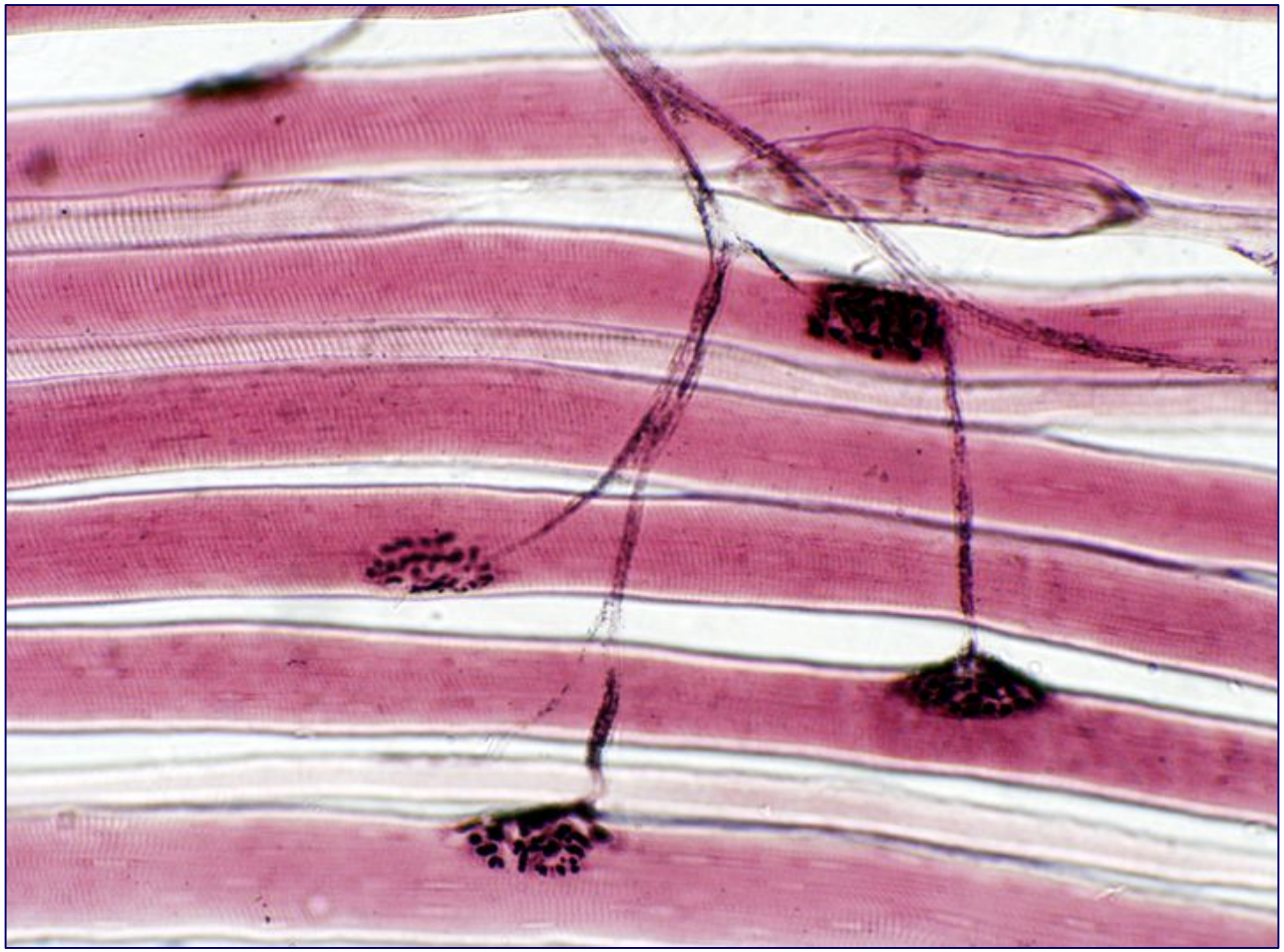
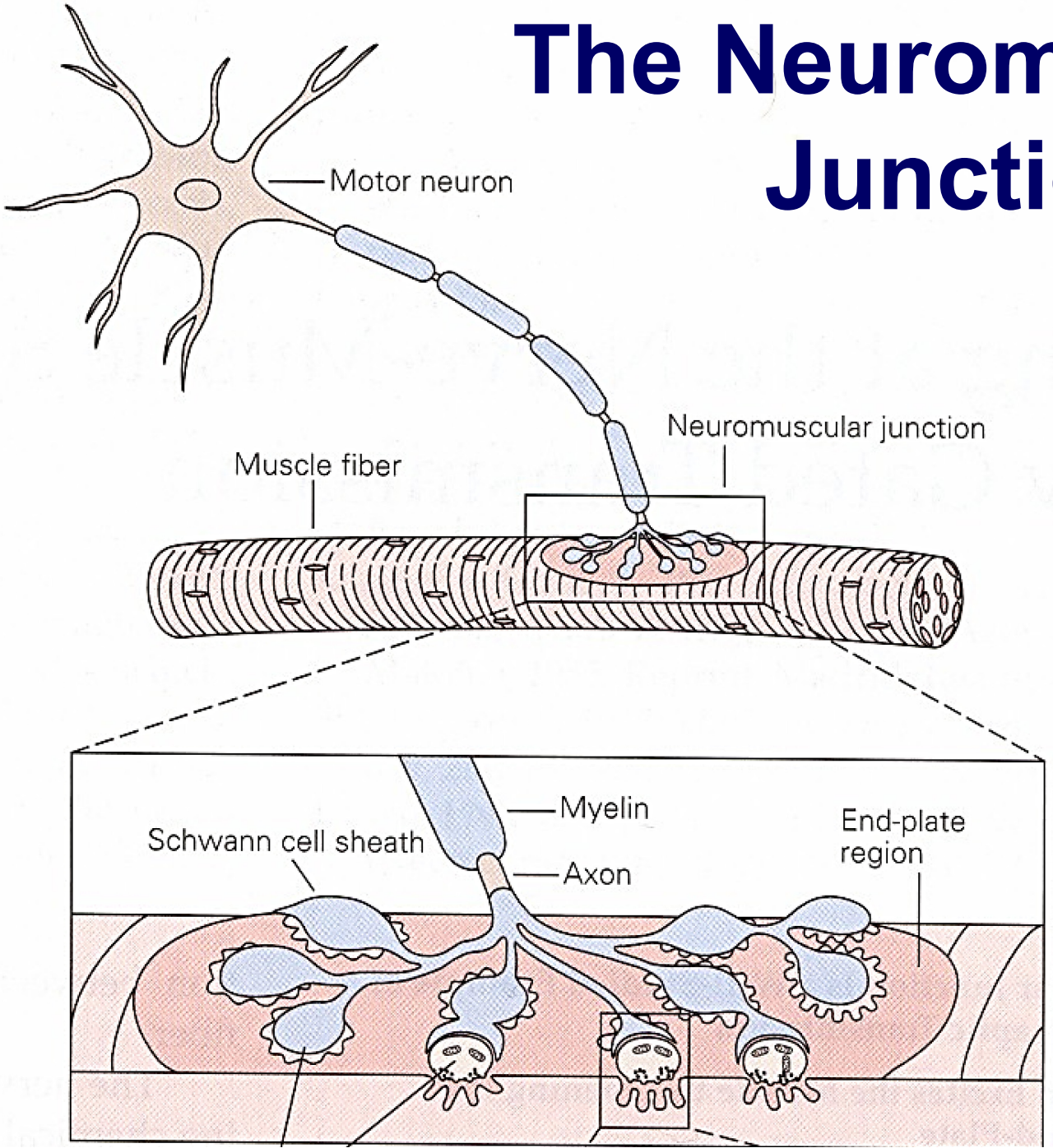
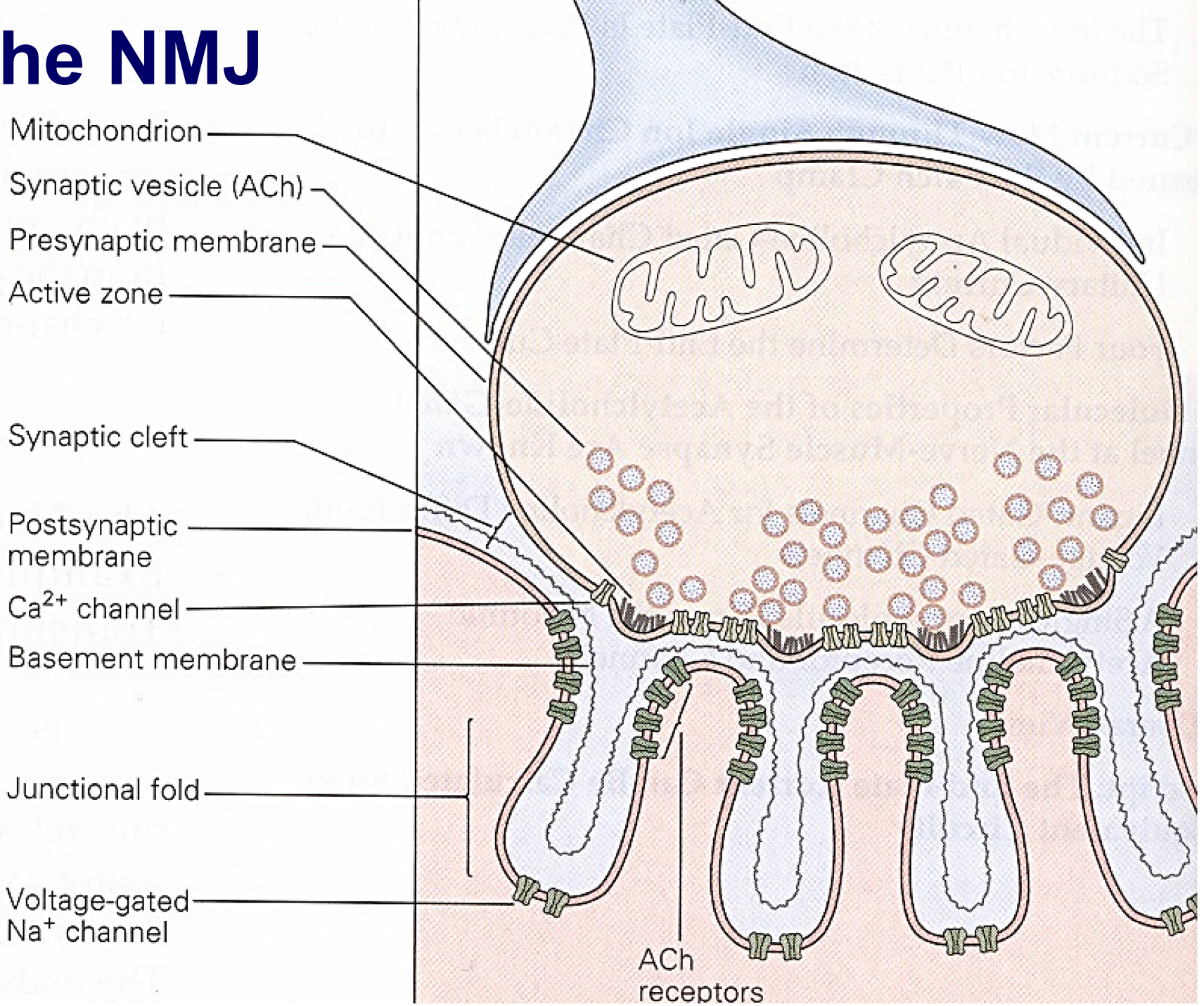
Chapter 12:
Directly Gated Transmission



