SINAPSI - ELETTRICHE

- CHIMICHE
  - ECCITATORIE
  - INIBITORIE

SINAPSI CHIMICHE

PRIME EVIDENZE

- Metodo di Golgi (TEORIA DEL NEURONE RAMON Y CAJAL)
  ↓
- MICROSCOPIA ELETTRONICA (1940-1950)
- ACh nel cuore ('VAGUSSTOFF')
  ↓
- ACh in vescicole presinaptiche
- RITARDO SINAPTICO (0,2 ms)

PREPARATO SPERIMENTALE CLASSICO:

- GIUNZIONE NEUROMUSCOLARE (RANA)

(- anche SINAPSI GIGANTI di INVERTEBRATI)

Dc: AIDLEY D.J. THE PHYSIOLOGY OF EXCITABLE CELLS. CAMBR. U.P.

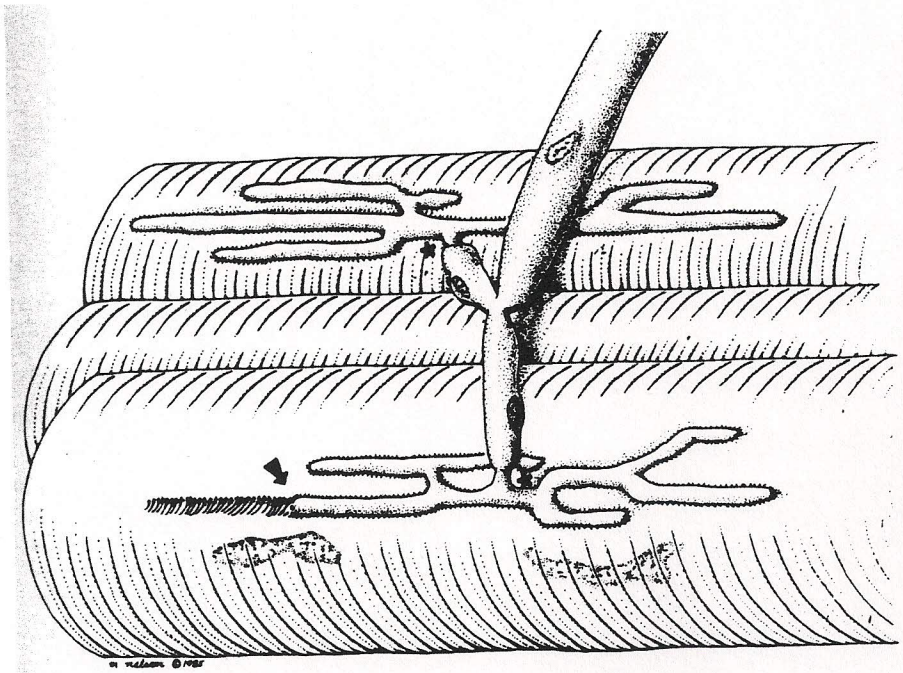


Figure 7.2. A schematic drawing of the frog neuromuscular junction, based mainly on light microscopy and scanning electron microscopy. The nerve terminal branches to contact a number of muscle fibres. The asterisks show where the myelin sheath ends. Part of a terminal branch has been pulled away at the arrow to show the postsynaptic gutter traversed by postsynaptic folds. (From Salpeter, 1987 in *The Vertebrate Neuromuscular Junction*, ed. M. M. Saltpeter, © 1987 Alan R. Liss. Reprinted by permission of John Wiley & Sons, Inc.)

