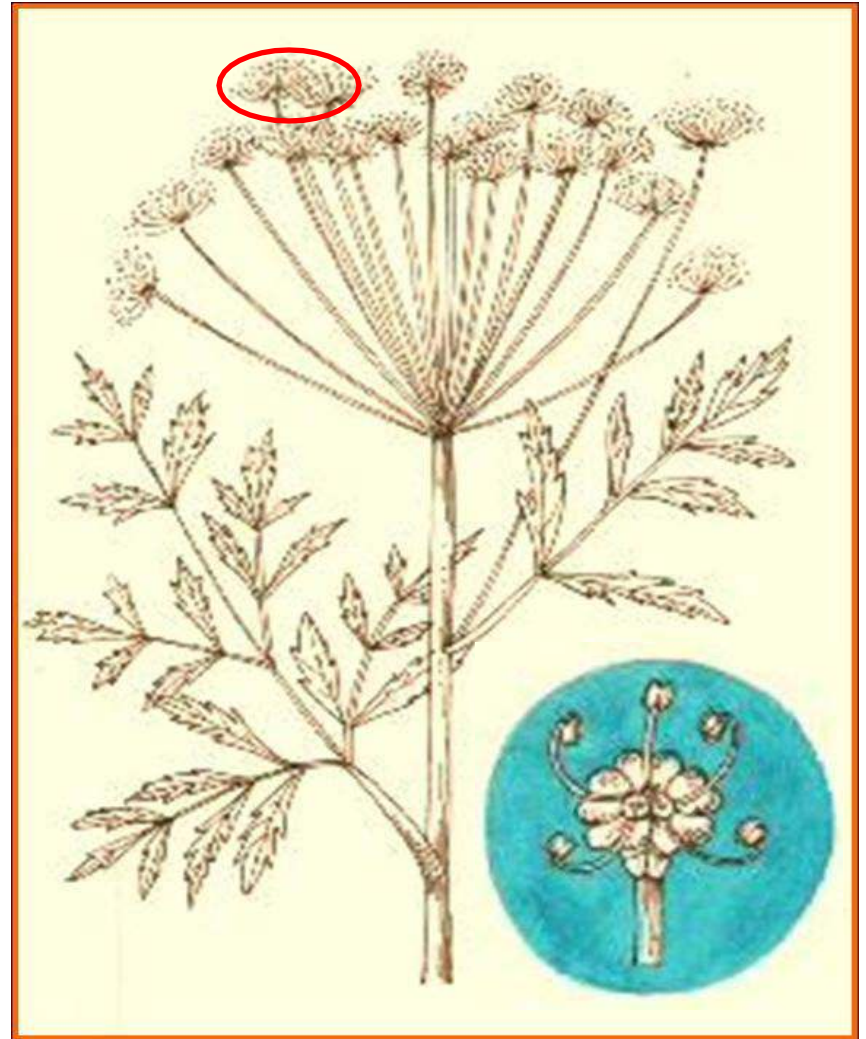




# 神经肌肉传导电生理

# Acetylcholine

- **curare**是一种取自热带植物的剧毒药物，被南美的土著猎人用作制作毒箭的材料



# Acetylcholine

- **Bernard** 认为 Curare 的作用位点是神经与肌肉相接触的区域 (N M J )
- **John Langley** 发现 Nicotine 能刺激蛙的离体骨骼肌的收缩, 但 Curare 会使 Nicotine 失效
- 1906 **John Langley** 提出化学递质假说
- 1921 **Loewi** 发现化学递质 — Ach