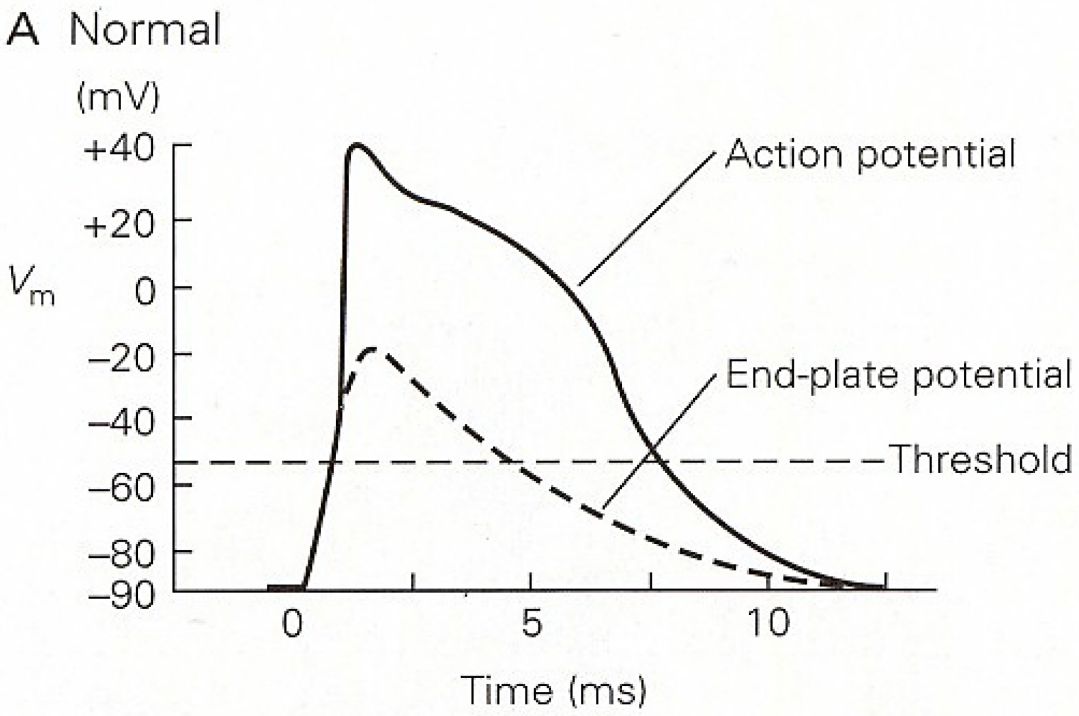
The Neuromuscular Junction



The NMJ

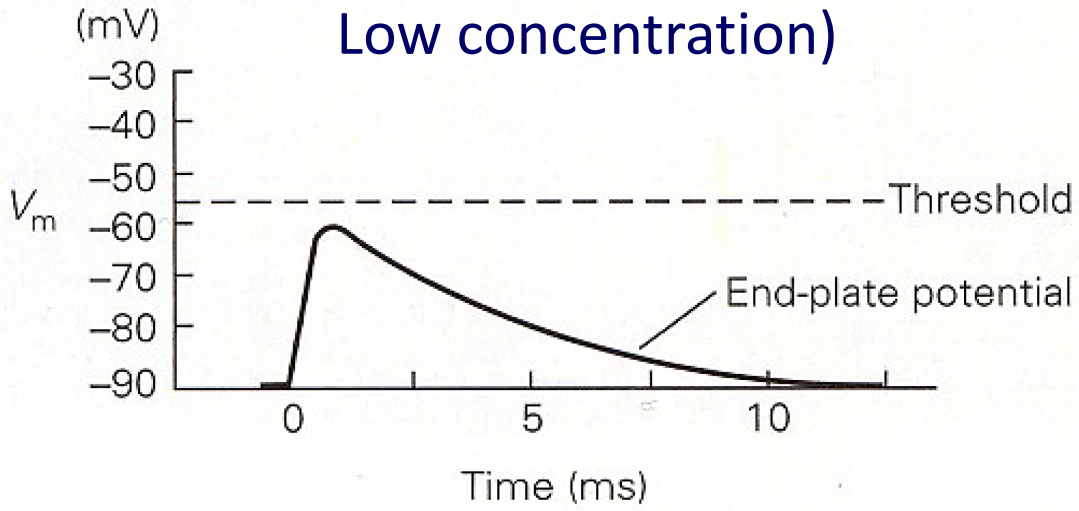

Mitochondrion
Synaptic vesicle (ACh)
Presynaptic membrane
Active zone
Synaptic cleft
Postsynaptic membrane
Ca^{2+} channel
Basement membrane
Junctional fold
Voltage-gated Na^{+} channel
ACh receptors

The Muscle End-Plate Potential

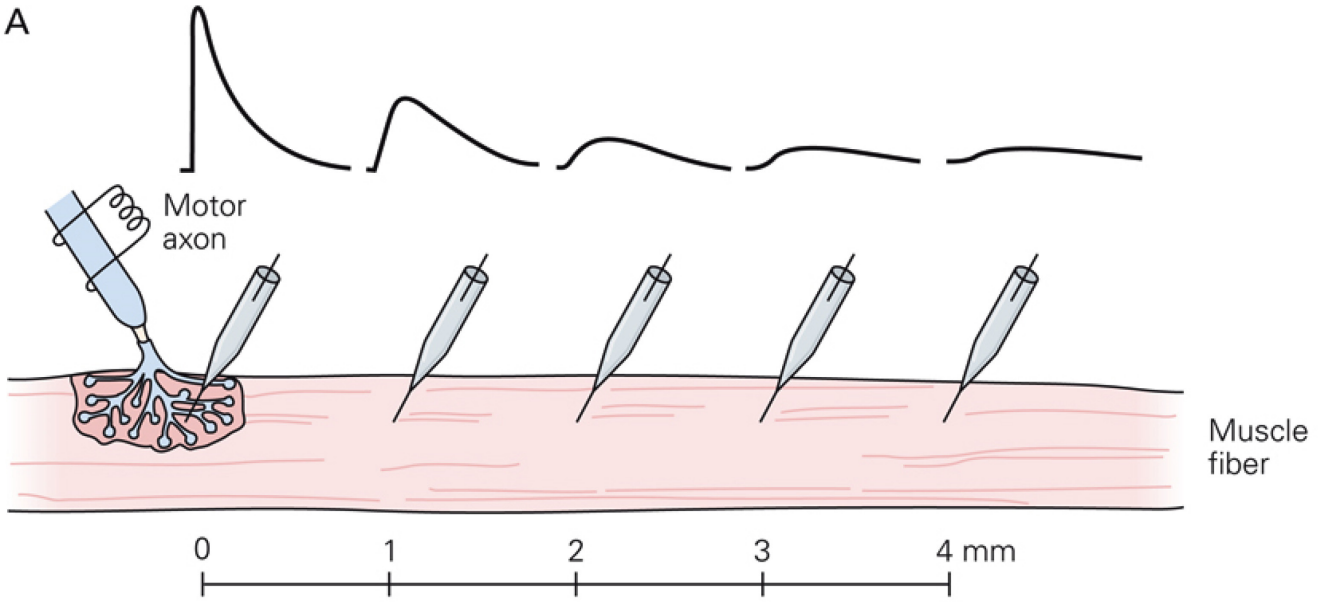


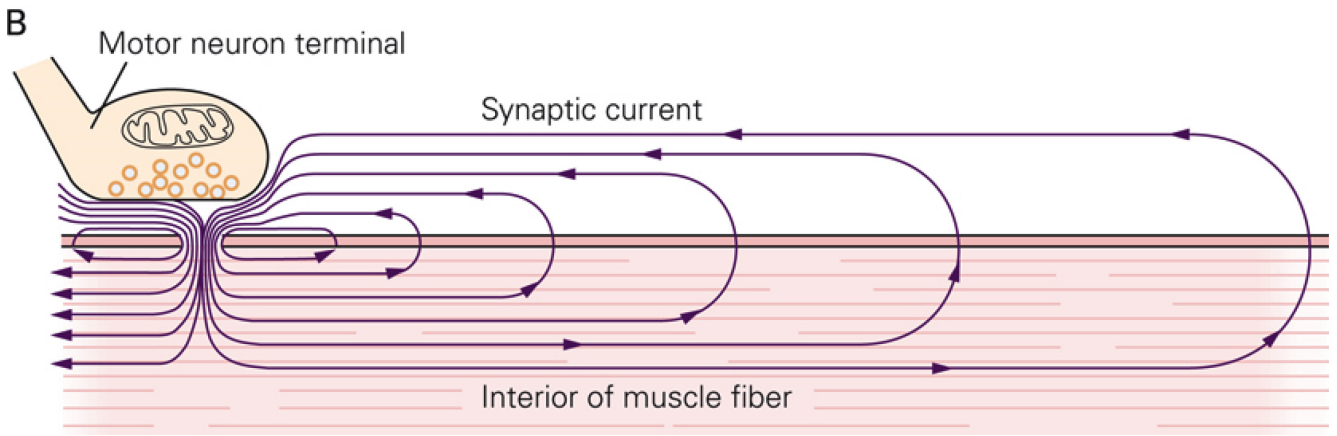
B With curare

(nAChR antagonist…
Low concentration)

