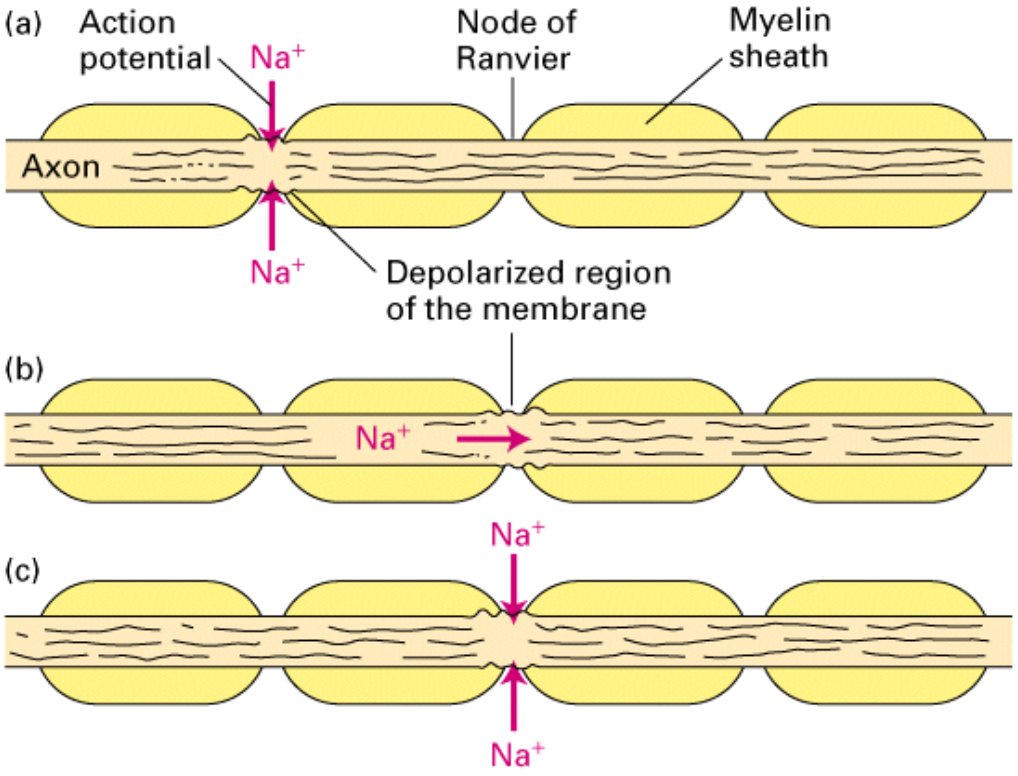
$$V_m = \frac{(E_{Na}g_{Na} + E_K g_K)}{g_{Na} + g_K}$$

Length Constant $\lambda = \sqrt{r_m / r_a}$



PNAS, Fig 8-5


Status of Na+ channels:
Closed and inactivated
Open
Closed
Axon
Time: 0
Passive spread
Refractory period
Depolarization
Membrane potential (mV)
50
0
−50
0
1
2
3
4
5
6
Distance along axon (mm)
Closed
Closed and inactivated
Open
Closed
Time: 1 ms
Hyperpolarization
Membrane potential (mV)
50
0
−50
0
1
2
3
4
5
6
Distance along axon (mm)



Action potentials travel down myelinated nerves at 100 m/s vs ~1 m/s for unmyelinated nerves. Why?

动作电位在有髓鞘包裹的神经纤维上传递速度是100m/s,在非髓鞘包裹的神经纤维上传递速度是1m/s

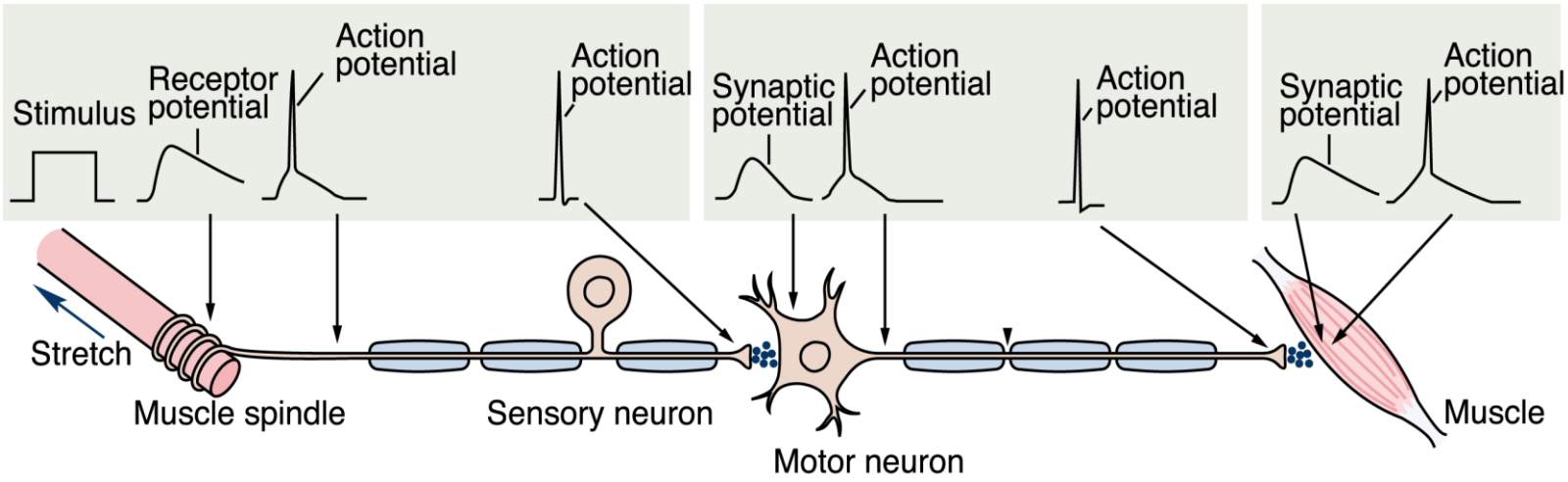
All Na+ channels concentrated at the nodes of Ranvier-very few between nodes. When Na+ rushes in at one node-it can't leak out over the intervening membrane-so it travels within the cell down the axon-all these positive charges start to depolarize the next node-which is picked up by voltage-gated sodium channels, action potential, on and on.