# Acetylcholine

荣获1936年诺贝尔生理学或医学奖

发现了神经冲动的化学传递



戴尔

Sir Henry Hallett Dale

英国

国家医学研究所

1875年--1968年



洛伊

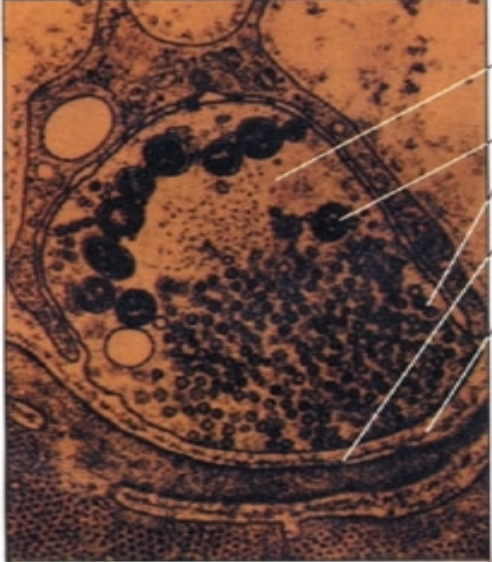
Otto Loewi

英国

奥地利格拉茨大学

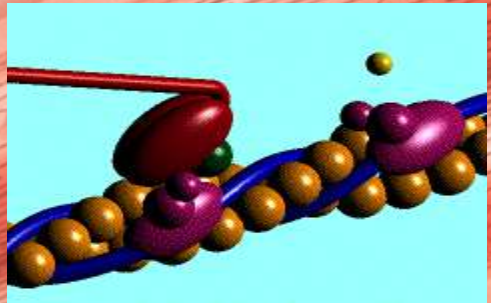
1873年--1961年



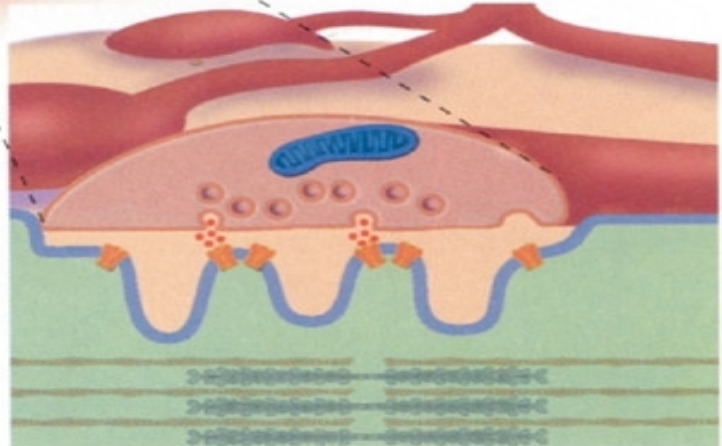


Terminal knob of presynaptic neuron  
Synaptic vesicles  
Membrane of postsynaptic target cell  
Synaptic cleft