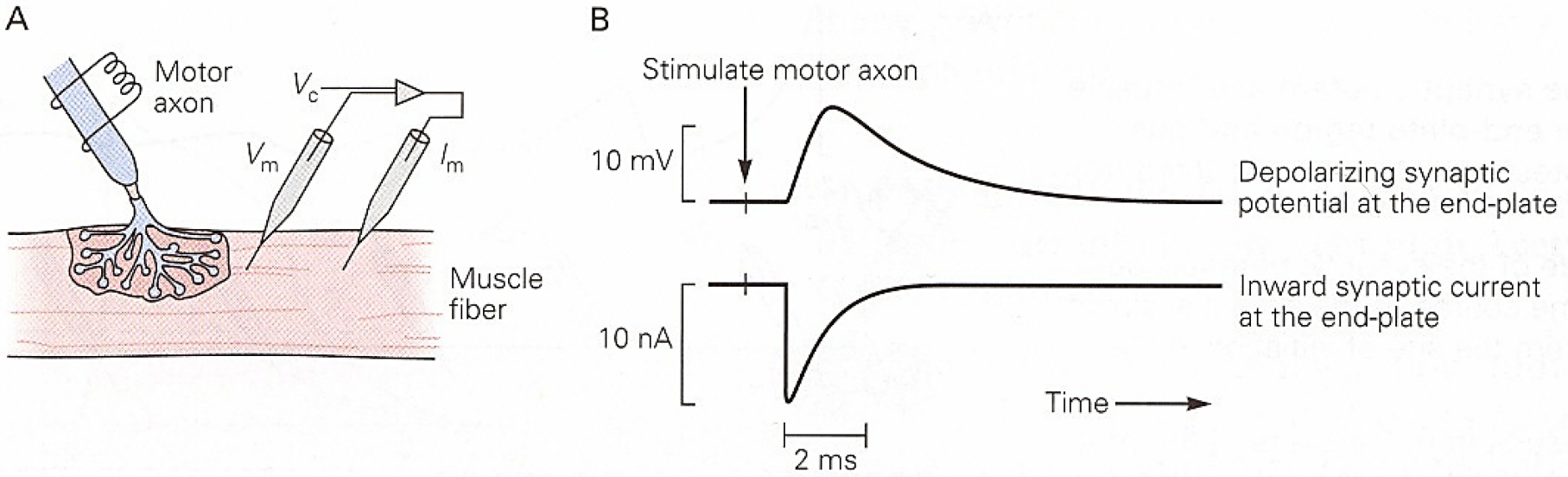


The end-plate potential decays with distance



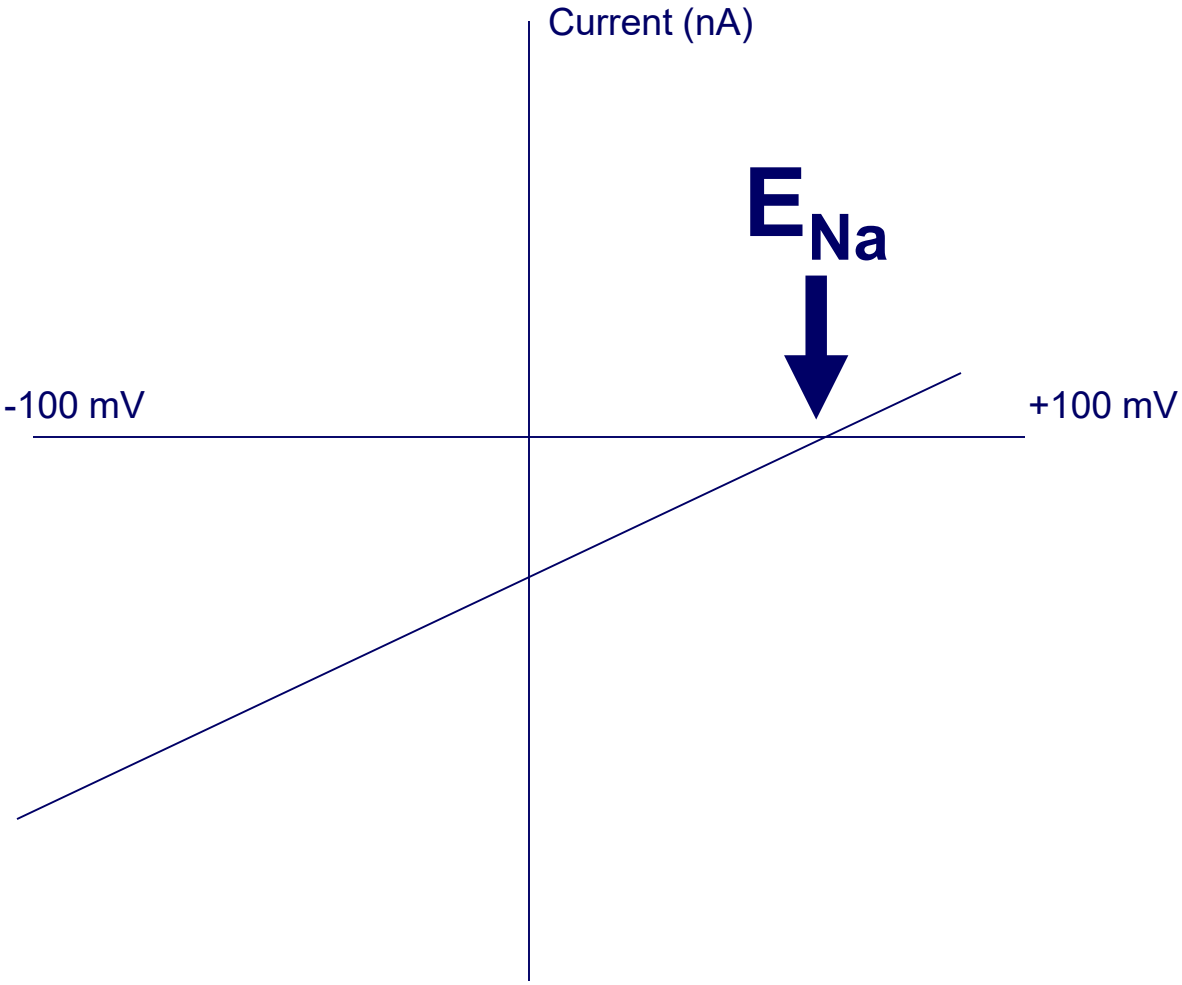


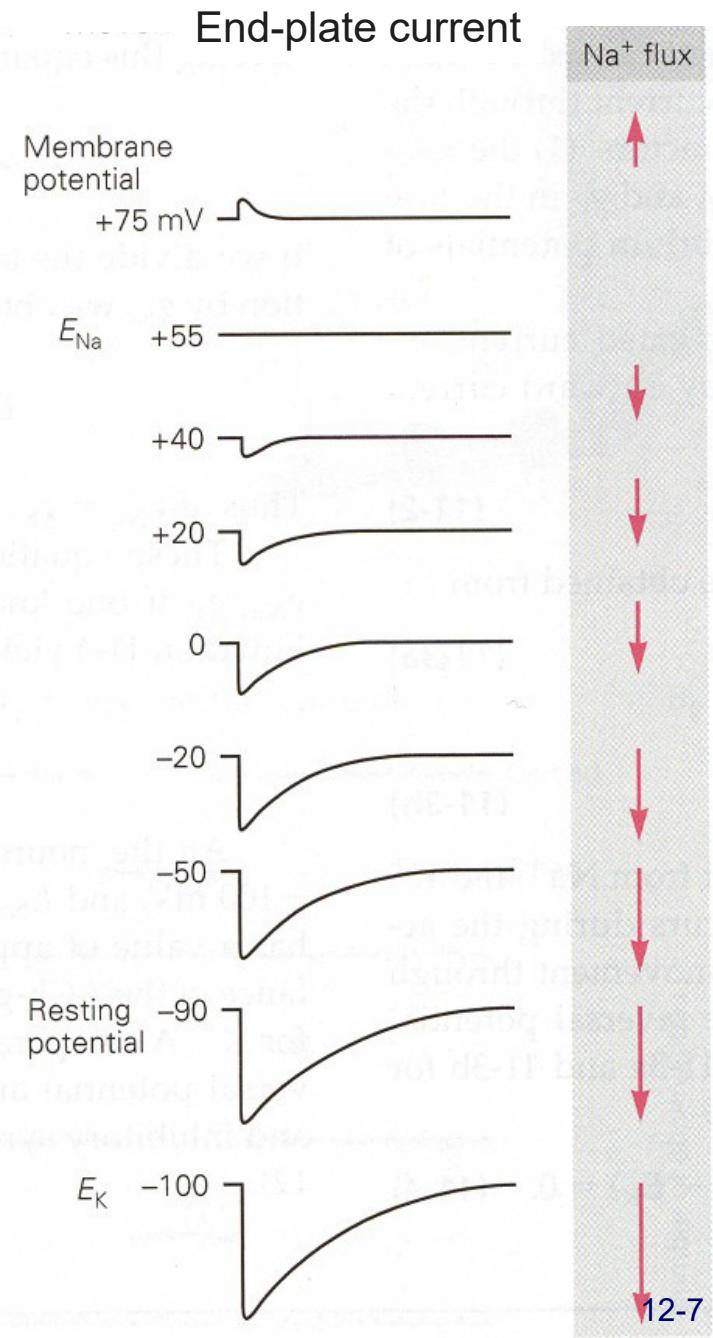
An inward current underlies the end-plate potential



What are the ions underlying this current?

IV Plot for a Hypothetical Na^+ Channel





IV Plots for Selective Channels

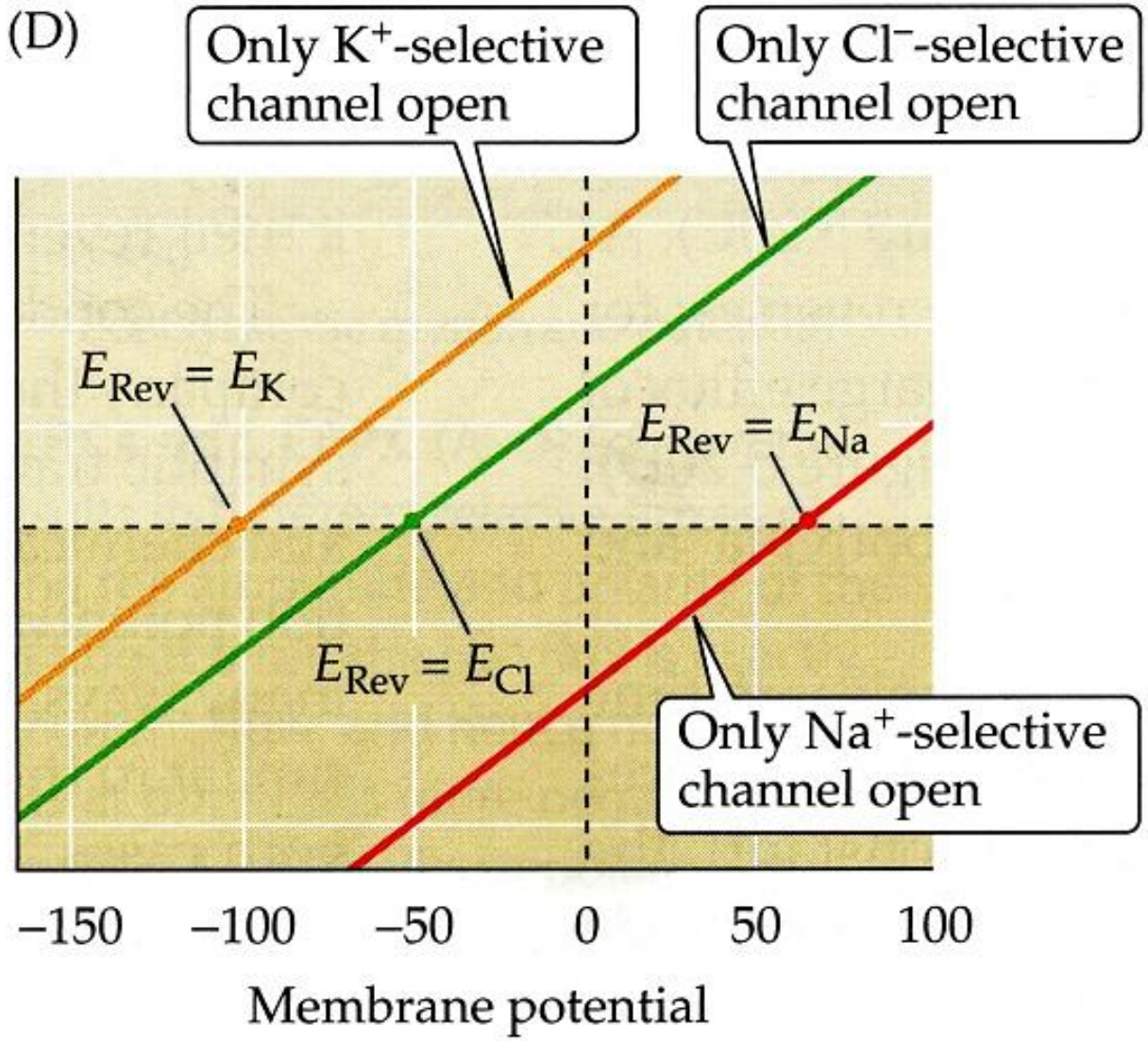
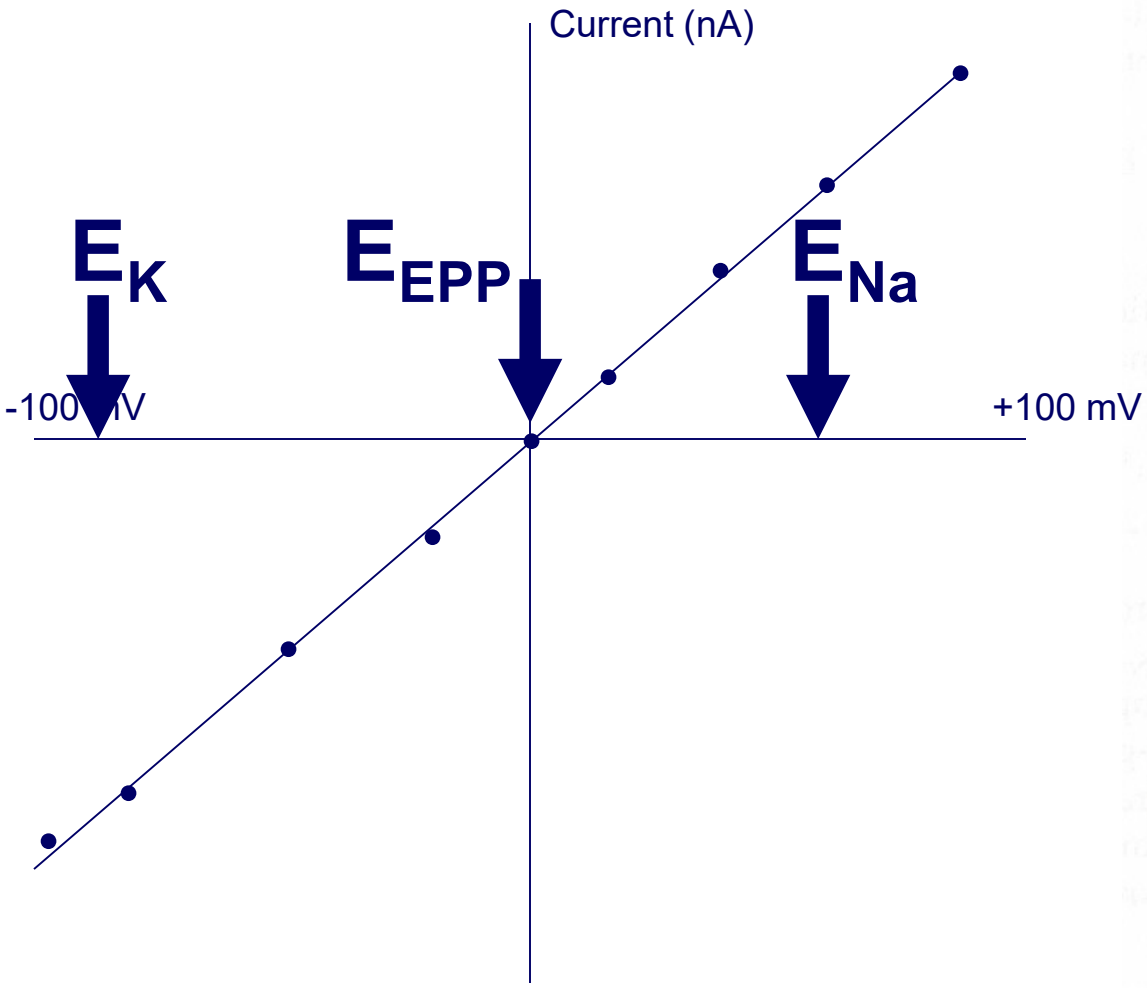
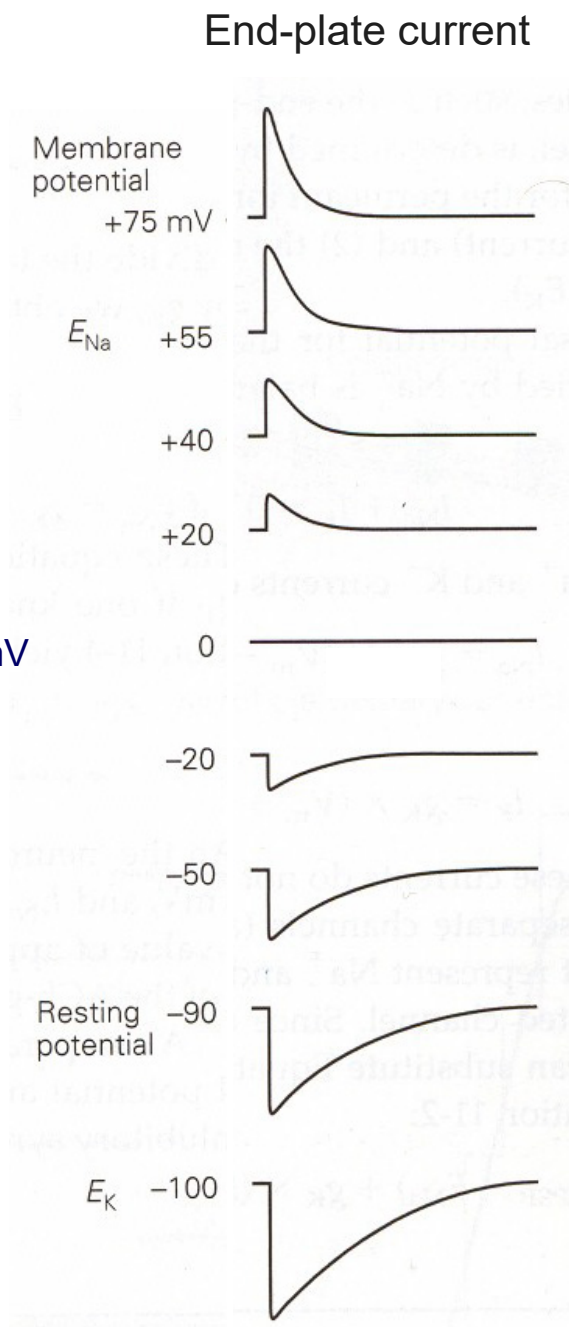