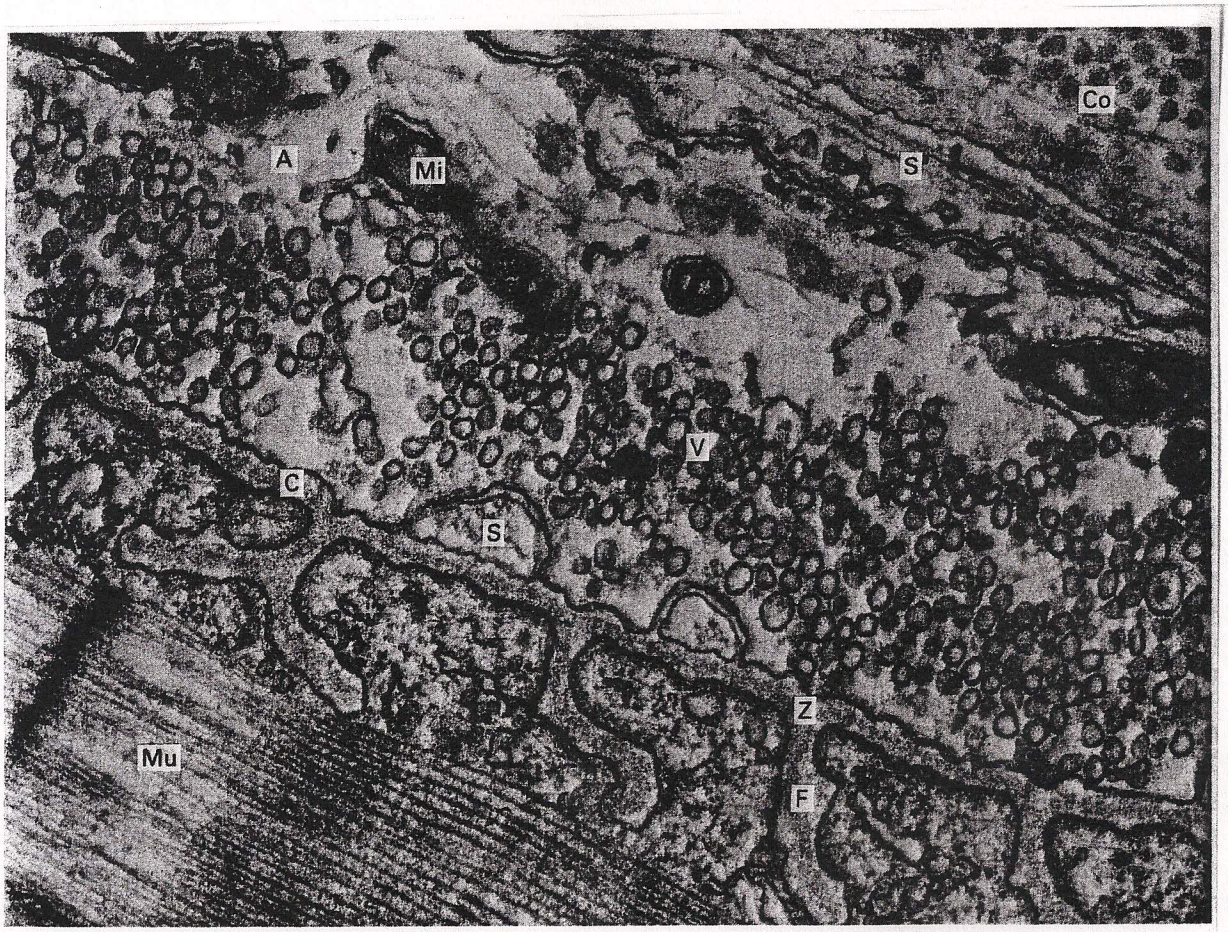
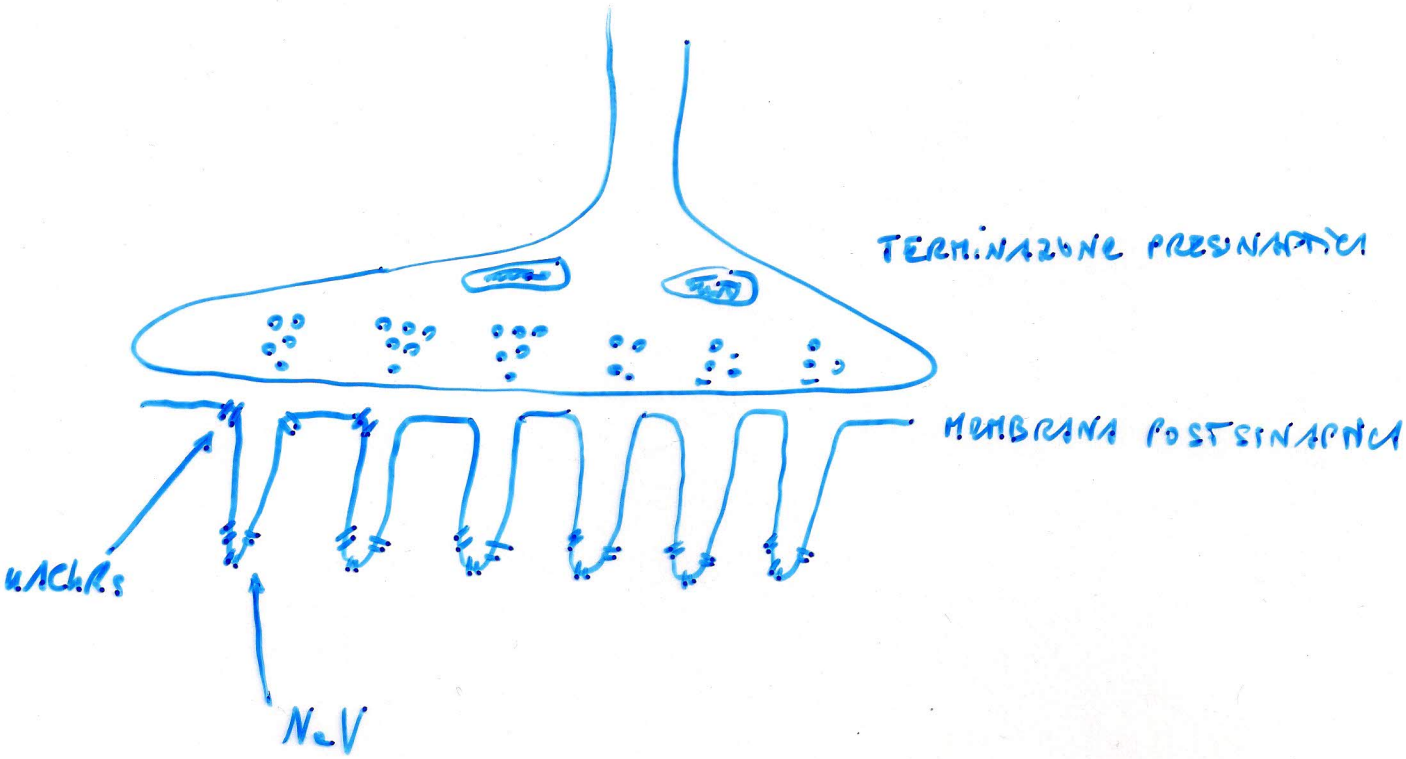