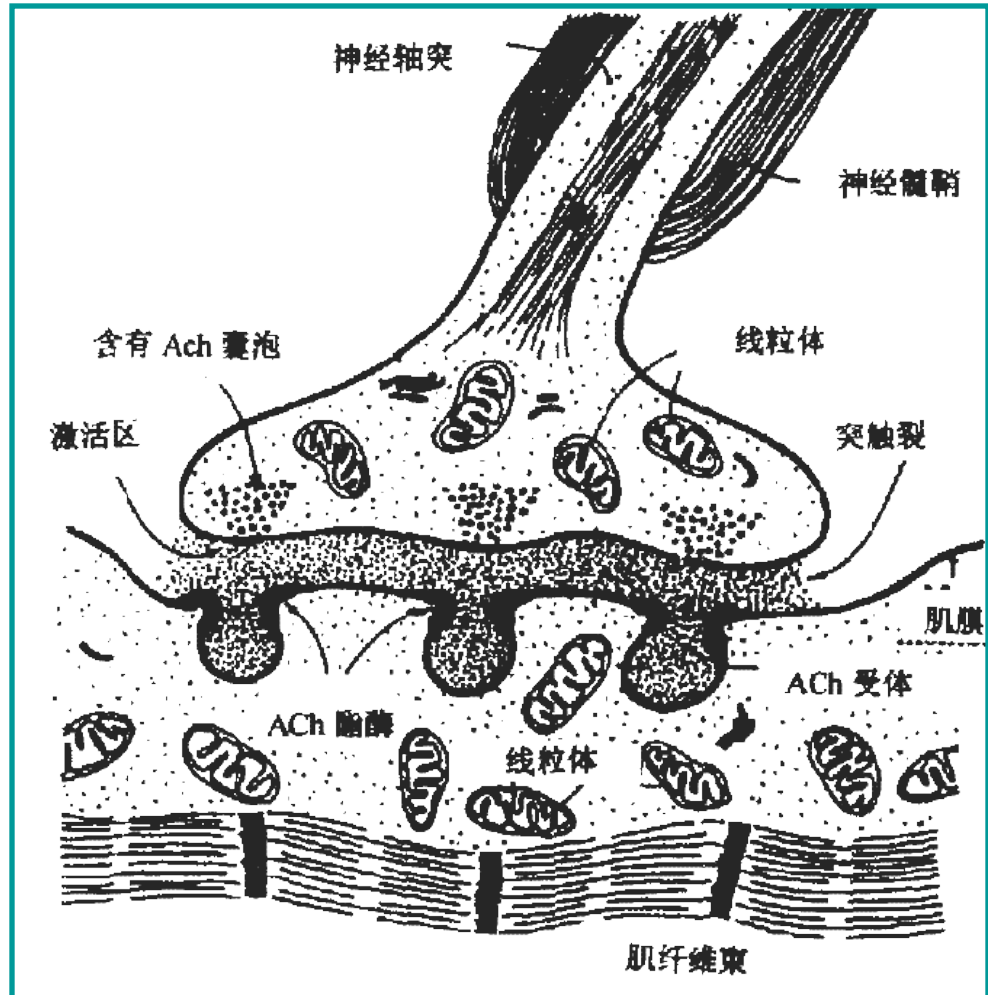
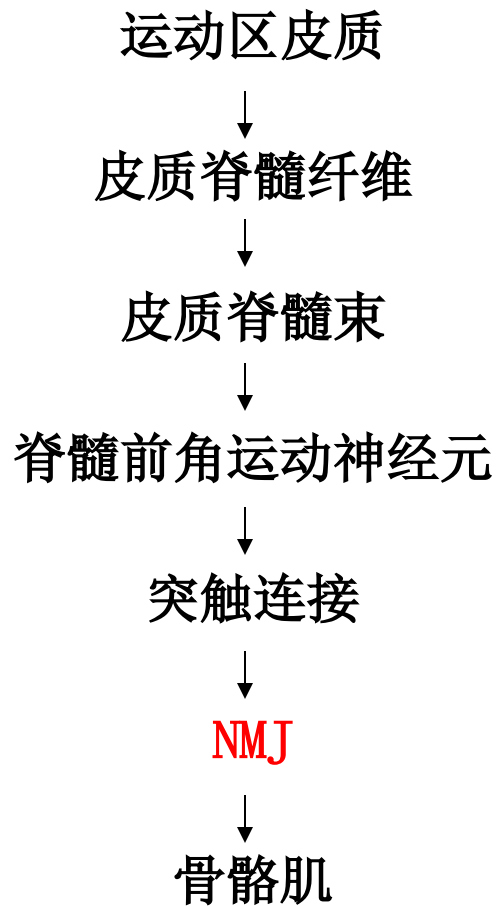
Axon of nerve cell