Fig. 21-18 p. 927

绝大部分的钠离子通道集中在郎飞结，只有极少数在郎飞结之间存在。由于髓鞘具有高度绝缘性，不可以使带电粒子通过。所以当钠离子进入细胞内产生动作电位后，郎飞结与相邻静息的郎飞结之间形成局部电流，激活下一个郎飞结。

Diagram of information transfer in the nervous system

神经系统中的信息传递



Generator Potentials, Synaptic Potentials and Action Potentials All Can Be Described by the Equivalent Circuit Model of the Membrane

发生电位，突触电位，动作电位都可以通过细胞膜平衡环路模型描述。

PNS, Fig 2-1

Neurotransmission

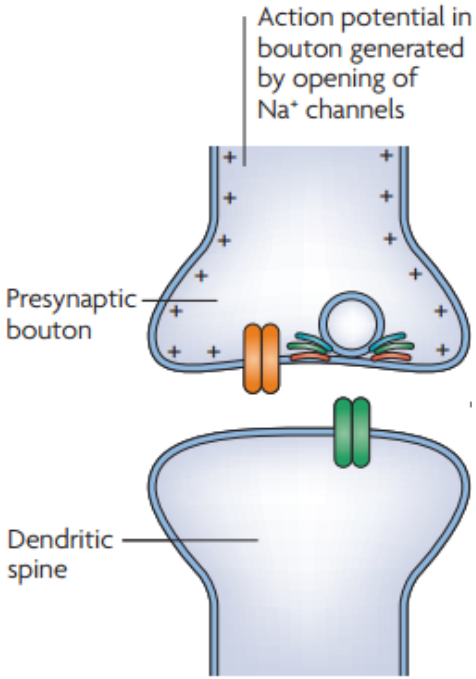
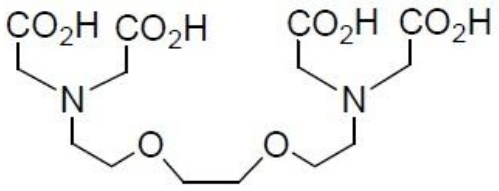
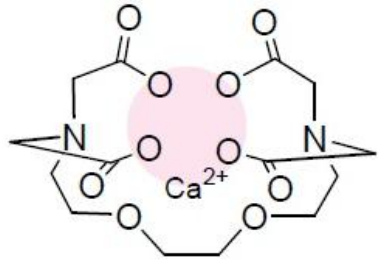


Figure 1 | **Steps in the process of chemical synaptic transmission.** These steps occur in both vertebrates and invertebrates, at the neuromuscular junction and central synapses. Cartoons based on a drawing by J. A. Ernst and A. Brunger.

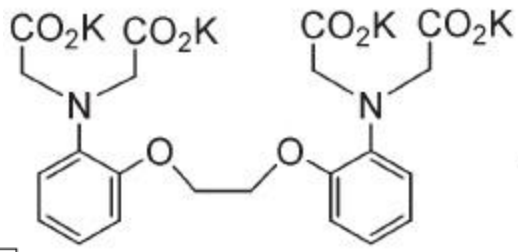
The sequence of events that underlie quantal transmission at central glutamatergic synapses. Nat Rev Neurosci. 2007 Aug

Calcium Chelators

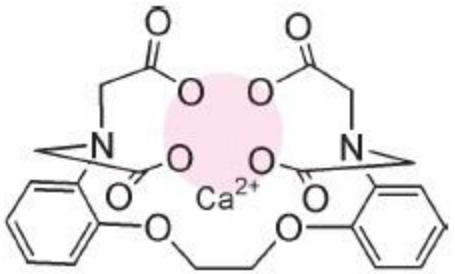




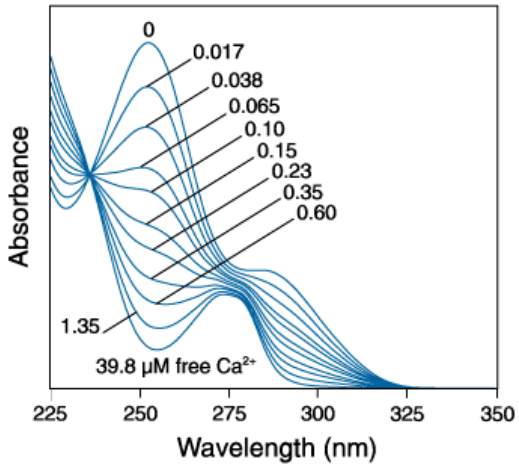
EGTA



BAPTA



BAPTA-Ca complex



Tsien, R.Y. (1980) New calcium indicators and buffers with high selectivity against magnesium and

Ca2+ dependence

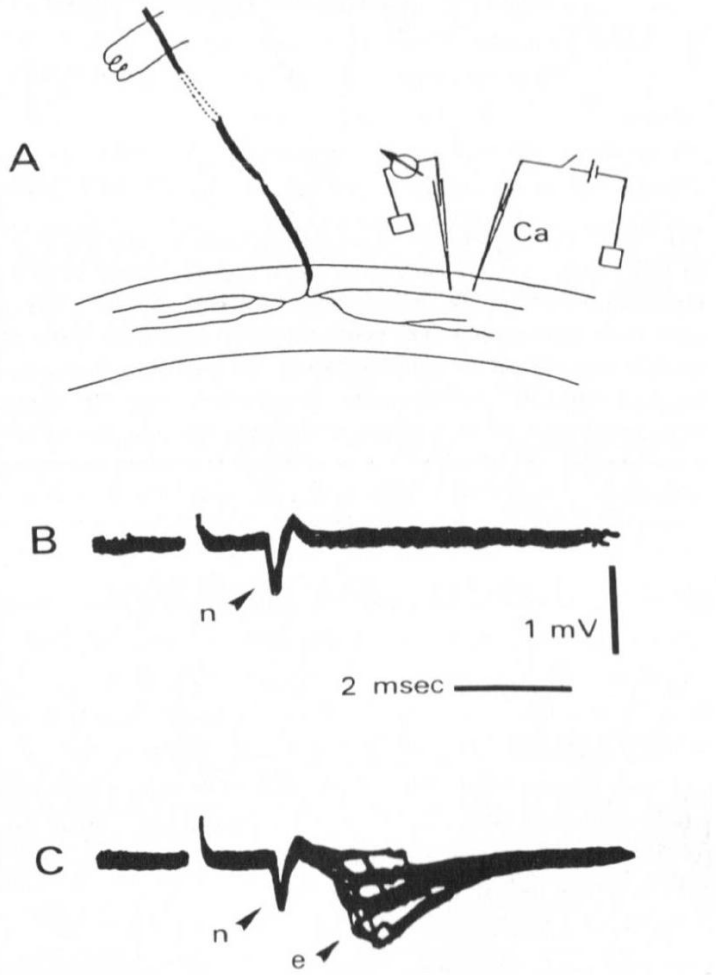


Fig. 2.1. Focal recordings of end-plate currents (e.p.c.s) with an extracellular electrode in a Ca^{2+}-free solution. A, schematic diagram of the recording procedure. B, without Ca^{2+} efflux from the Ca^{2+} pipette, nerve stimulation produces only a nerve terminal action current (n) not followed by the generation of e.p.c.s. C, when Ca^{2+} is applied from the pipette, nerve stimulation evokes e.p.c.s (e) as well as the nerve terminal action current (n). (Adapted from Katz and Miledi 1965c.)