Figure 5.18D, Purves

IV Plot for the End-Plate Potential





Confirming Selectivity of a Channel

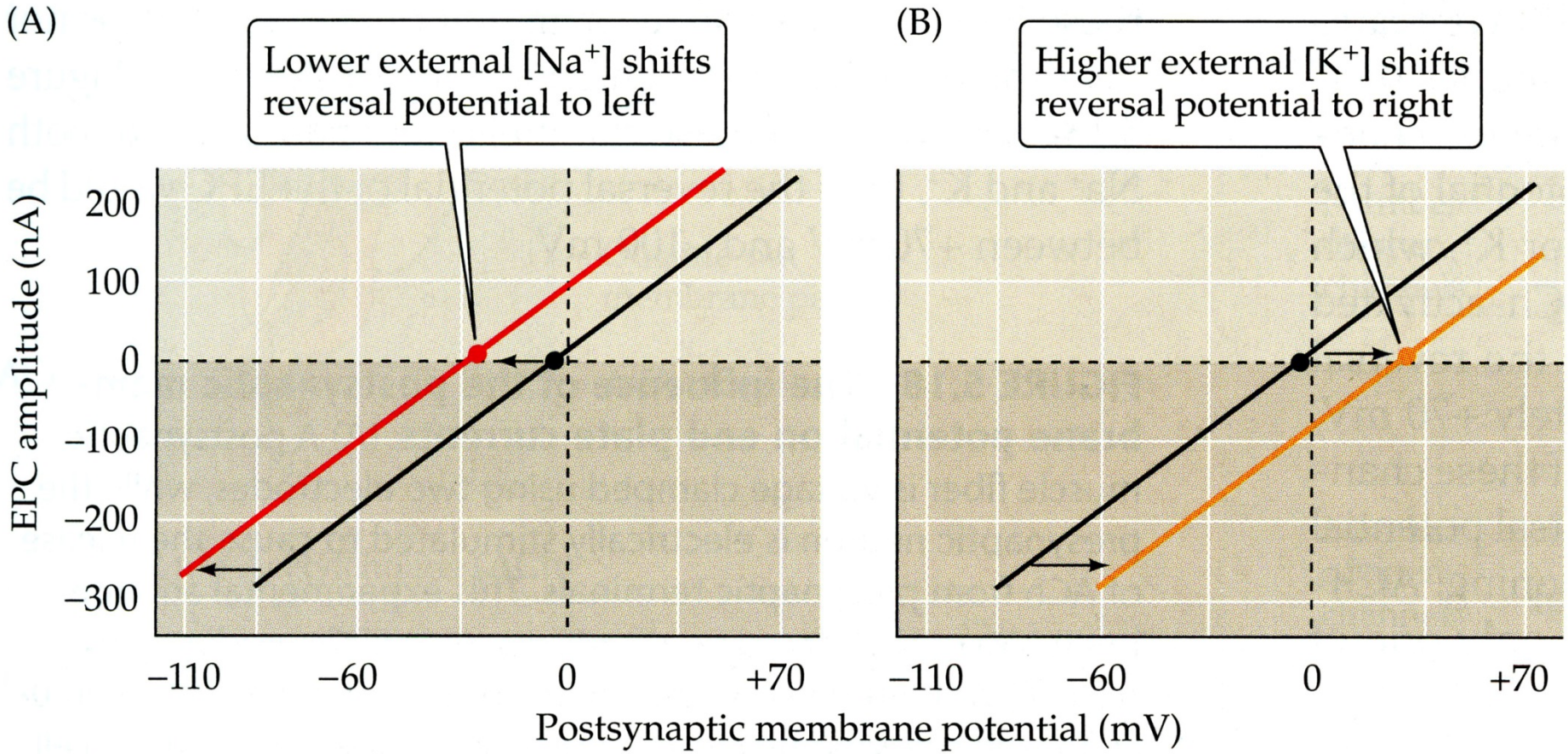
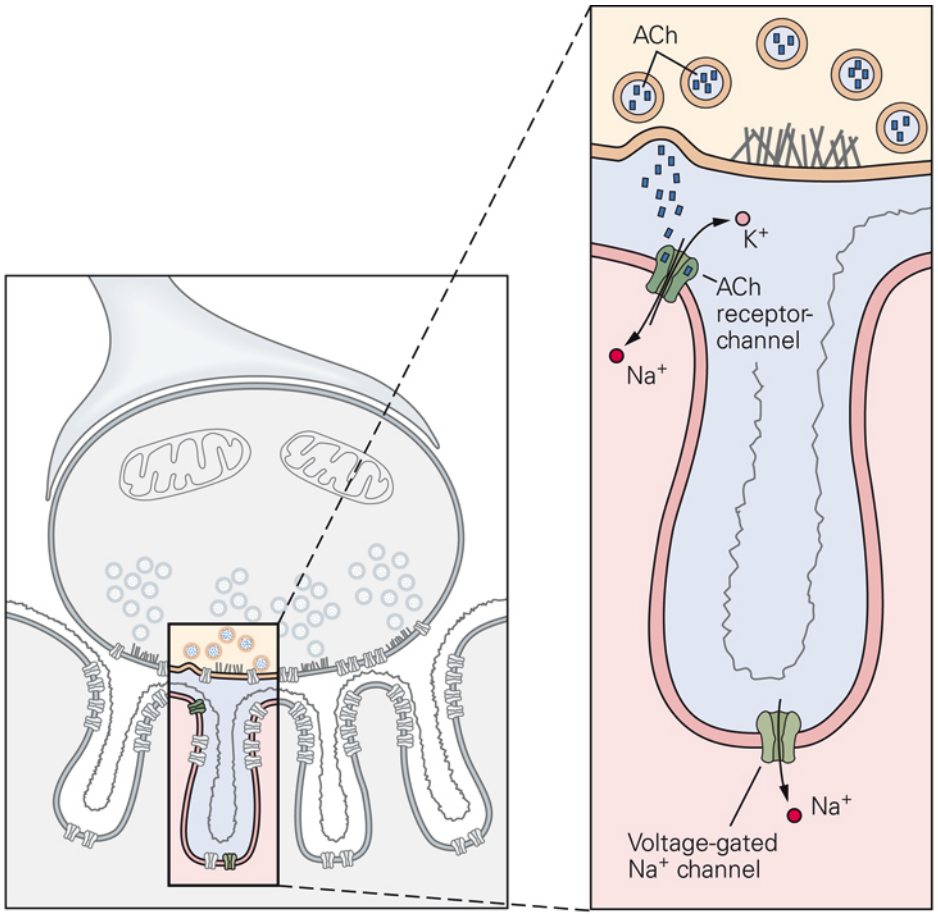
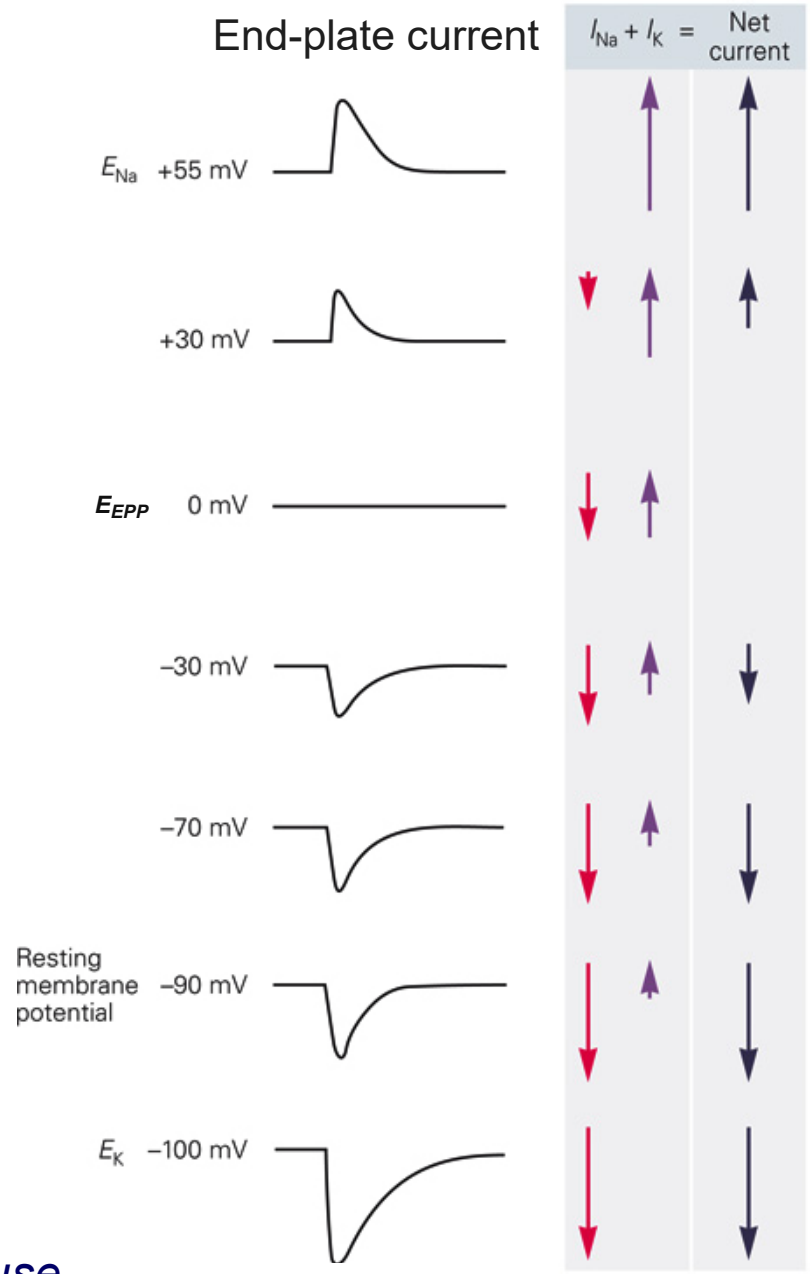


Figure 5.19, Purves

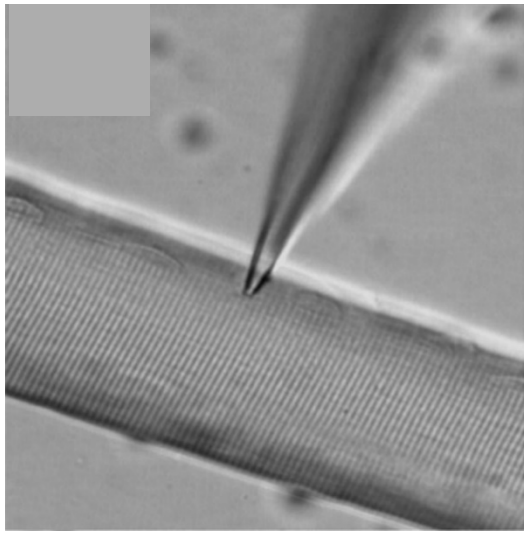
The Nicotinic ACh Receptor is a Mixed Cation Channel

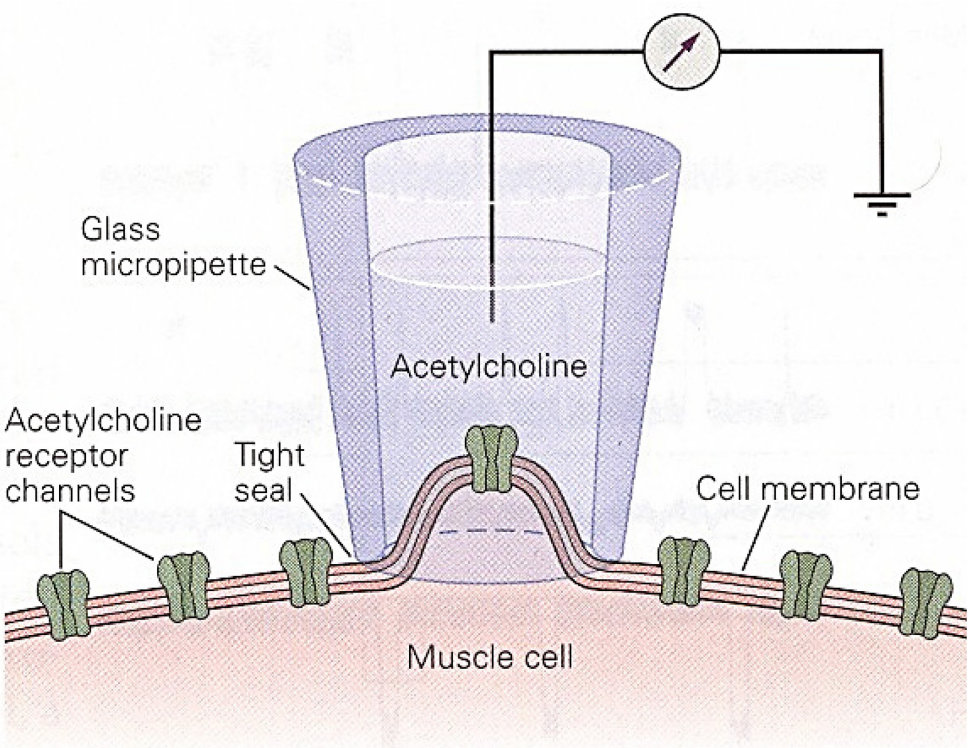


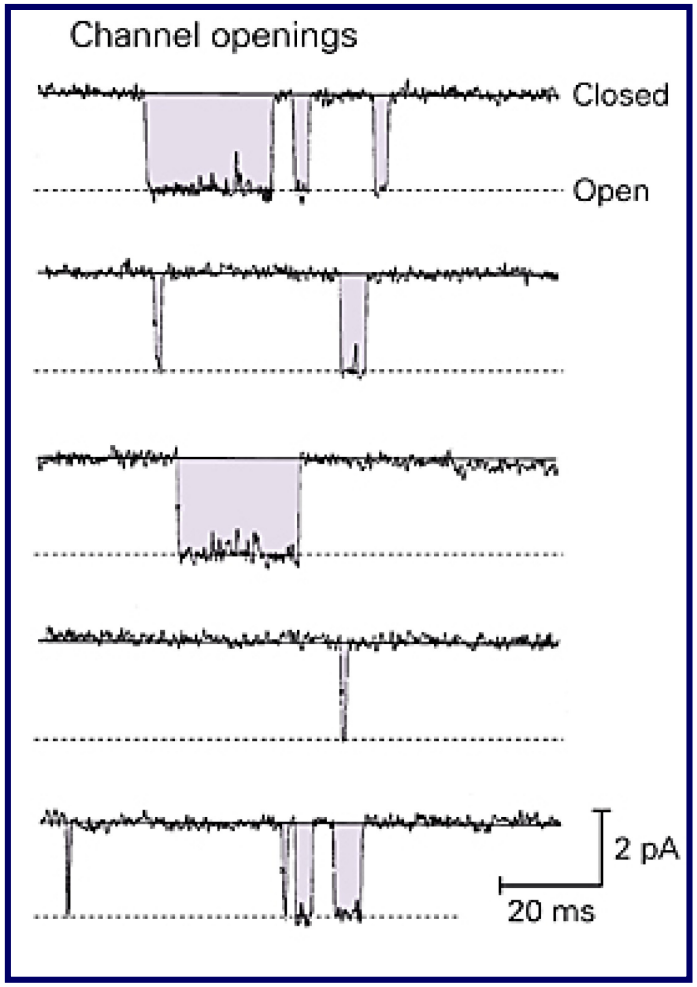


Why does opening a mixed cation channel cause depolarization at resting membrane potential?