Muscle fiber

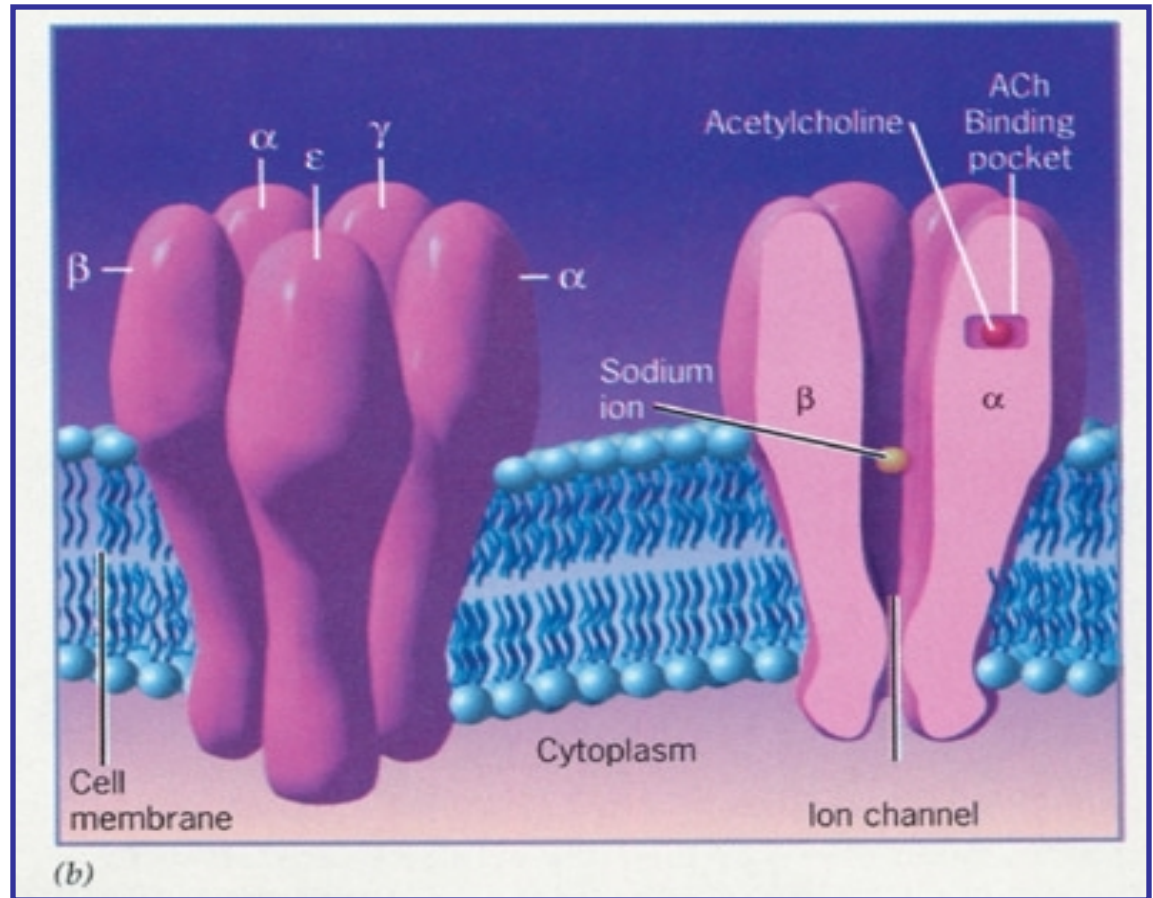


# 神经-肌接头NMJ (neuromuscular junction)

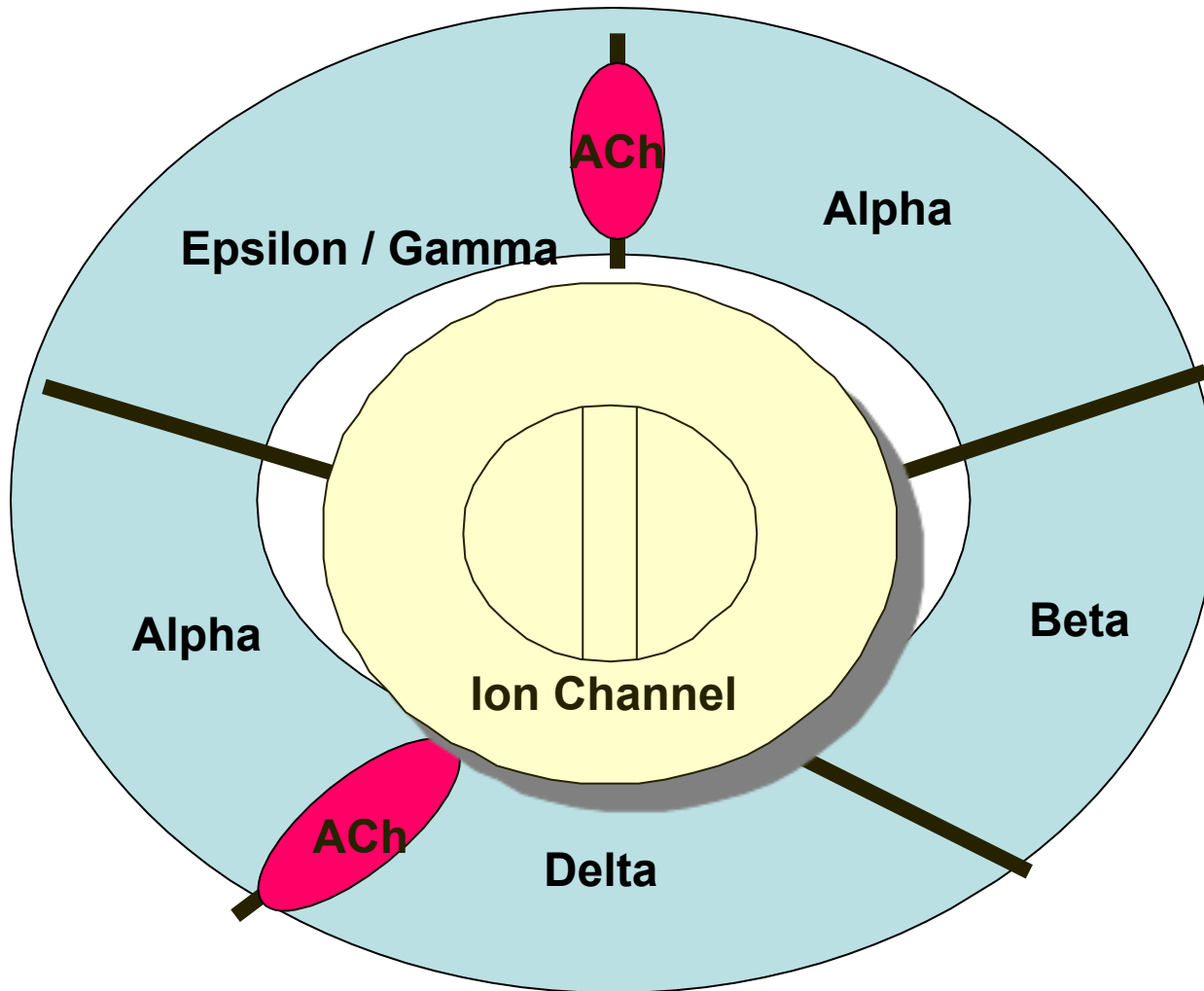


# nAChR

- Arthur Karlin
- nAChR是一个五聚体
  - $\alpha$ 亚基 2个
  - $\beta$ 、 $\delta$ 亚基各一个
  - $\epsilon$  或  $\gamma$ 亚基