Katz and Miledi J Physiol. 1965

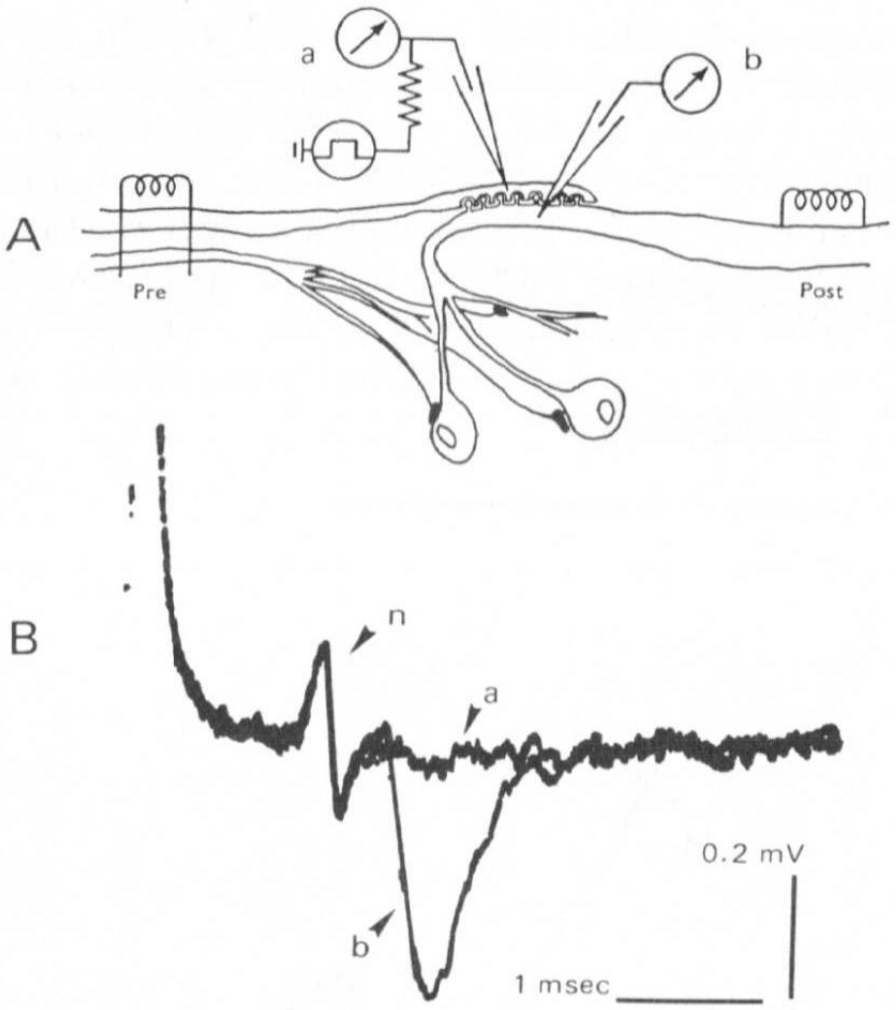
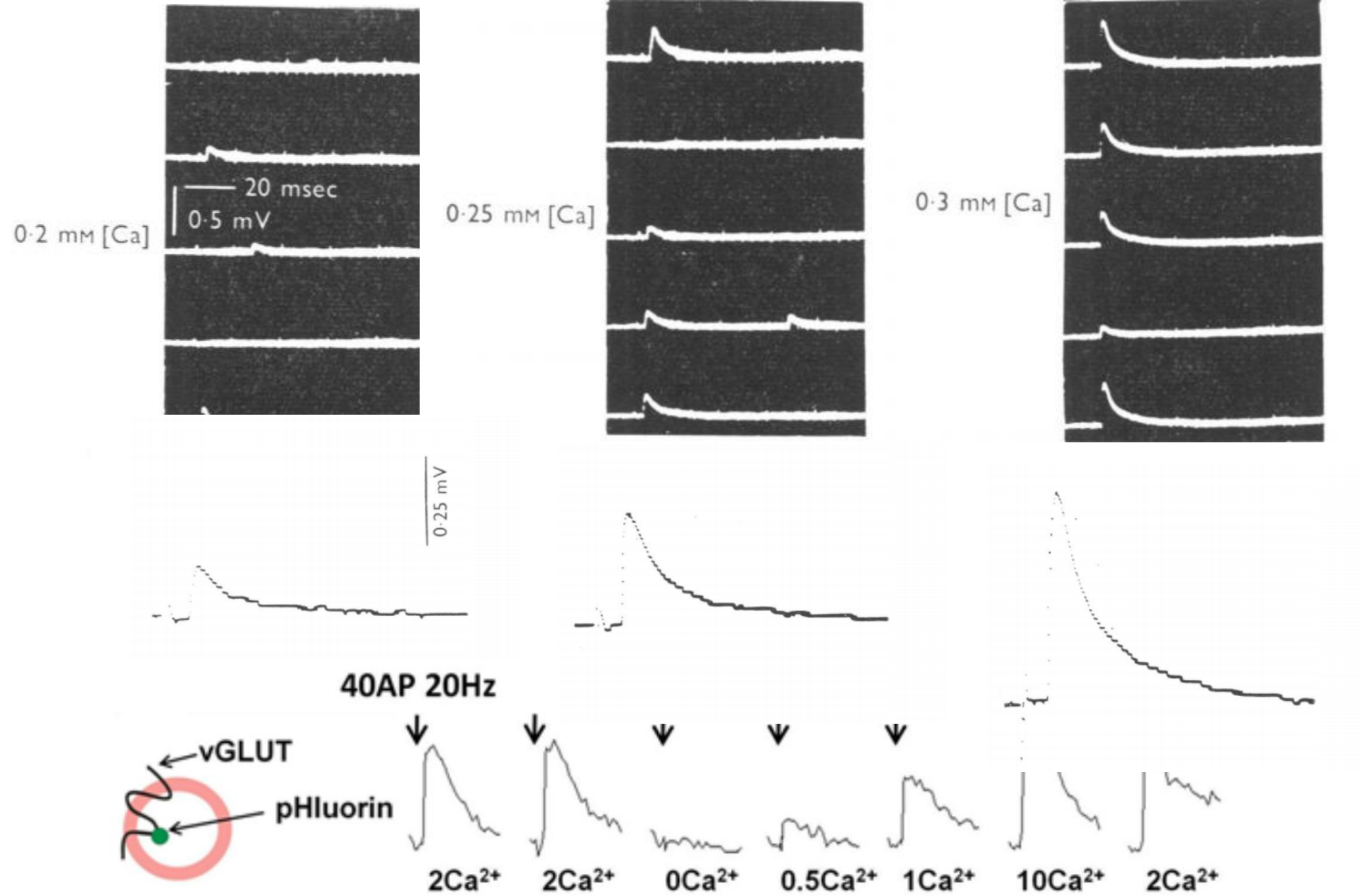
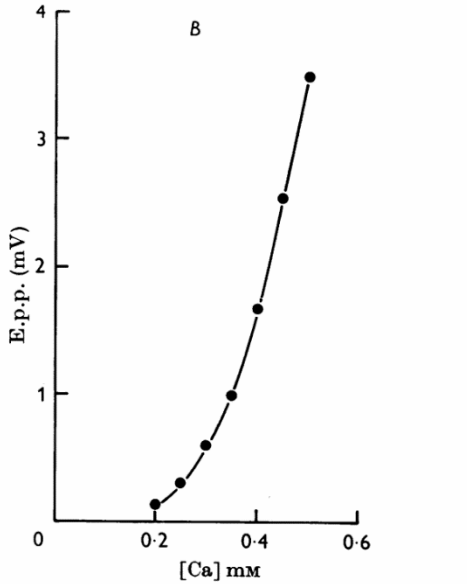