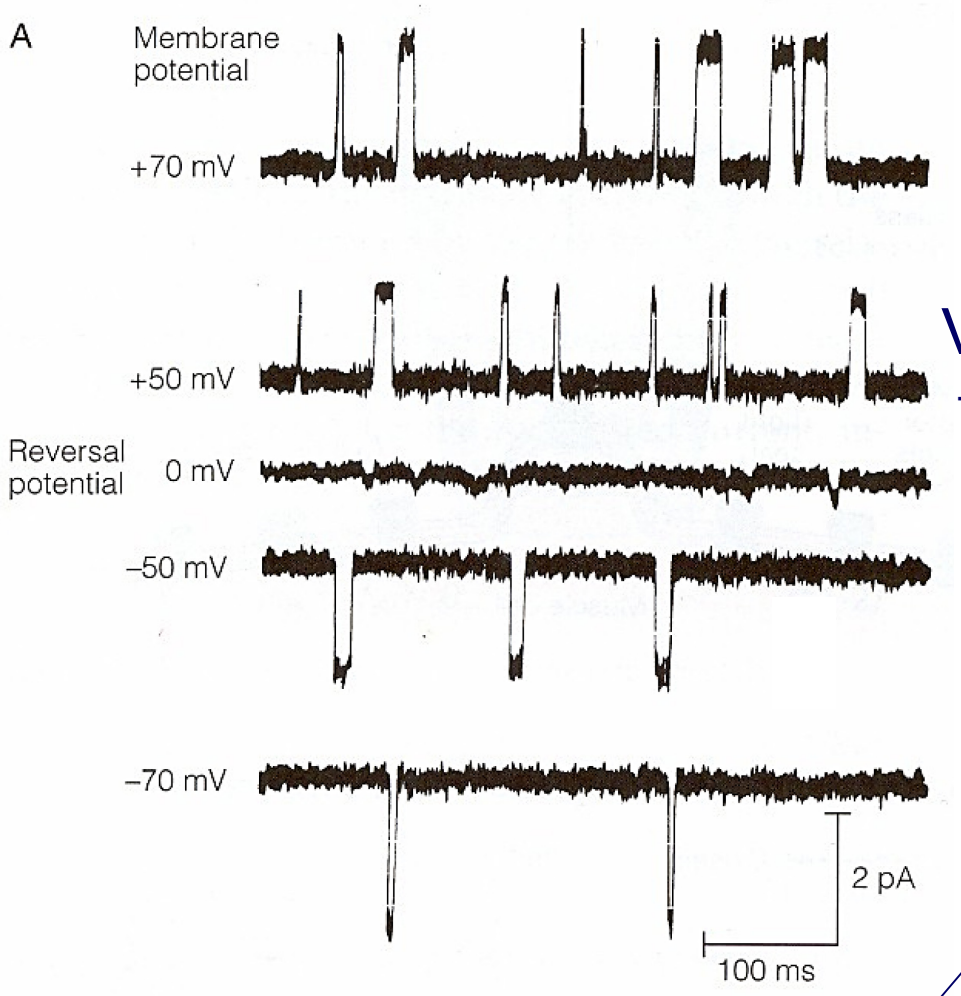
Patch Clamping the Nicotinic AChR

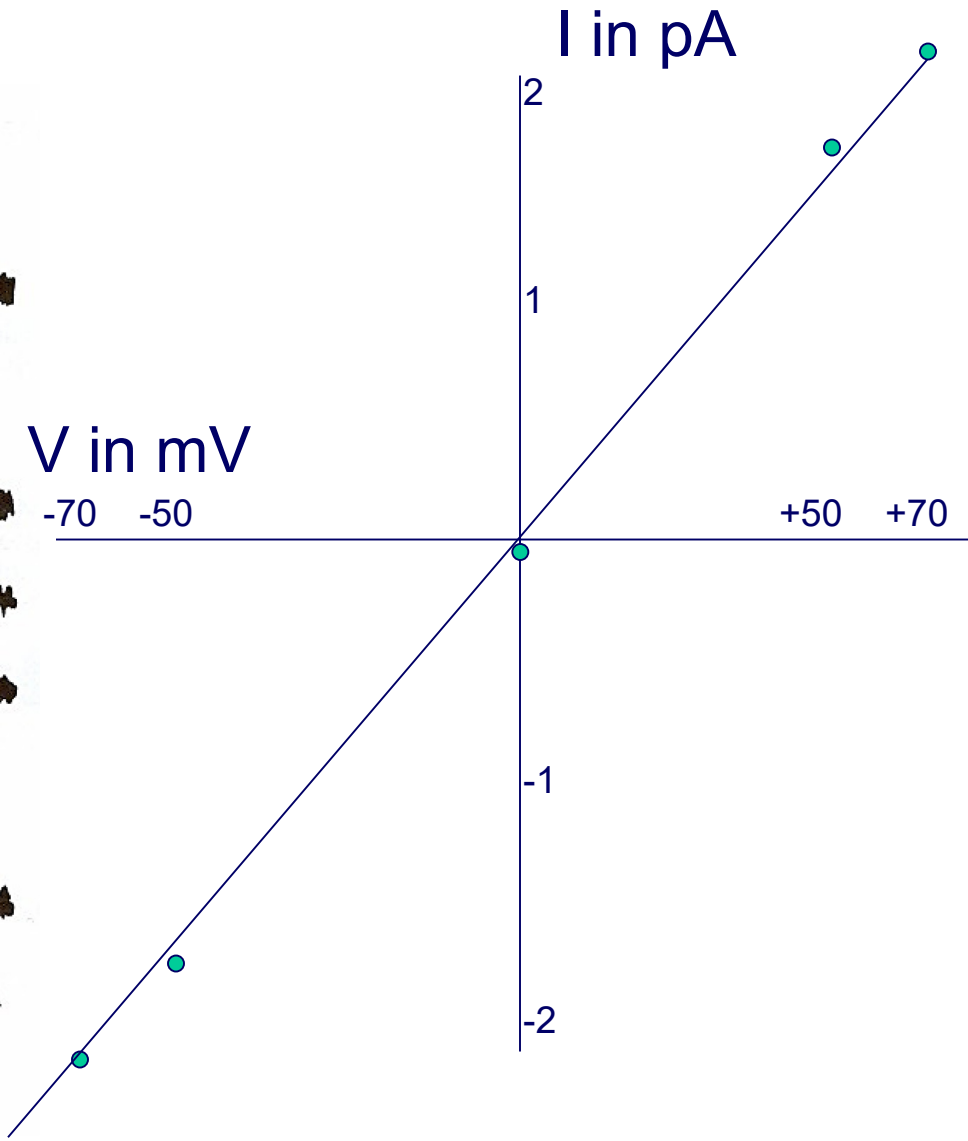






Single-Channel IV Plot for the nAChR



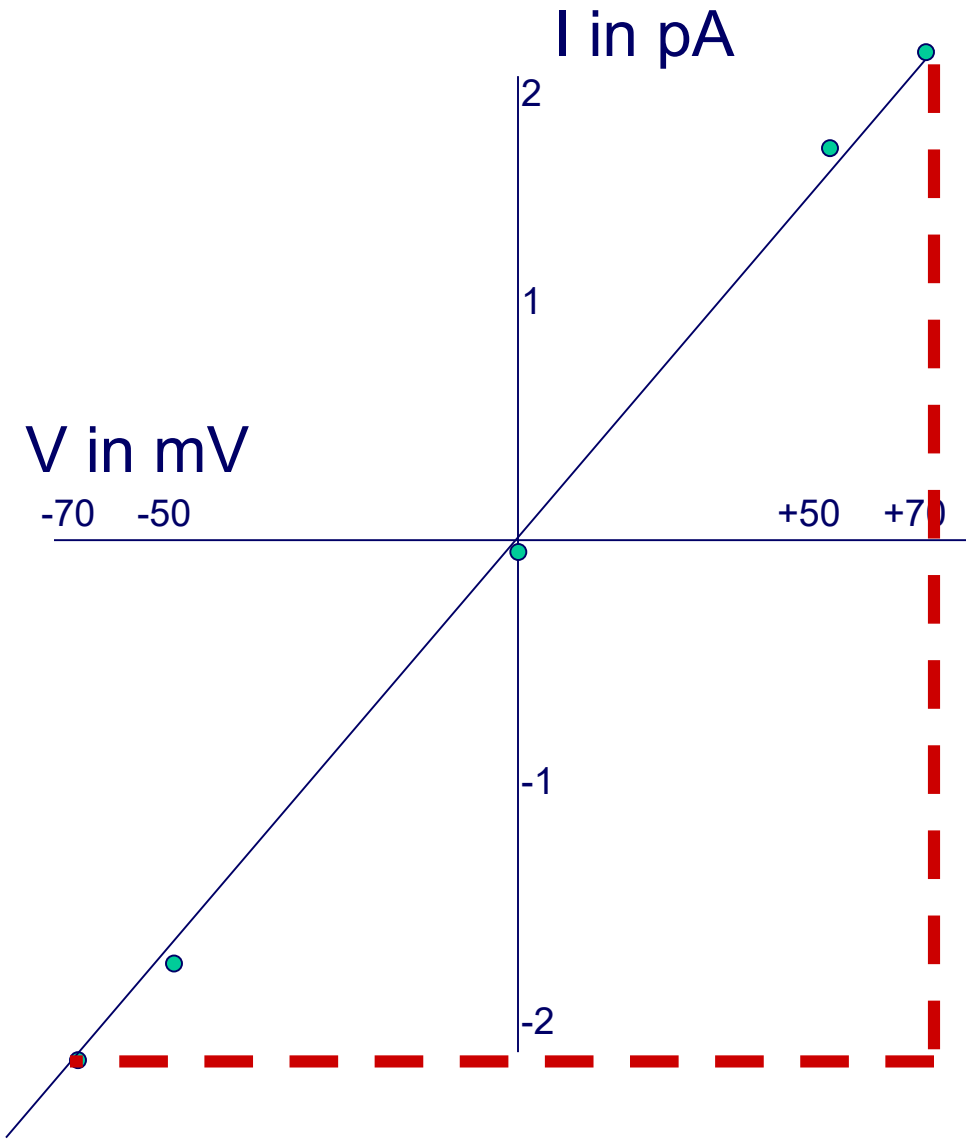


Single-Channel Conductance

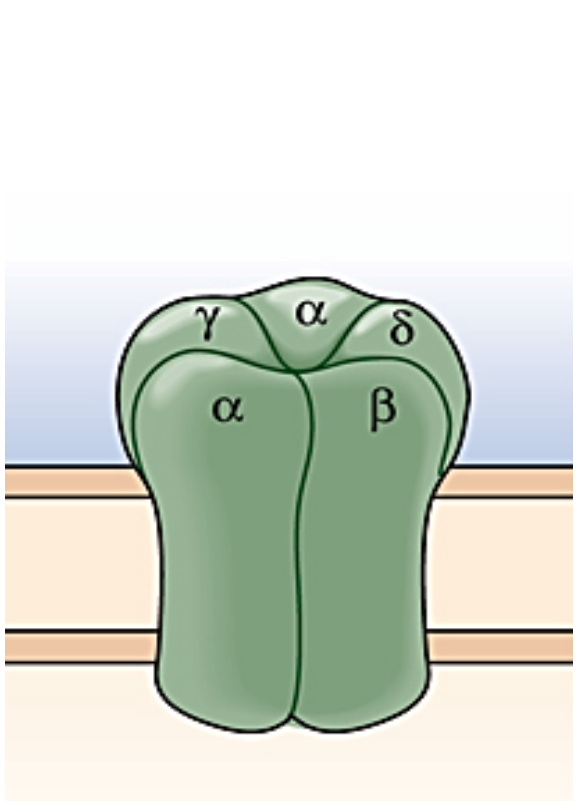
Conductance = slope

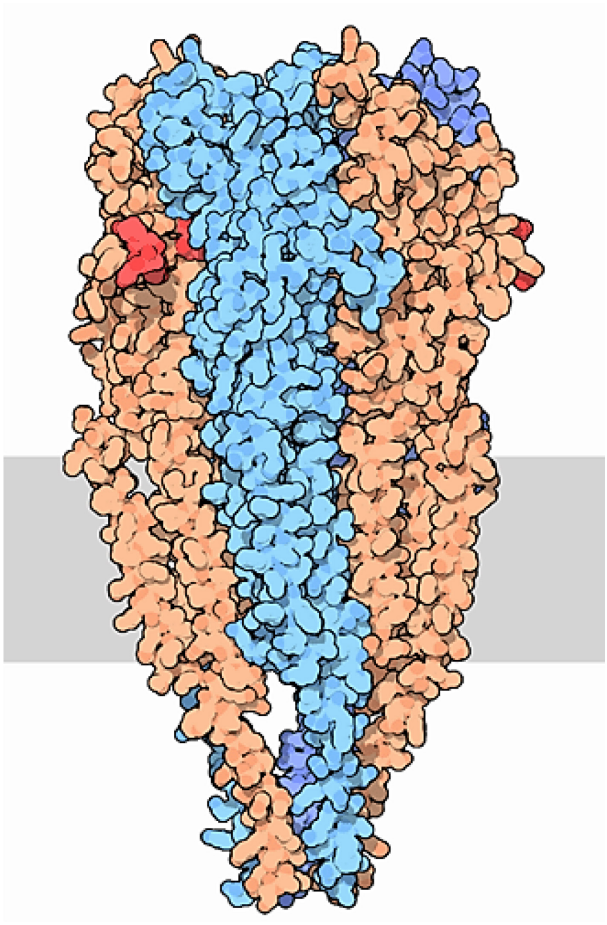
$$\frac{4.2 \times 10^{-12}\ A}{140 \times 10^{-3}\ V}$$

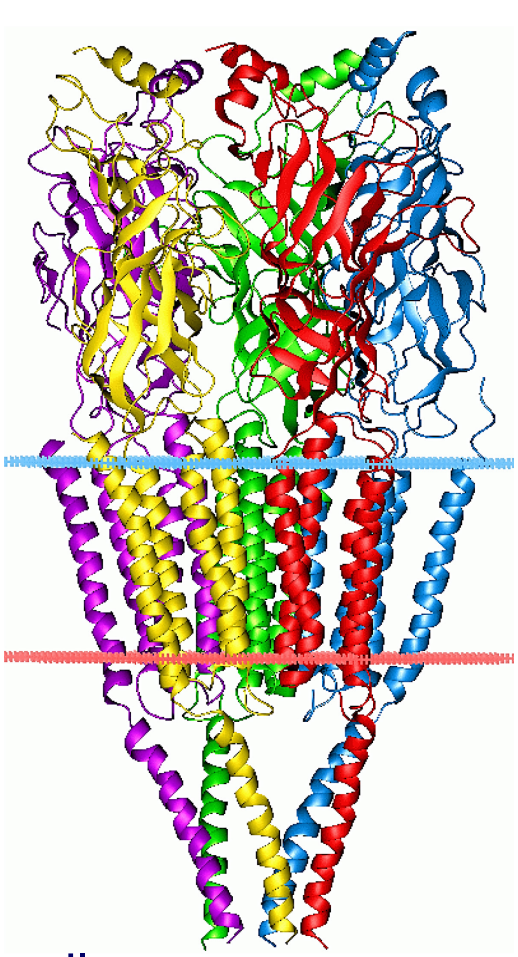
$$\gamma = 30 \times 10^{-12}\ S$$



The Muscle nAChR

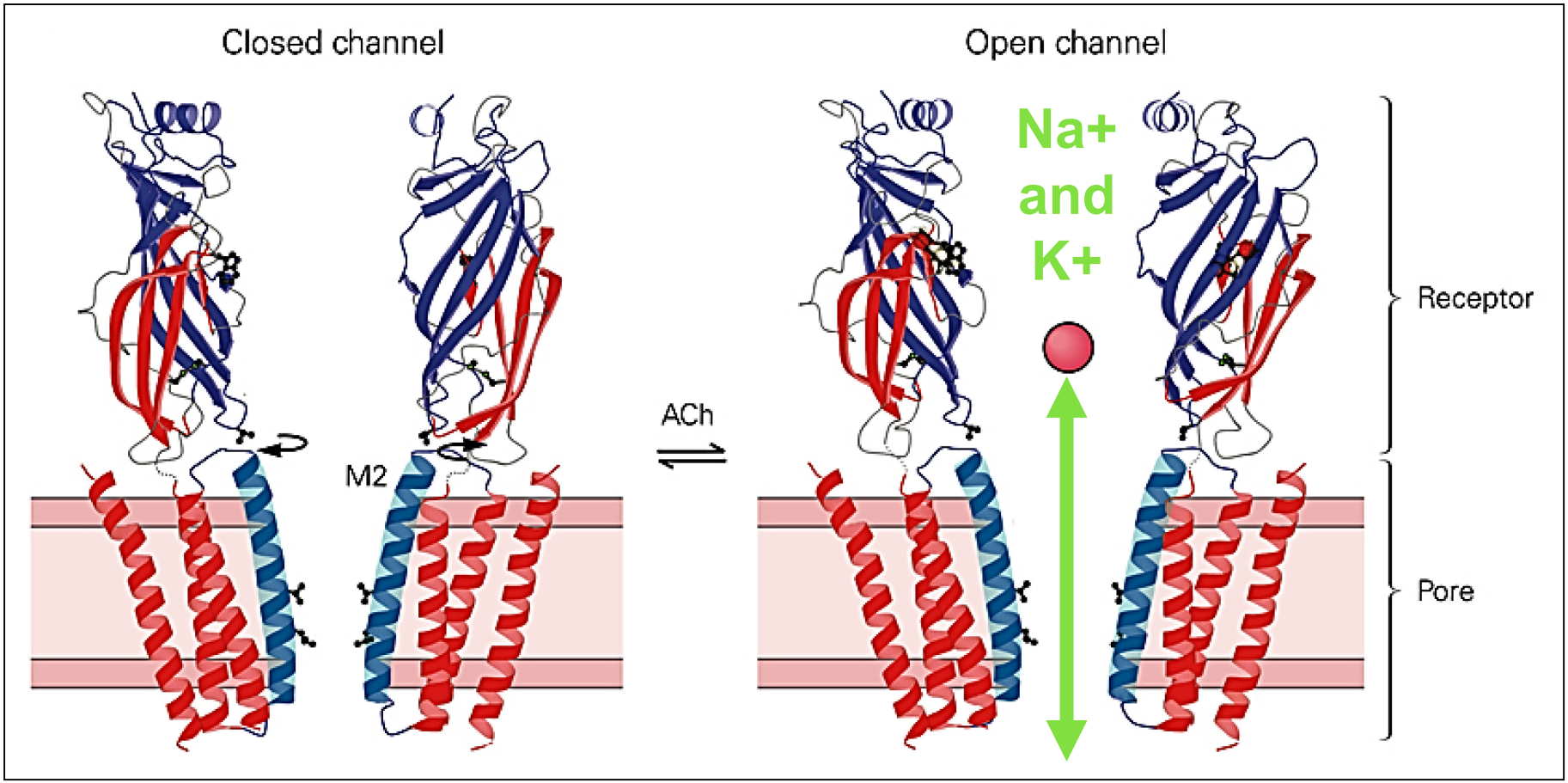