Figure 7.3. Electron micrograph of a frog neuromuscular junction. The axon terminal (A) is seen in longitudinal section. It contains mitochondria (Mi) and numerous synaptic vesicles (V), and is covered by a Schwann cell (S). Collagen fibres (Co) can be seen over the Schwann cell. The muscle fibre (Mu) is separated from the axon terminal by the synaptic cleft (C), which contains some darkly staining material. The muscle fibre postsynaptic membrane is indented to form junctional folds (F), and is underlaid by dense material at the top of them, where the acetylcholine receptors are concentrated. Presynaptic active zones (Z) occur opposite some of the junctional folds; notice the slight protrusion of the presynaptic membrane, the dense cytoplasmic material and the concentration of synaptic vesicles there. Magnification 43 000×, i.e. 1 mm is equivalent to 230 Å. (Photograph kindly supplied by Professor J. E. Heuser.)

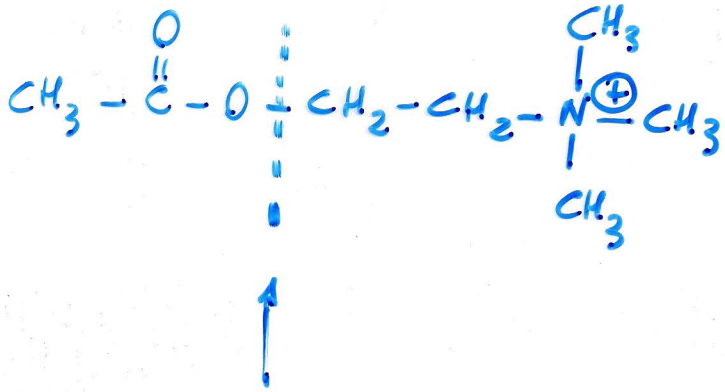
GIUNZIONE NEUROMUSCOLARE (PLACCA MOTRICE)