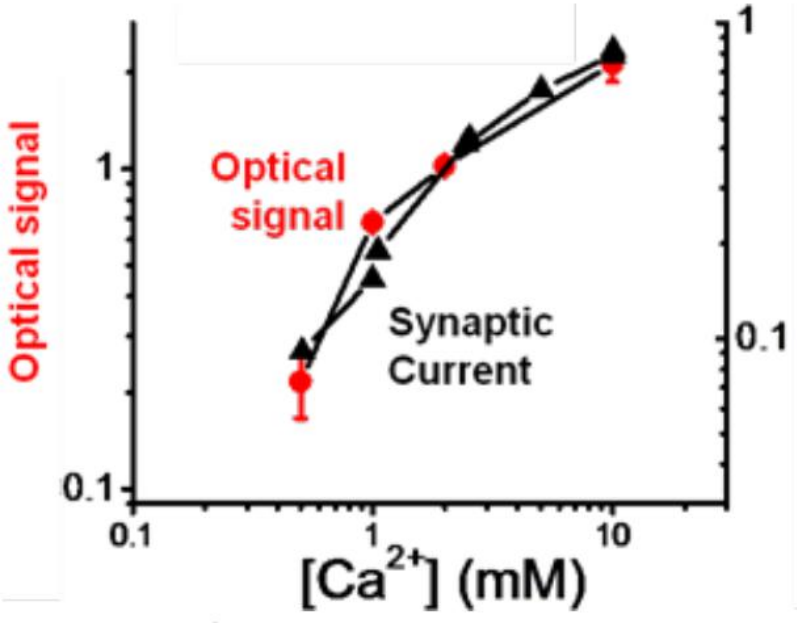
Fig. 2.2. Effects of Ca^{2+} on transmission in the giant synapse of the squid stellate ganglion. A, a pipette filled with a Ca^{2+}-rich solution (a) delivered Ca^{2+} focally while extracellular responses were recorded with another electrode (b). The response was elicited by stimulating the presynaptic axon (Pre). B, without Ca^{2+} efflux from the pipette presynaptic stimulation produced only a nerve action current (a) in a Ca^{2+}-free solution (a). When Ca^{2+} was applied from the pipette extracellularly, a synaptic response (b) followed the terminal action current (n). (Adapted from Miledi and Slater 1966.)

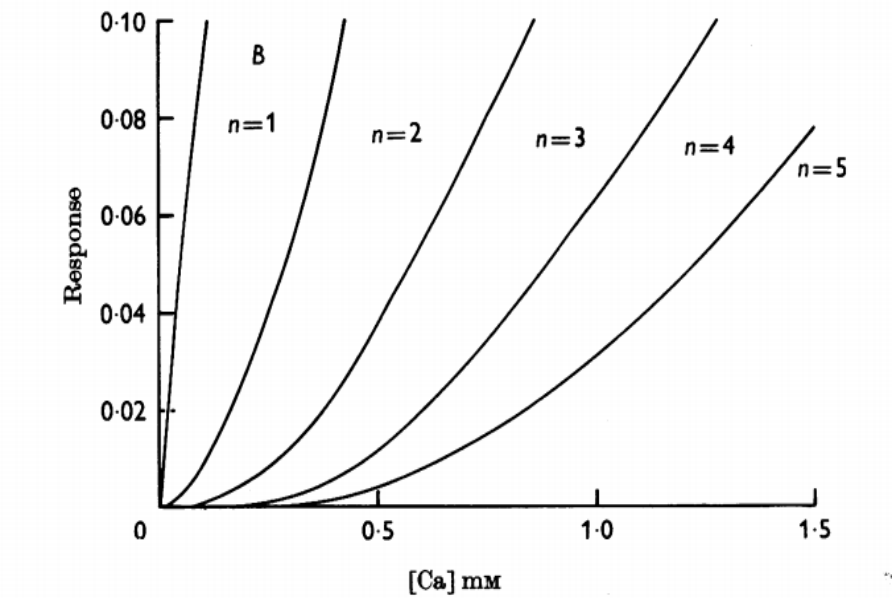
Miledi and Slater . J Physiol. 1966



Dodge, F A, & Rahamimoff, R. Physiol. (Lond.)