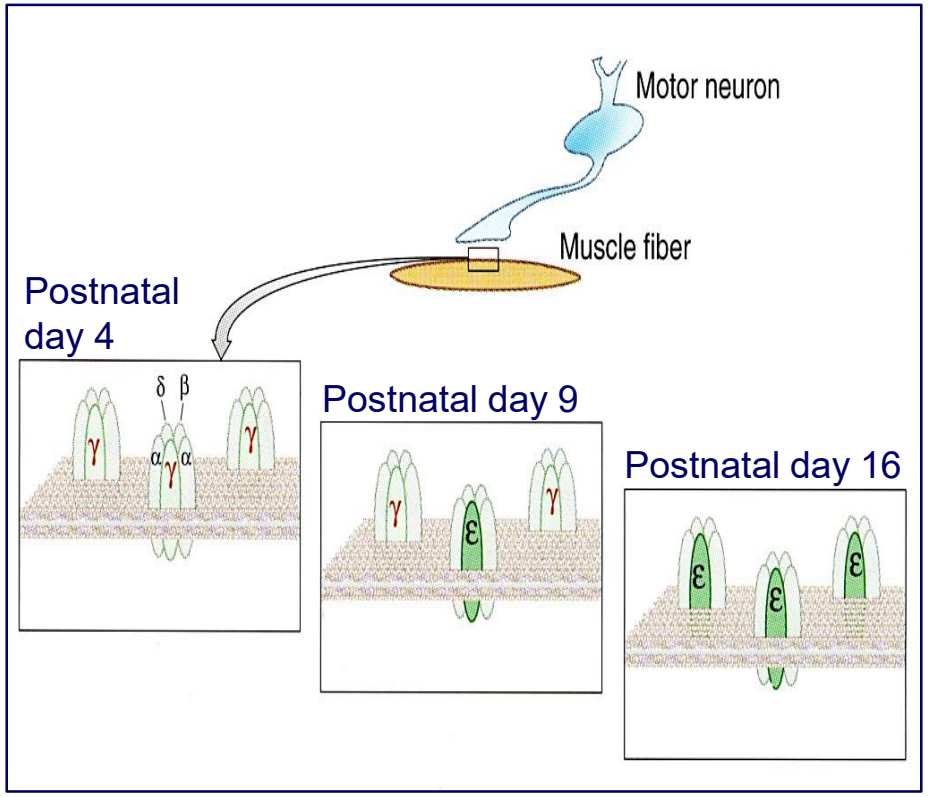


- Subunit composition: 2 alpha, beta, delta, gamma/epsilon *(gamma in embryonic muscle, epsilon in adult muscle)*
- *Binding of two ACh molecules (one to each alpha subunit) opens the channel*

The Muscle nAChR

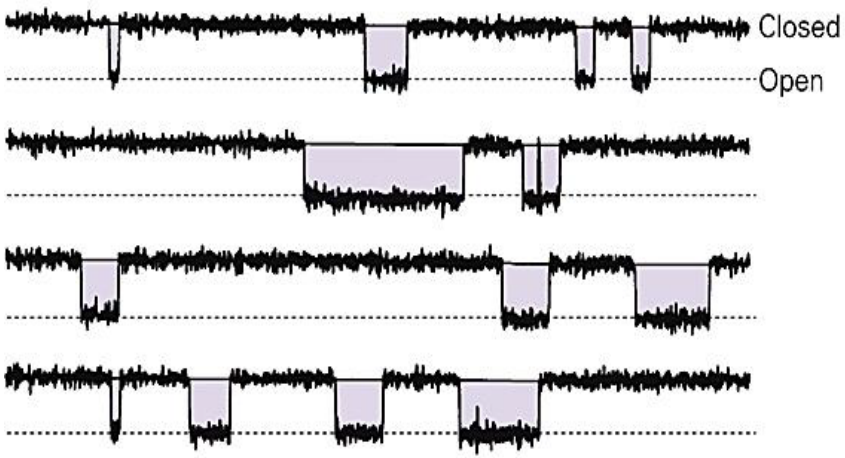


Maturation of the Muscle nAChR (γ to ε subunit change)

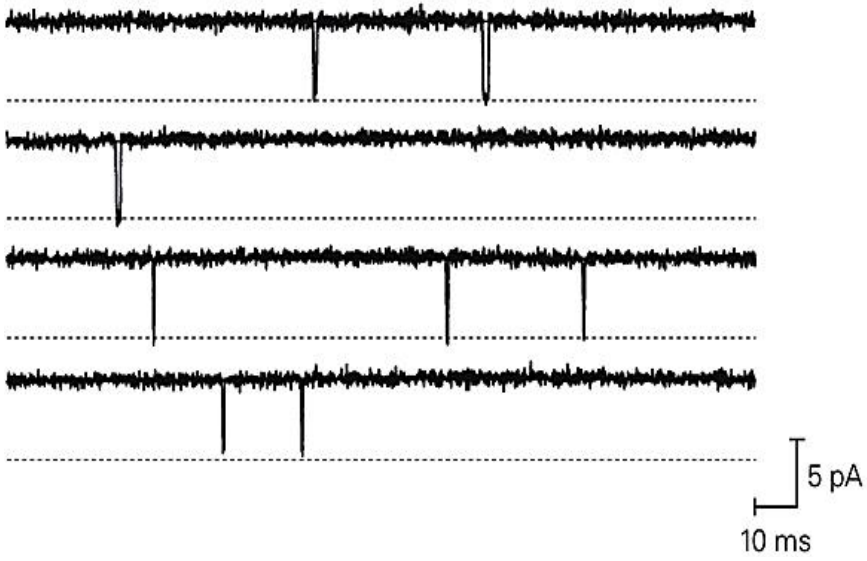


Frog skeletal muscle at different times of development

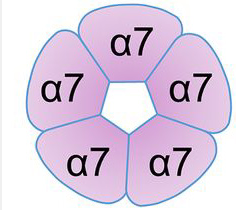
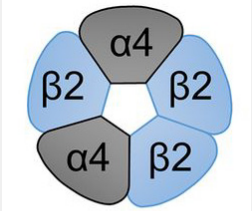
nAChR activity at postnatal day 4