ENDPLATE

EP



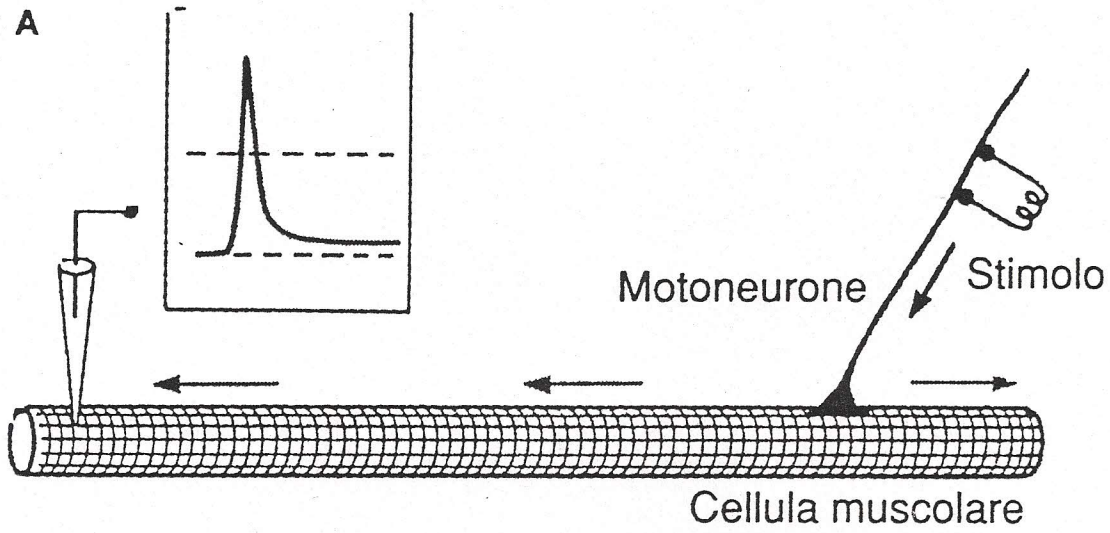
ACh

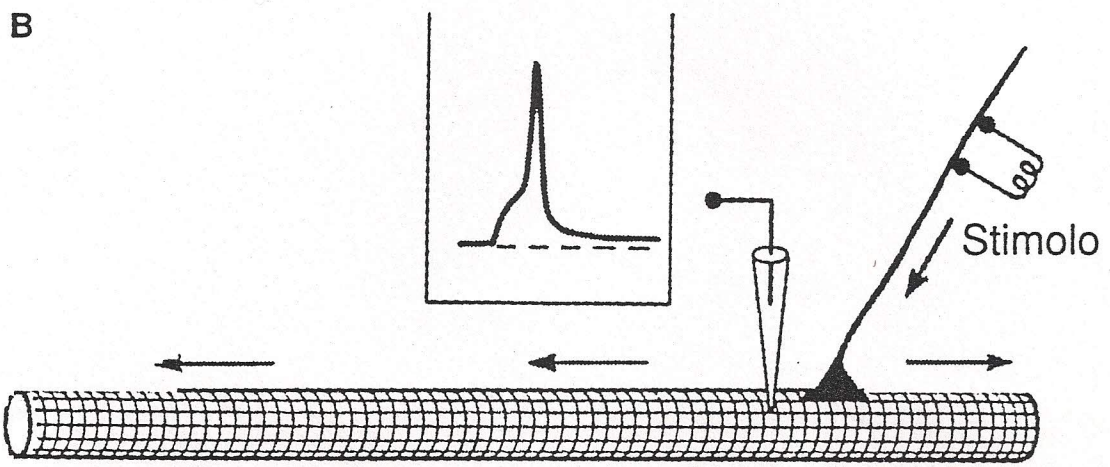


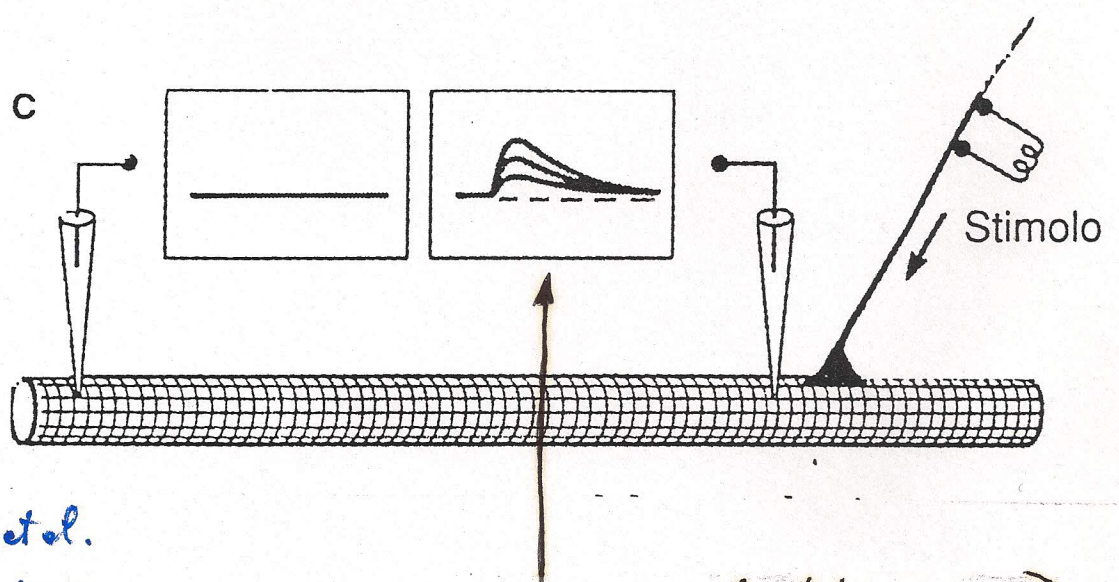
ACETILCOLINESTERASI

(AChE)

nello spazio sinaptico







Da: RANDALL et al.
FISIOLOGIA ANIMALE
2 ED. ZANICHELLI

CON CURARO (D-tubocurarina) PER BLOCCARE PARZIALMENTE LA TRASMISSIONE E GENERARE POTENZIALI DI PLACCA CHE NON RAGGIUNGANO LA SOGLIA

Da: AIDLEY D.J. THE PHYSIOLOGY OF EXCITABLE CELLS

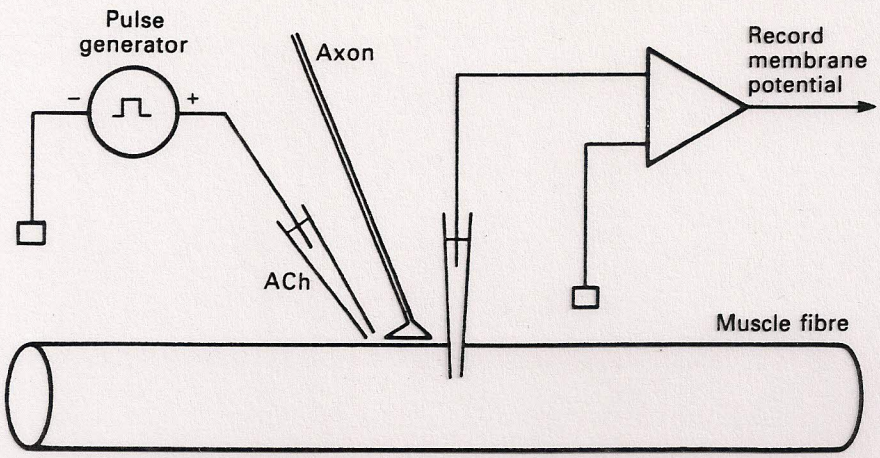


Figure 7.11. Arrangement for ionophoretic application of acetylcholine at the neuromuscular junction. The intracellular microelectrode is inserted in the end-plate region and connected to the circuit on the right to record the membrane potential. The ionophoresis circuit is shown on the left: a pulse generator is connected to an extracellular micropipette which contains a solution of acetylcholine (ACh).