Dodge, F A, FA & Rahamimoff, R, R. Physiol. (Lond.) 1967

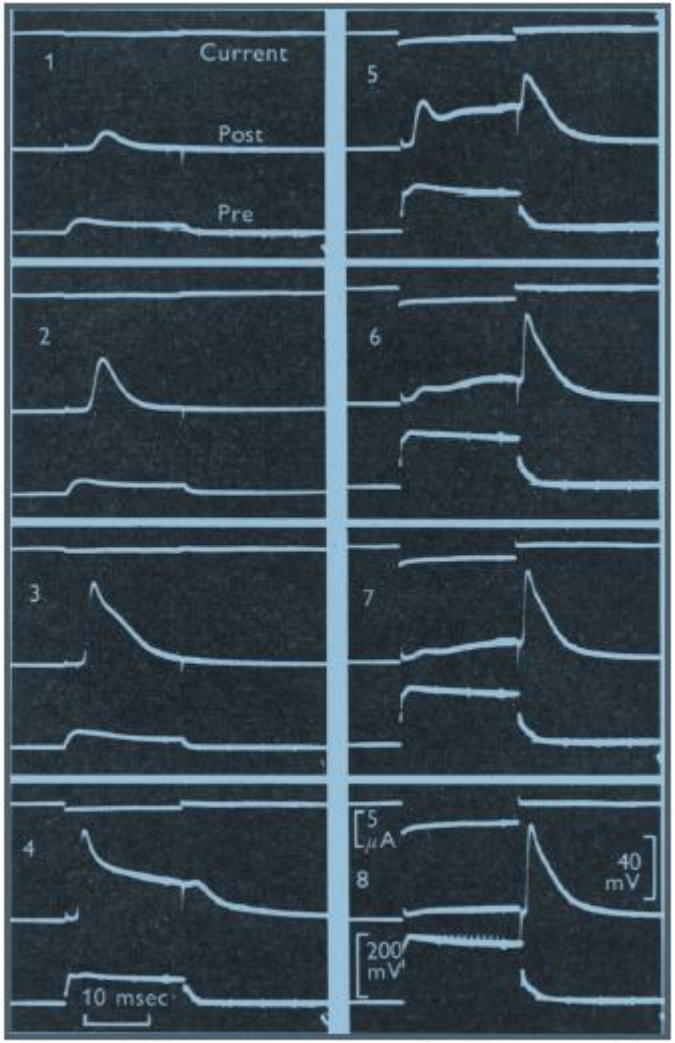


Fig. 10. Sample records of long current pulses and resulting pre- and post-potentials after iontophoretic loading of the terminal with tetraethylammonium. 1–8: increasing pulse intensity. Note gradual change from ON- to OFF-response.

J. Physiol. (Lond.) (1967) .A study of synaptic transmission in the absence of nerve impulses

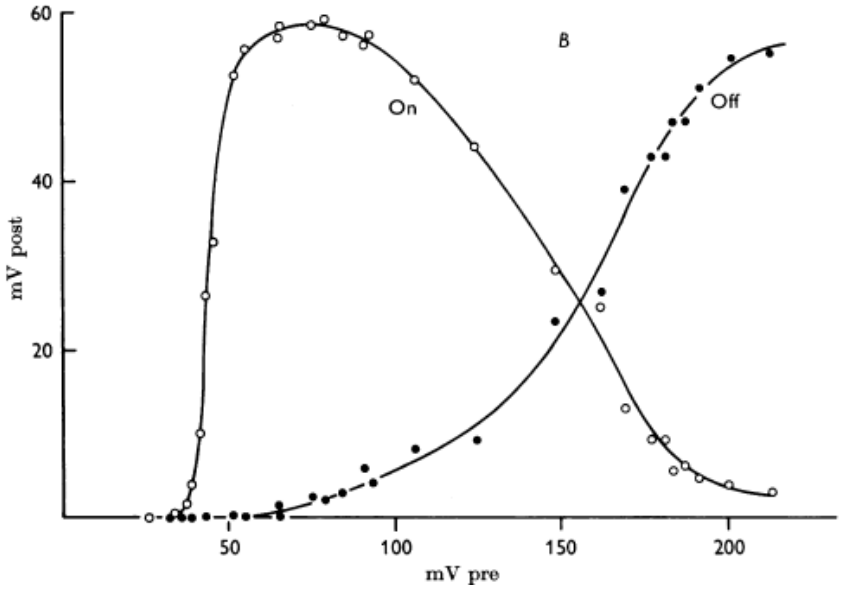


Fig. 11. Input/output curves from experiment illustrated in Fig. 10.

A study of synaptic transmission in the absence of nerve impulses. J.