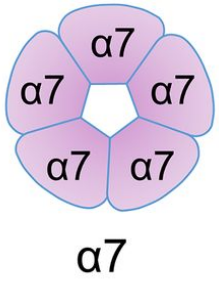


nAChR activity at postnatal day 16

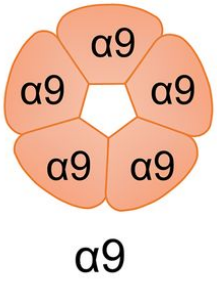


Neuronal nAChR Composition

Channel Composition		
Ion Selectivity	Na^+, K^+, Ca^{+2}	Na^+ and K^+
Pharmacology	blocked by α-bungaro-toxin	NOT blocked by α-bungaro-toxin

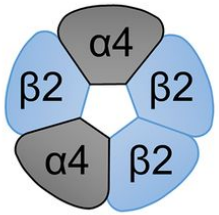


α7

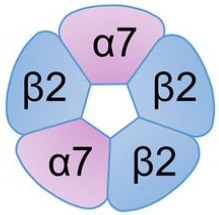


α9

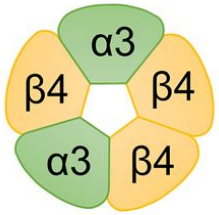
Homomeric nAChRs



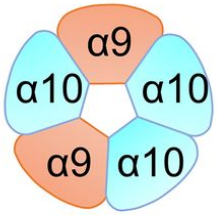
α4β2



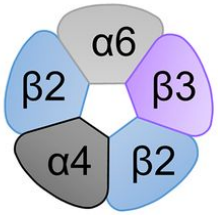
α7β2



α3β4



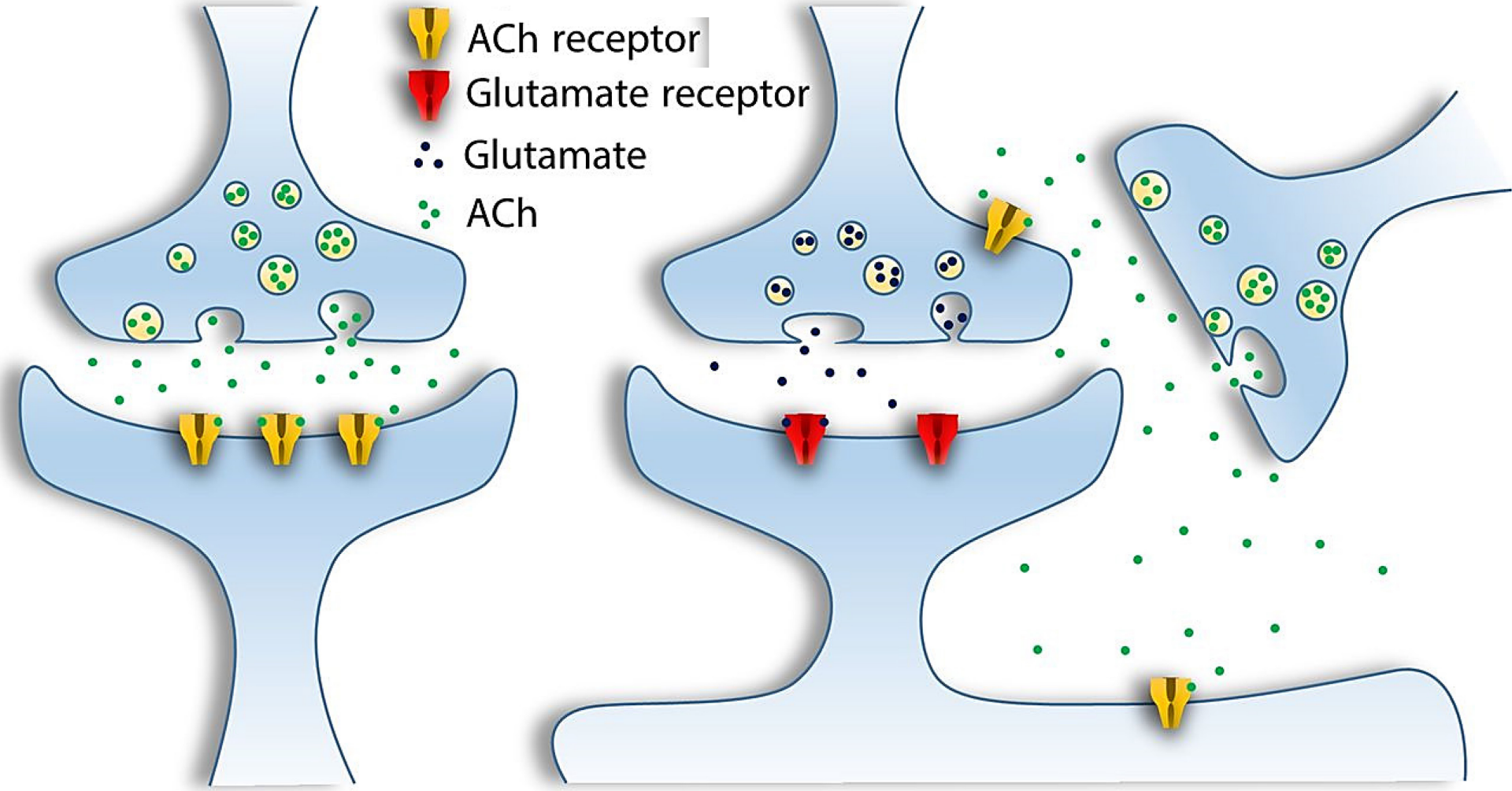
α9α10



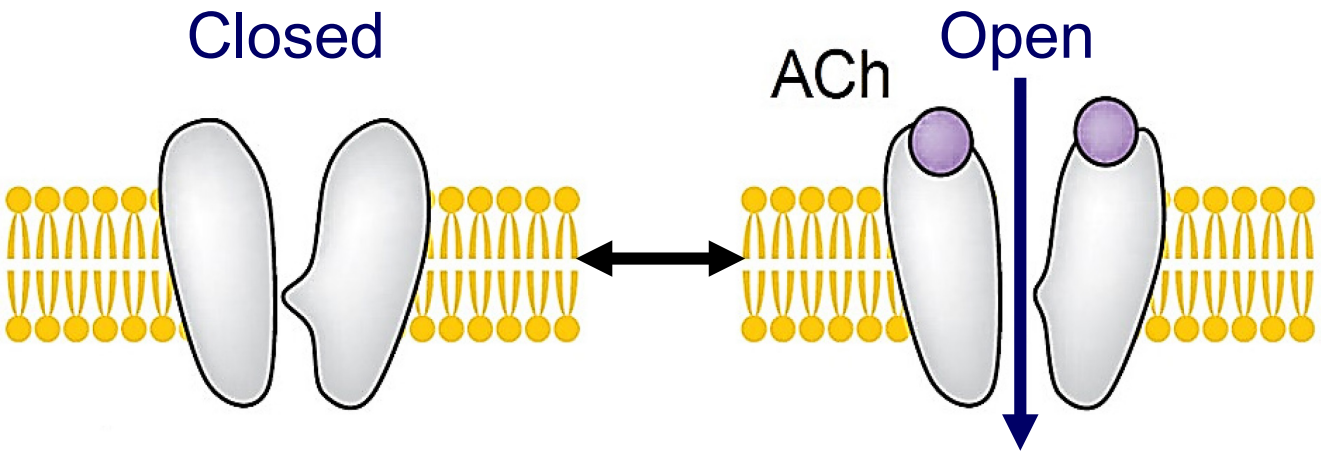
α4α6β2β3

Heteromeric nAChRs

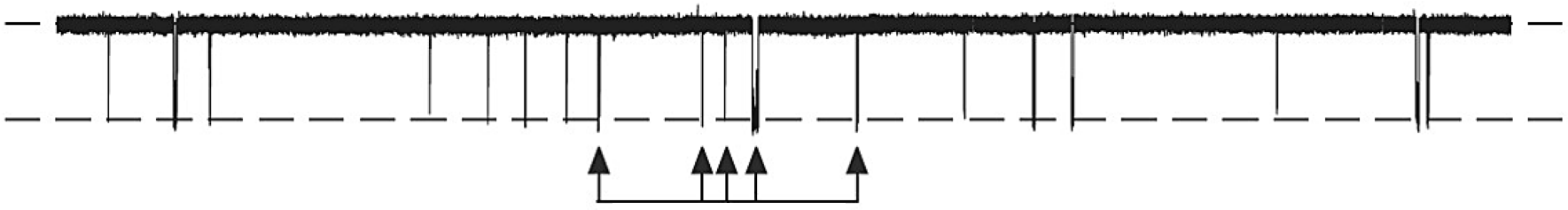
Neuronal nAChR Location



Single-Channel Recording of a Neuronal nAChR

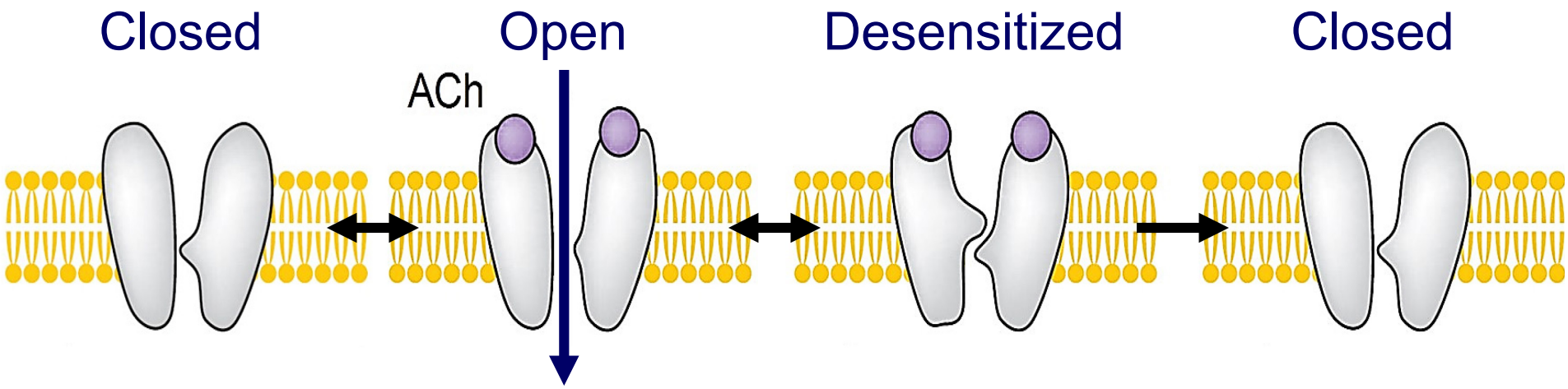


Agonist (low concentration)

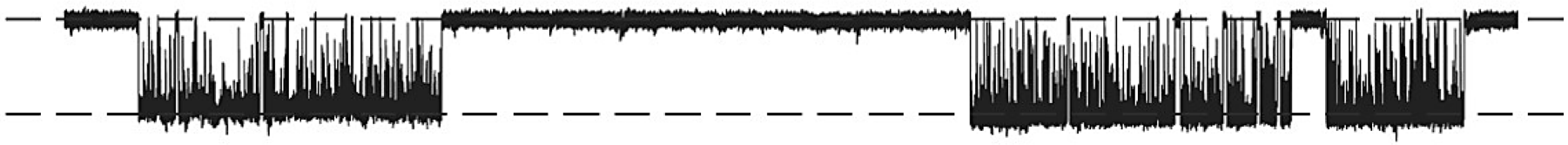


TINS 28(7):371 and
Cell Mol Life Sci 70:1241

Single-Channel Recording of a Neuronal nAChR



Agonist (high concentration)