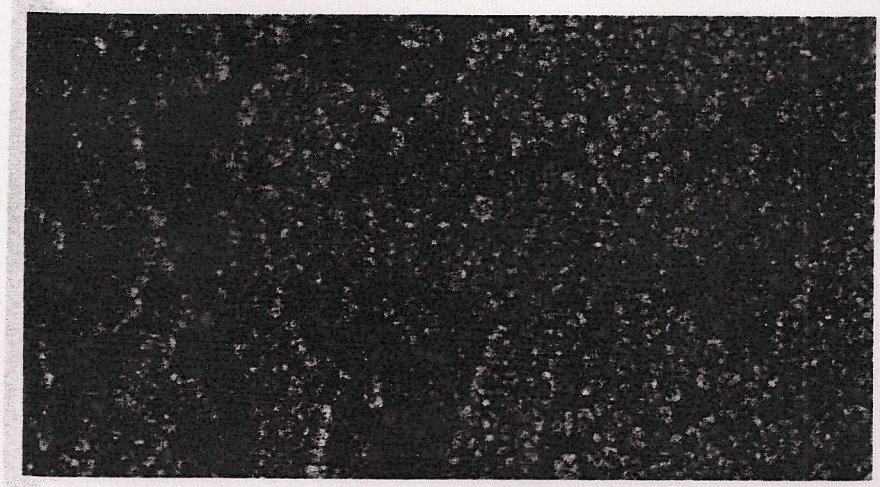


Figure 7.13. Array of acetylcholine receptors on the electrocyte postsynaptic membrane in the electric ray *Torpedo*. Notice the tendency for the receptors to form rows of four abreast, and that each receptor consists of a number of subunits around a central hollow. The picture is of a platinum replica of the surface of a fragment of postsynaptic membrane, quick-frozen and freeze-etched. Magnification 296 000×, i.e. 1 mm is equivalent to 34 Å. (Photograph kindly supplied by Professor J. E. Heuser, from Heuser & Salpeter, 1979.)

IDEA DEI RECETTORI:

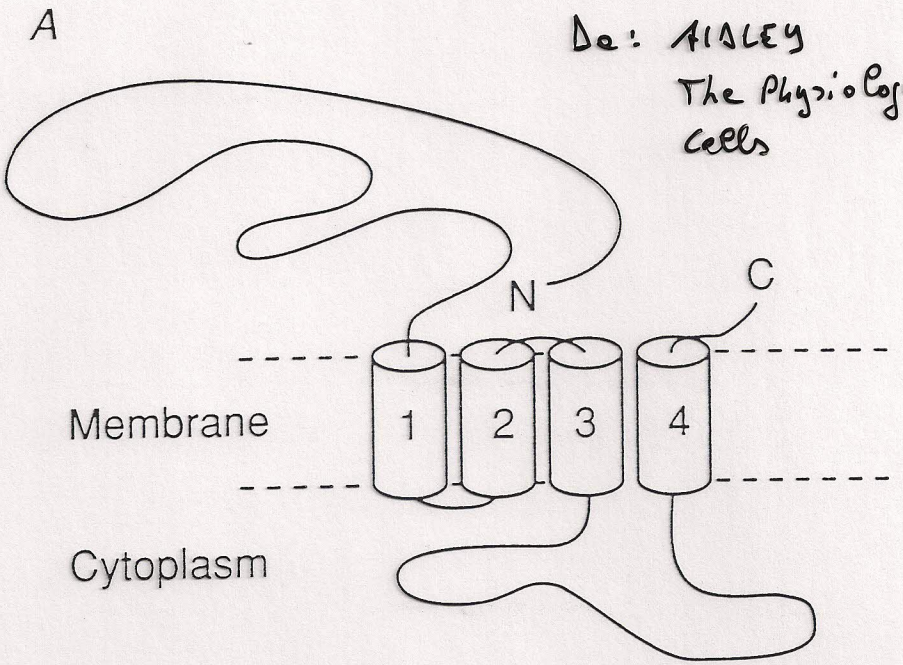
IONOFORESI: rapida
manipolabile (p.es. conc.
distanza dalla placca)

Ach funziona solo dall'esterno

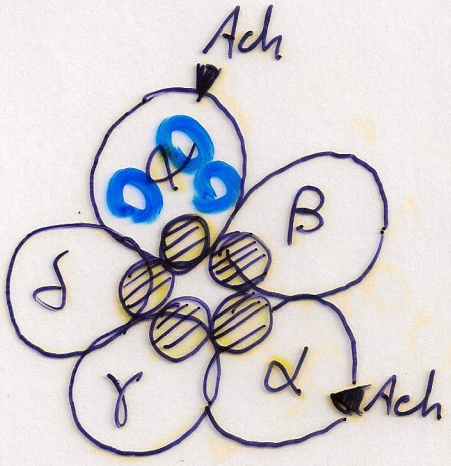
LOCALIZZAZIONE: IONOFORESI
α-BTX*
M.E.

RECETTORE NICOTINICO PER L'ACETILCOLINA

(IONOTROPO)