# nAChR



In fetal & denervated receptors: Gamma replaces Epsilon



# nAChR

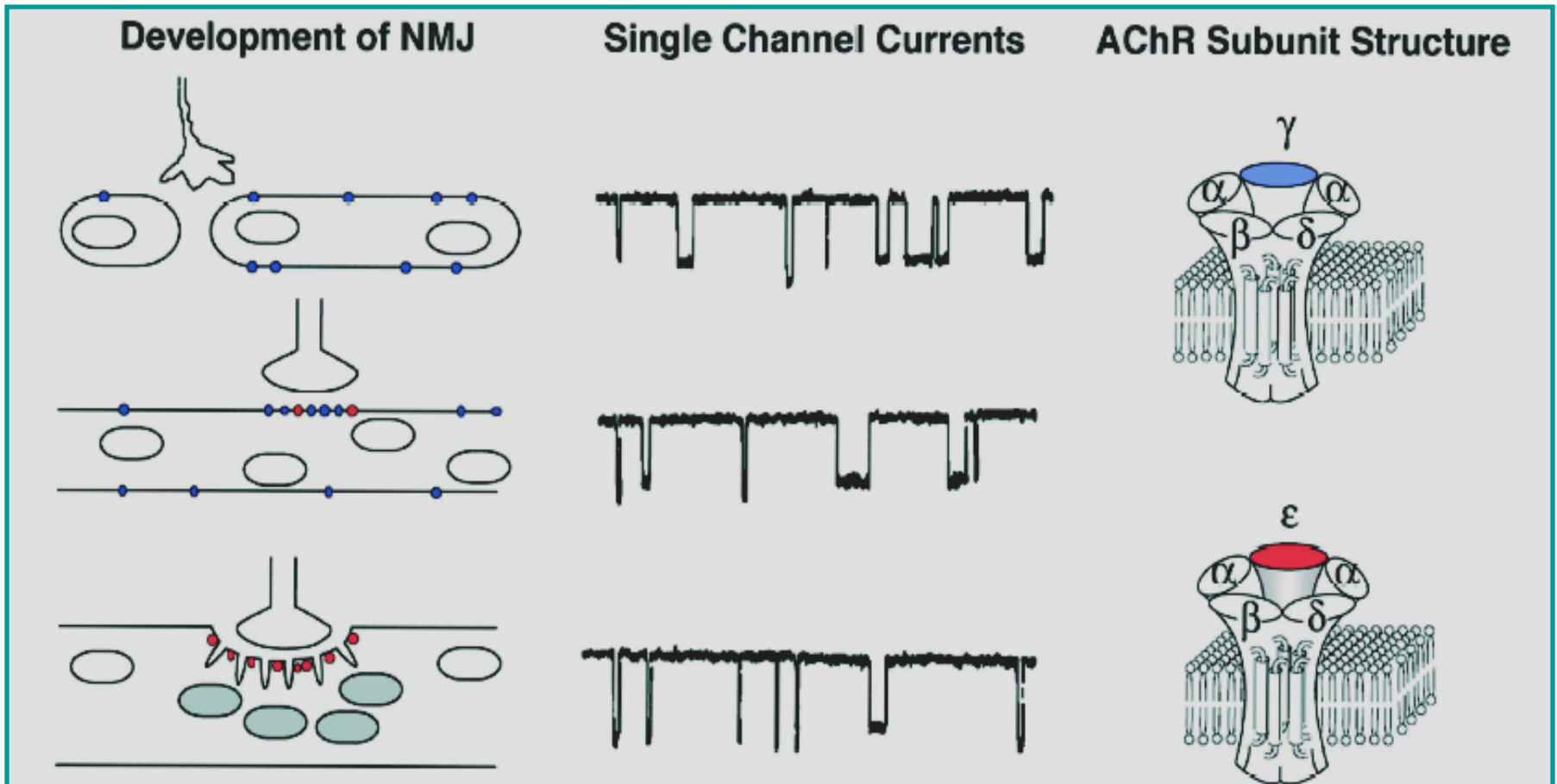


Fig. 1. Development of the neuromuscular junction. (Left) Motor neuron growth cones contact myotubes as they fuse from myoblasts and express mostly fetal nicotinic acetylcholine receptors (nAChRs; marked in blue) in their surface membranes. In adult muscle, adult nAChRs (marked in red) predominate and are largely concentrated at the neuromuscular junction. (Center) Records of AChR channel openings from muscle membranes at different stages of neuromuscular development. Fetal (top) and adult nAChRs (bottom) are activated by acetylcholine to form ion channels of different conductance and gating properties. (Right) Subunit composition of fetal and adult AChR subtypes. Fetal and adult AChR subtypes are characterized by the presence of a  $\gamma$  and  $\epsilon$  subunit, respectively.

# nAChR

## Immature

- Spread
- Unstable
- $\frac{1}{2}$  life 24 hrs
- Longer burst duration
- Smaller conductance
- 2-10 times longer channel opening (slow closing)

## Mature

- Localized
- Stable
- $\frac{1}{2}$  life 2 weeks
- Burst activity
- Normal conductance
- Channel opens for 0.5 millisecond

# nAChR

- **10 %** receptors must be open for muscle **action potential** generation
- **70 %** receptors can be occupied before **fade** is observed
- **95 %** receptor occupancy required for **complete twitch suppression**

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