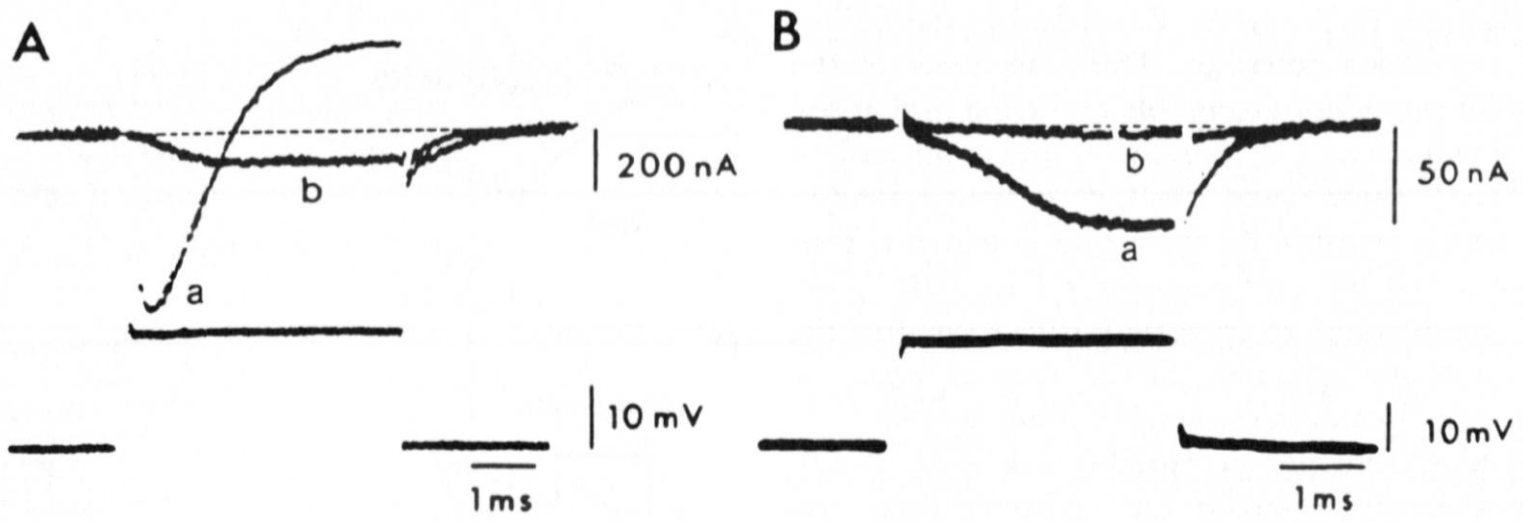


Fig. 2.8. Ca^{2+} currents recorded from a presynaptic terminal of the squid giant synapse under voltage clamp. The terminal was depolarized from a holding potential of −70 mV (lower traces). A: a, with low doses of TTX and 3–aminopyridine (3–AP), an initial inward Na^+ current followed by an outward K^+; b, a slow inward Ca^{2+} current was unmasked by additional TTX and 3–AP plus intracellularly injected TEA. B: a, with blockage of the Na^+ and K^+ conductances a depolarizing pulse elicited an inward Ca^{2+} current; b, the Ca^{2+} current was blocked by 1 mM Cd^{2+}. External Ca^{2+} concentration, 10 mM. (From Llinás *et al.* 1981.)

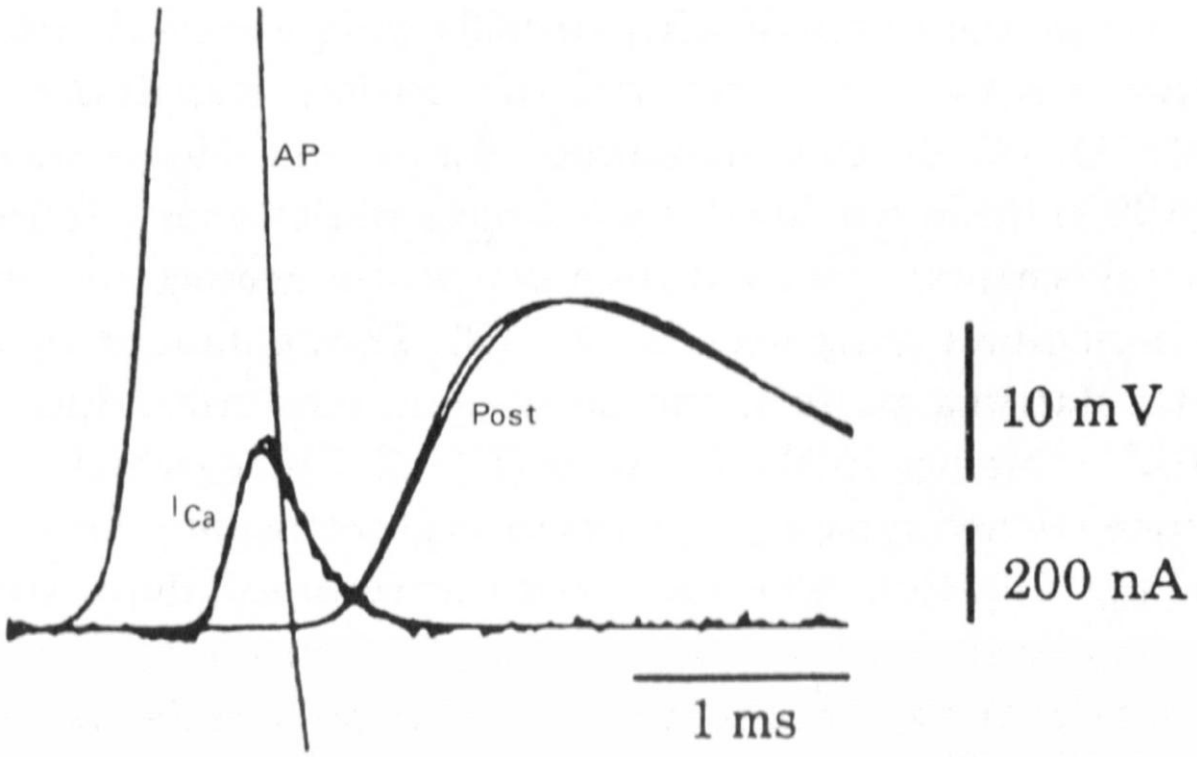


Fig. 2.10. Calcium currents (I_{Ca}) generated in a presynaptic terminal of the squid giant synapse by a replicated action potential. The presynaptic terminal was voltage-clamped with a waveform identical to the normal presynaptic action potential (AP). Post, synaptic potential simultaneously recorded from the postsynaptic axon. (From Llinás *et al.* 1982.)