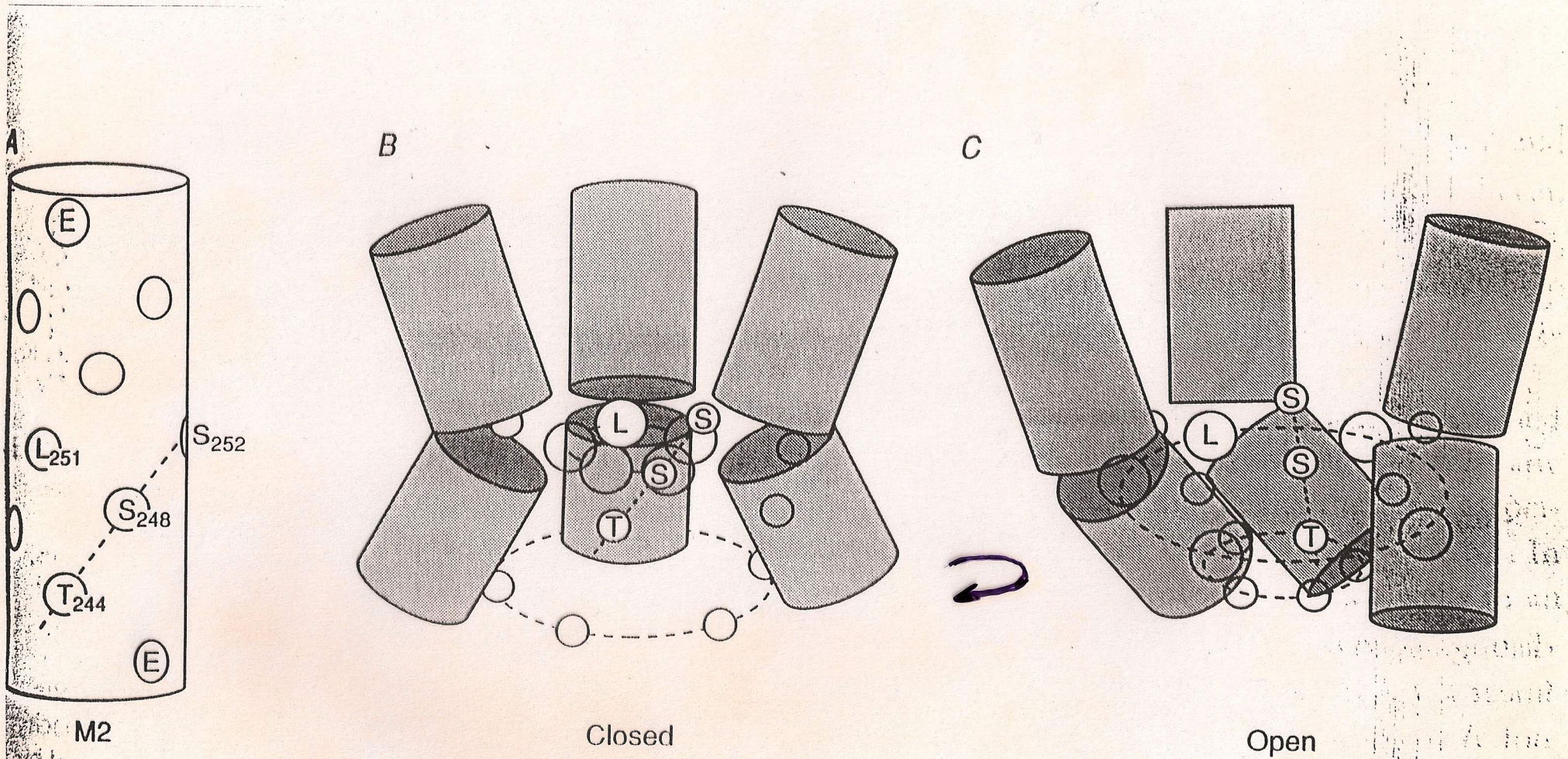
Da: ALDLEY
The Physiology of Excitable cells



= M2

SUBUNITÀ NEL MUSCOLO

IL GATING E IL FILTRO DI SELETTIVITA'
NON SONO PROCESSI INDIPENDENTI



FROM: AIDLEY. THE PHYSIOLOGY OF EXCITABLE CELLS. 1998 CAMBR. UN. PRESS
ORIGINAL FROM UNWIN N. 1995 Nature 373, 42

POTENZIALE D'INVERSIONE DEL RECETTORE NICOTINICO

$$I_{Na} = g_{Na}(V_m - E_{Na})$$

$$I_K = g_K(V_m - E_K)$$

(assumendo flussi indipendenti per i due ioni e nessun altro ione permeante)

Al V_{INV} (pot. di inversione, o V_{REV}):

$$I_{Na} + I_K = 0$$

Cioè $$V_{INV} = \frac{g_{Na}}{g_{Na}+g_K} E_{Na} + \frac{g_K}{g_{Na}+g_K} E_K$$

Se $g_{Na} \simeq g_K \rightarrow V_{INV} \simeq -20\ mV$

(in realtà è $\simeq -10\ mV$)

ACh

$V_m = E_{Na}$ (N+60)

I USCENTE (tutto K^+)

$E_{Na} > V_m > E_{INV}$

PREVALE K^+ USCENTE

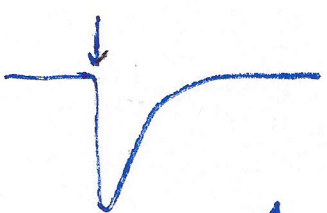
$V_m = E_{INV}$ (N-10)

$I = 0$ $I_{Na} = -I_K$

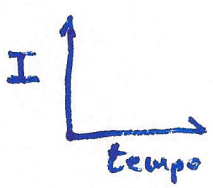
$E_{INV} > V_m > E_K$

PREVALE Na^+ entrante

$V_m = E_K$ (N-90)



I ENTRANTE (tutto Na^+)



DIMOSTRAZIONE CHE È UN TIPO UNICO DI CANALE IONICO:

- SINGOLO CANALE
- BLOCCANTI SPECIFICI
- MARKATORI, ecc.