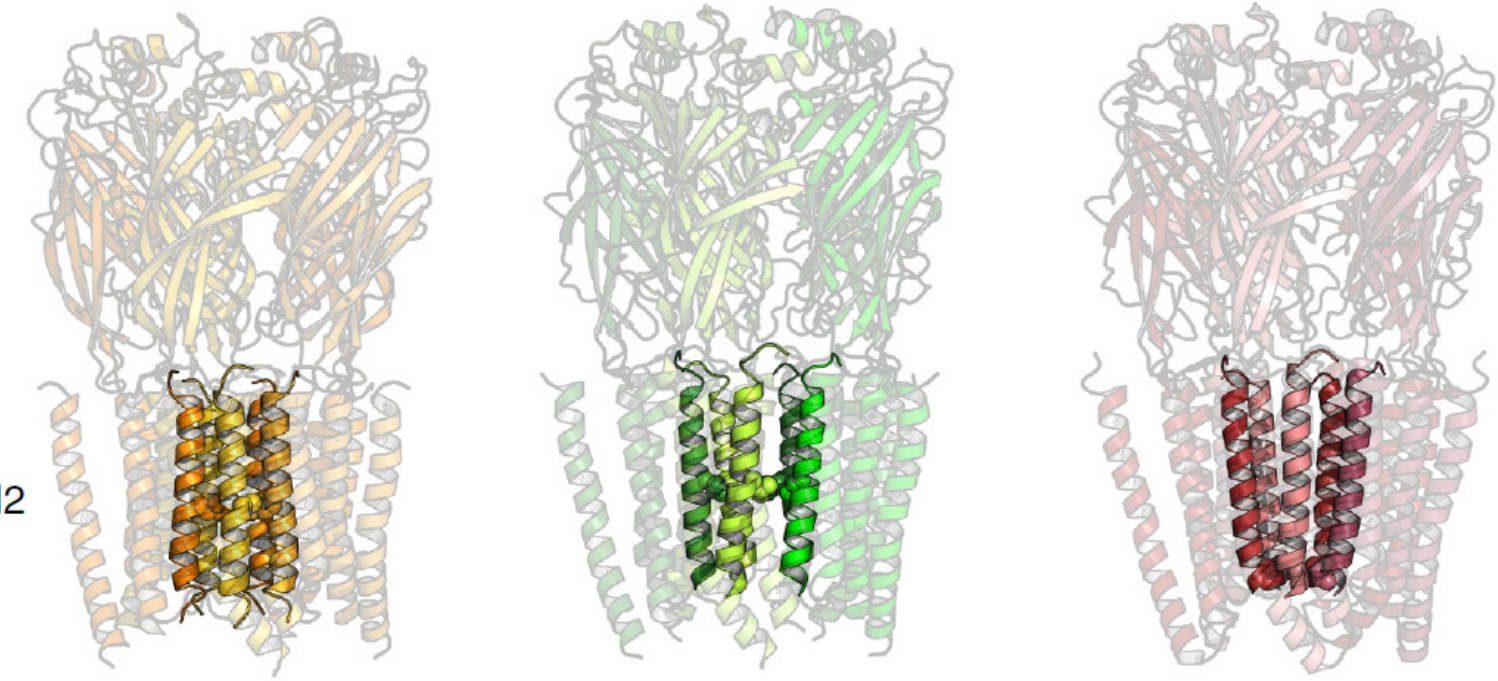
5 pA
1 s

TINS 28(7):371 and
Cell Mol Life Sci 70:1241

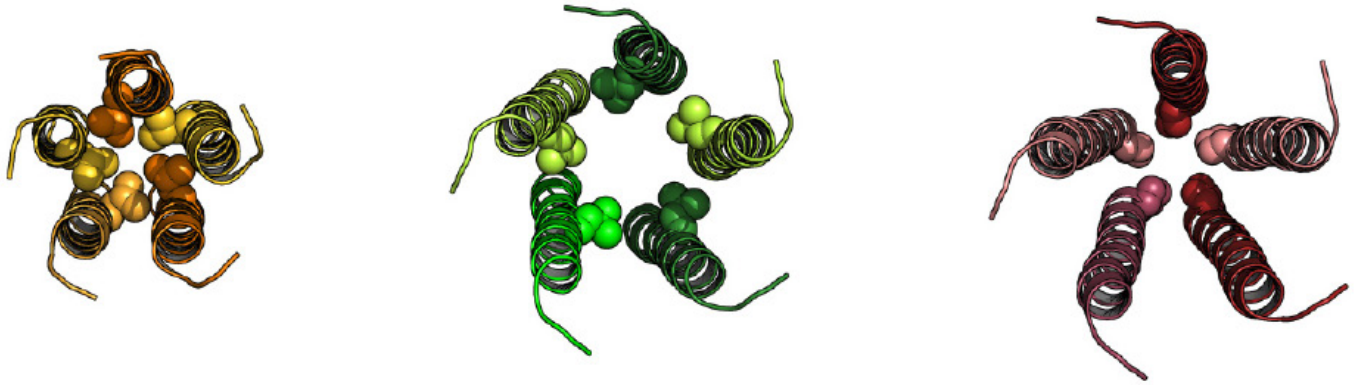
Neuronal nAChR Desensitization

Side view

M2



Extra-cellular view



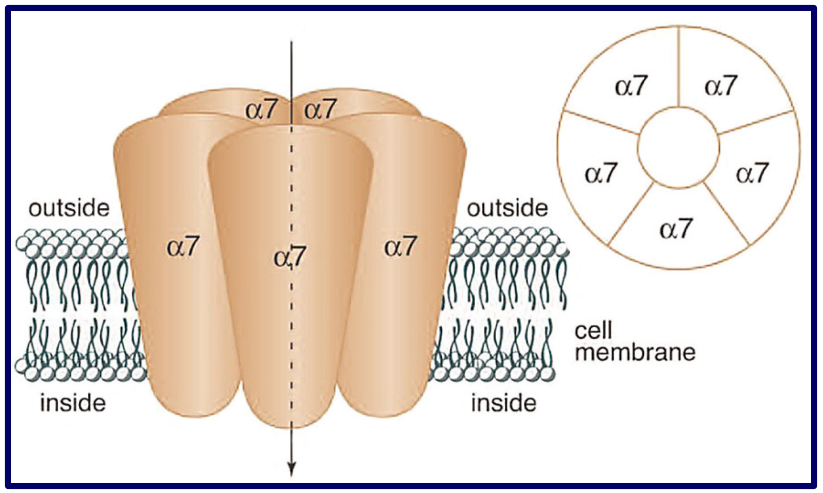
Resting

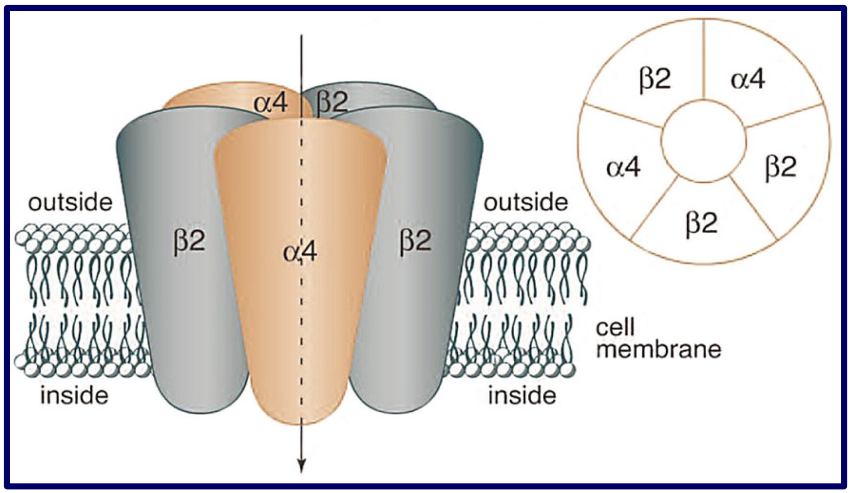
Active

Desensitized

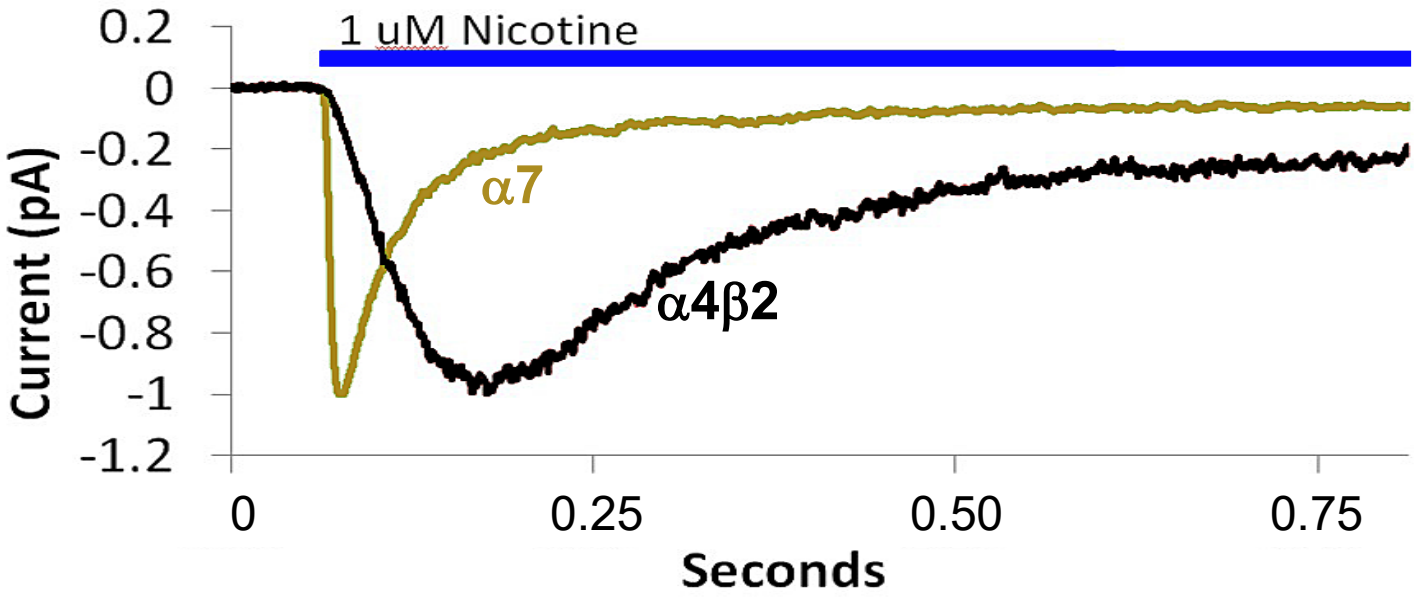
Nature 23(6):494

nAChR Subunit Composition Influences Desensitization Kinetics



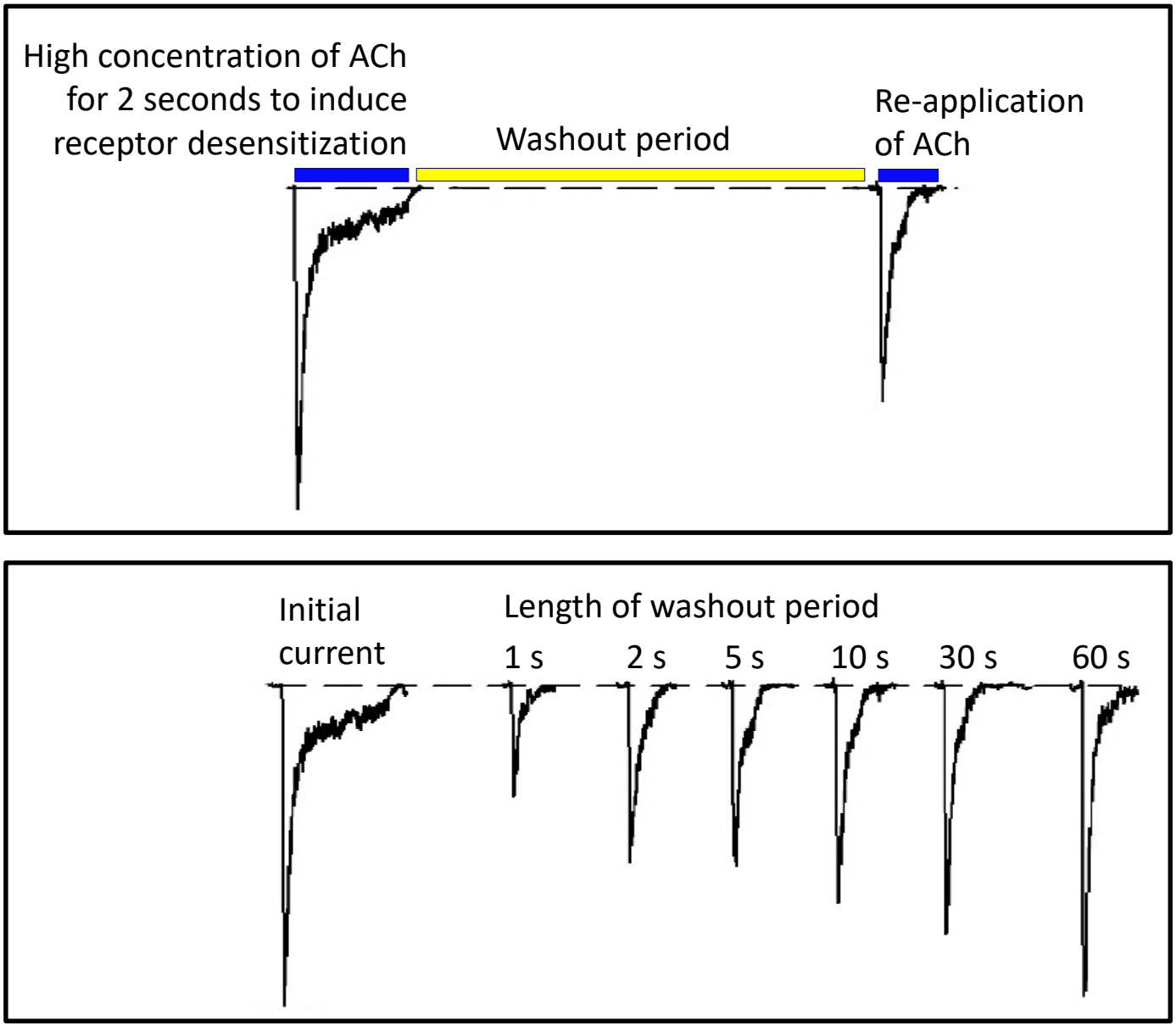


Whole-cell recordings



Recovery from Desensitization

Whole-cell recordings of neuronal nAChRs



Neuronal nAChR Desensitization and Recovery