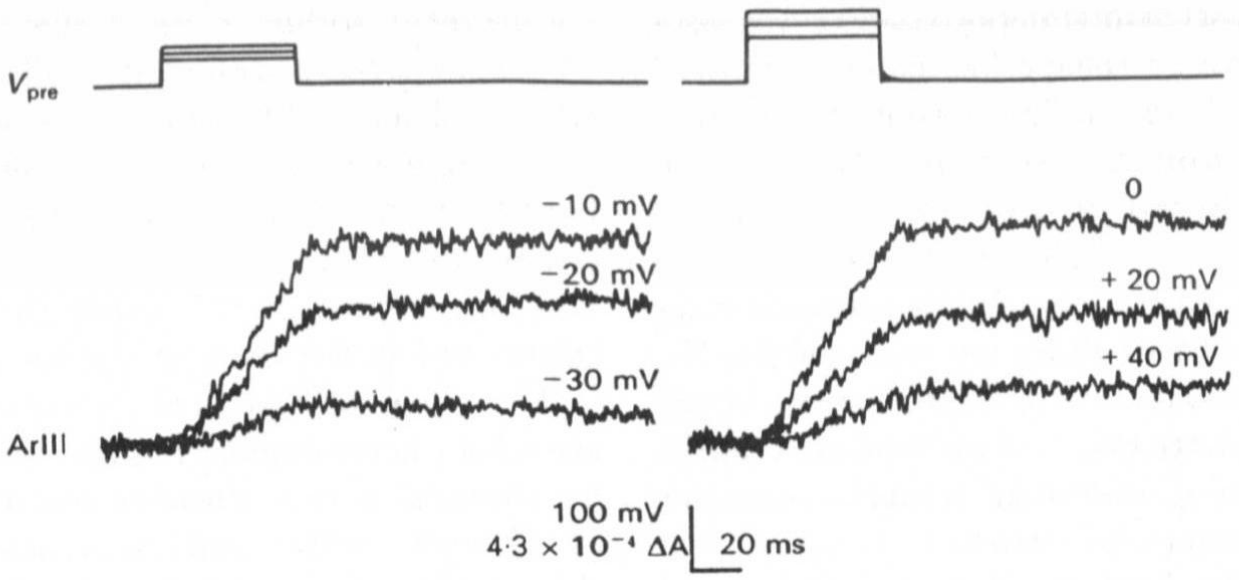
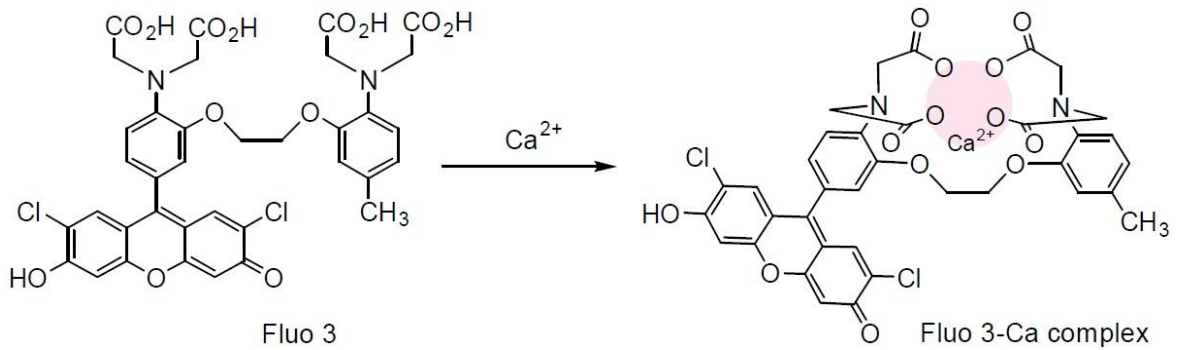
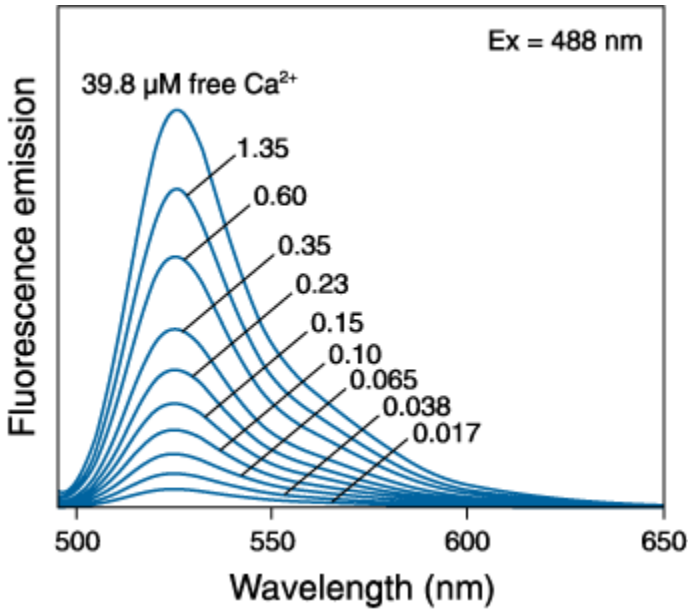


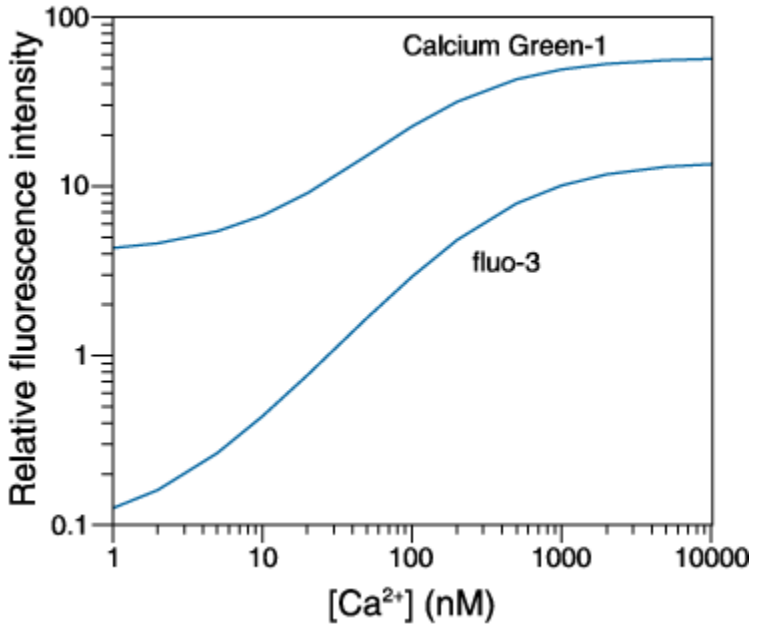
Fig. 2.4. Signals of arsenazo III (ArIII) detected in a presynaptic terminal of the squid giant synapse on depolarization of the presynaptic terminal. The presynaptic terminal was depolarized from a holding potential of −70 mV to varying levels indicated on each record under voltage clamp (V_{pre}). Note progressive increases in arsenazo III transients with stepwise depolarization to 0 mV, whereas the signals were reduced by further depolarization beyond 0 mV. (From Augustine *et al.* 1985.)