TABLE 5. SELECTED PERMEABILITY RATIOS FOR ENDPLATE CHANNELS

Ion or molecule	P_X/P_{Na}
Tl^+	2.51
$HONH_3^+$	1.92
NH_4^+	1.79
Guanidinium	1.59
Cs^+	1.42
Methylammonium	1.34
Ethylammonium	1.13
K^+	1.11
Na^+	1.00
Li^+	0.87
Isopropylammonium	0.82
Triaminoguanidinium	0.30
Diethylammonium	0.25
Urea	0.13
Triethylammonium	0.090
Arginine	<0.014
Tetrakisethanolammonium	<0.010

All values calculated from reversal potentials at the frog neuromuscular junction (Dwyer et al., 1980; Adams, Dwyer and Hille, 1980; where additional measurements can be found) except for urea, which is from isotope fluxes in cultured chick muscle (Huang et al., 1978).

From: Hille B., IONIC CHANNELS OF EXCITABLE MEMBRANES - SINAUER 1992

P_i: $Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$

U_i: $Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$

P_i = permeability

U_i = mobility

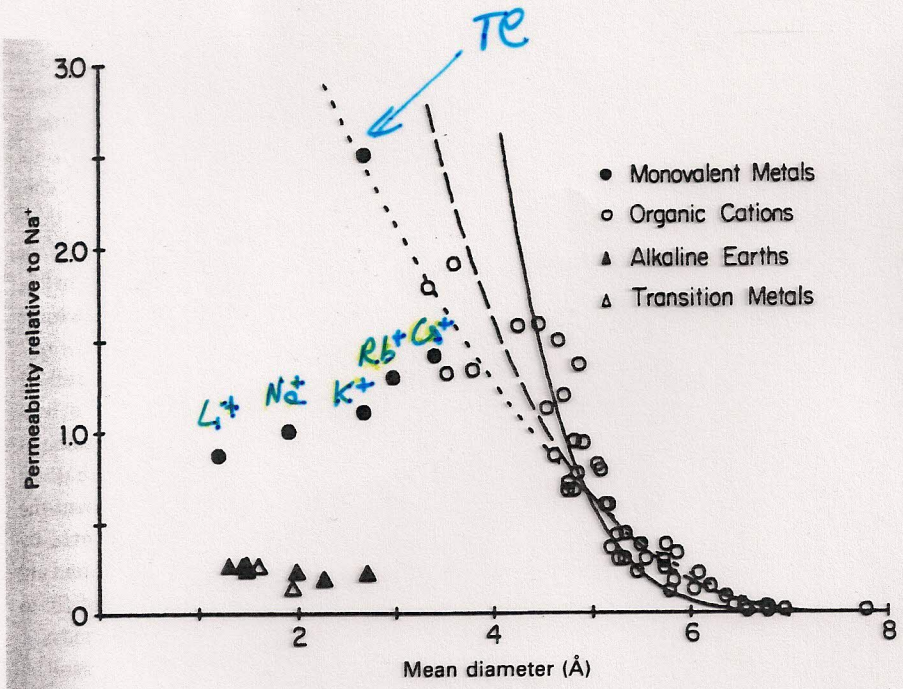


Figure 8.11. Relations between ionic diameter and the relative permeability of nicotinic acetylcholine receptor channels at the frog muscle end-plate. The three curves represent different theoretical models, all of them assuming a cylindrical pore with a diameter of 7.4 Å. (From Adams *et al.*, 1980. Reproduced from the *Journal of General Physiology*, by copyright permission of The Rockefeller University Press.)

From: AIDLEY, THE PHYSIOLOGY OF EXCITABLE CELLS.

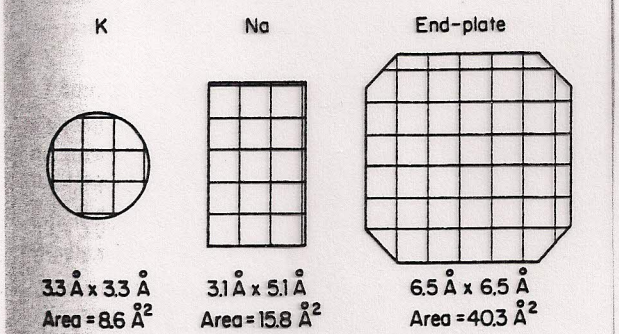


Figure 8.12. Hypothetical cross-sections of three types of ion channel in frog nerve and muscle, based on their permeabilities to ions of different sizes. The voltage-gated sodium and potassium (delayed rectifier) channels occur in nerve axons at the nodes of Ranvier. (From Dwyer *et al.*, 1980. Reproduced from the *Journal of General Physiology*, by copyright permission of The Rockefeller University Press.)