Typical Ca2+ dyes with intensity shift

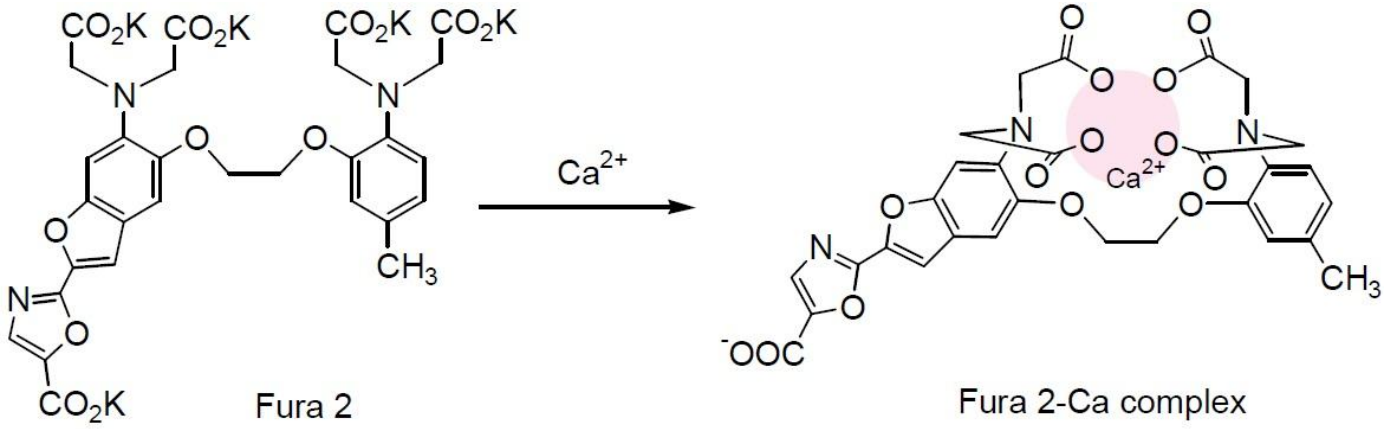
- Fluo-3, fluo-4

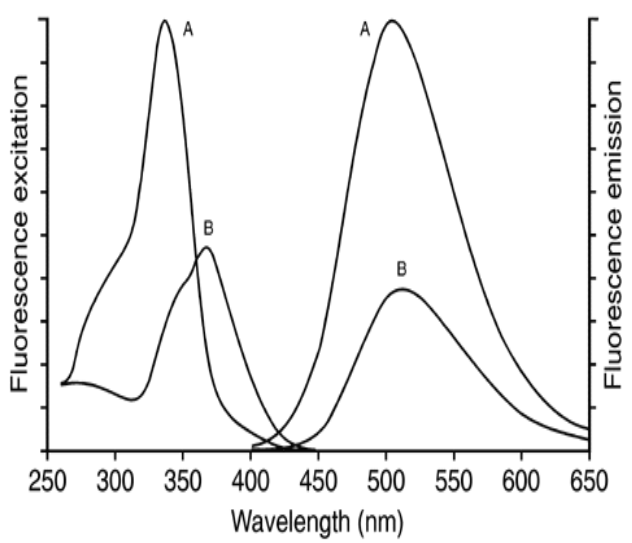


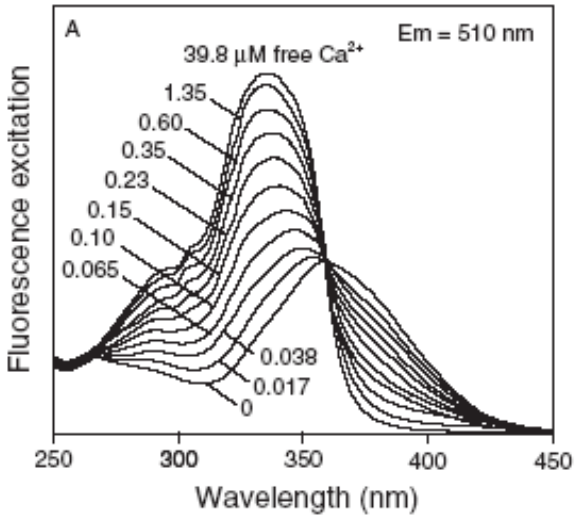




Fura-2







A: Ca2+ saturated B: Ca2+ free

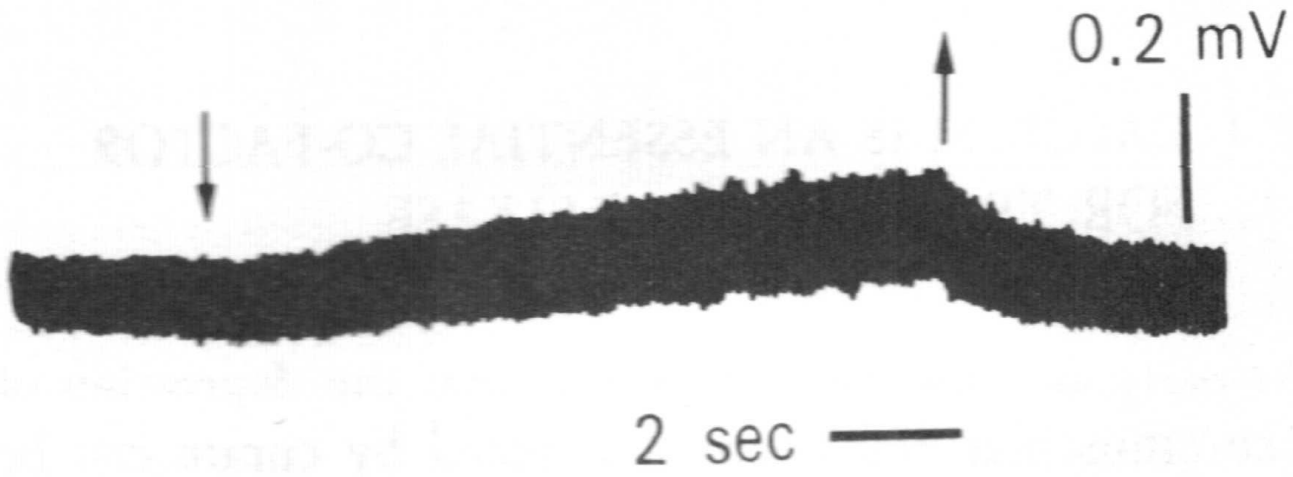


Fig. 2.3. A depolarizing response produced in the postsynaptic axon by injecting Ca^{2+} into the presynaptic axon in a squid giant synapse. The experimental procedure was similar to that illustrated in Fig. 2.2A, but the Ca^{2+}-filled pipette was inserted into the presynaptic axon, while recording the postsynaptic intracellular potentials with another electrode. The preparation was superfused with sea water containing tetrodotoxin. The bias current preventing Ca^{2+} efflux from the pipette was switched off during the period indicated by two arrows. (Adapted from Miledi 1973.)

Photolysis of Caged Calcium