$P_{Mg} > P_{Ca} > P_{Ba}$

$\frac{P_{Ca}}{P_{Na}} \approx 0.22$ in 20 mM $CaCl_2$

≈ 0.16 in 80 mM $CaCl_2$

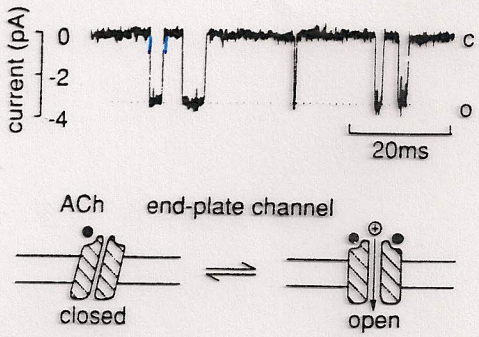


Figure 7.16. Currents through a single acetylcholine-gated channel in rat muscle, recorded with the patch clamp technique. Opening of the channel is seen as a downward deflection of the trace, indicating an inward current of about 3 pA. The membrane potential was −70 mV. The sketch indicates that normally two acetylcholine molecules have to be bound before the channel opens. (From Sakmann, 1992.)

$A \rightleftharpoons B$

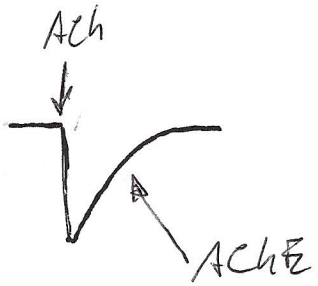
$A + B \rightleftharpoons C$

FROM: HILLE B. IONIC CHANNELS OF EXCITABLE MEMBRANES

SINAUER, 1992 (2nd Ed.)

DESENSITIZZAZIONE

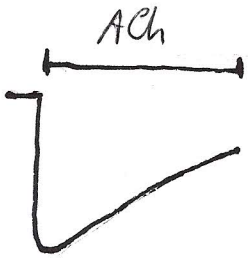
a) senza bloccante per AChE



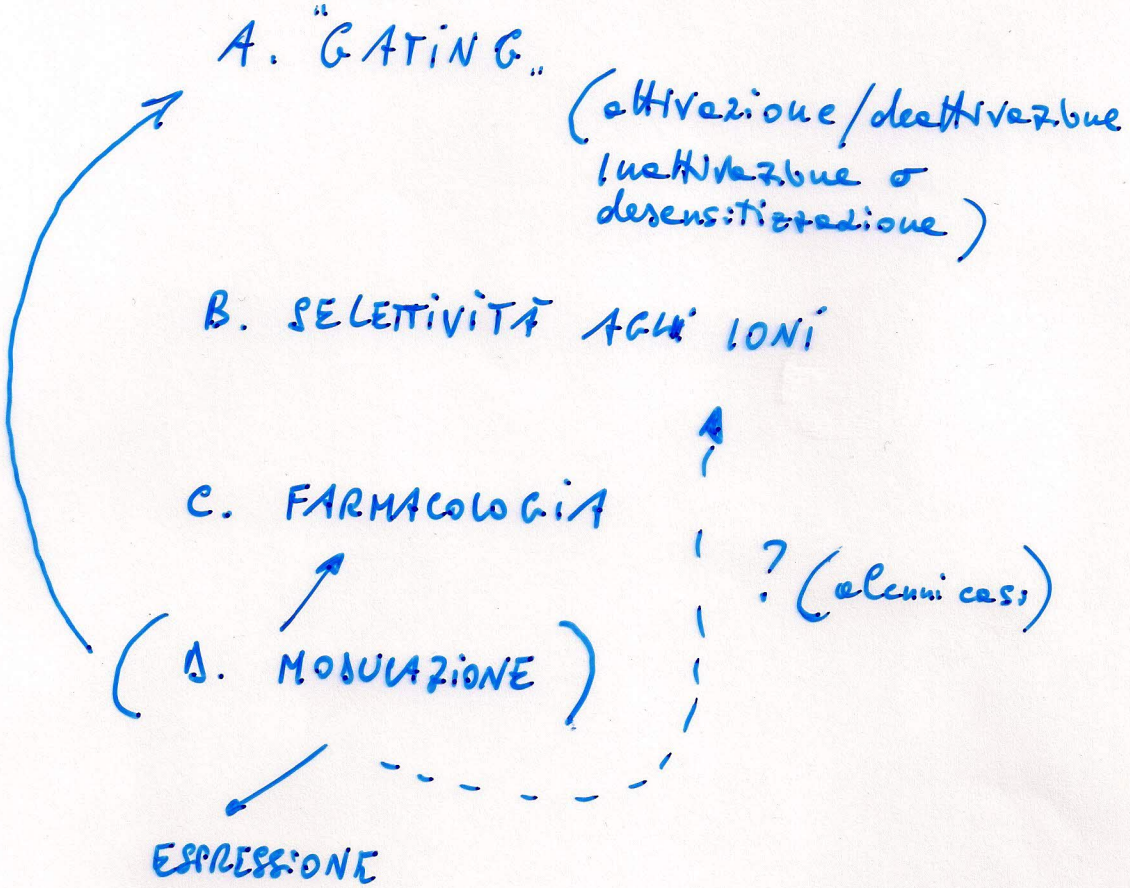
EPC
(END-PLATE CURRENT)

- 80 mV

b) con bloccante (p. es. ESERINA/FISOSTIGMINA) o canali isolati in un sistema d'espressione



- 80 mV


A. "GATING"
(attivazione/deattivazione
inattivazione o
desensitizzazione)
B. SELETTIVITÀ AGLI IONI
C. FARMACOLOGIA
? (alcuni casi)
D. MODULAZIONE
ESPRESSIONE