Neurotransmitter Receptors

End-plate channels

- receptor/channel protein
- gate opened by ACh
- binding site for ACh

Endplate channel is integral protein (5-subunits) forming ion channel and receptor for ACh.

Channel is permeable to both Na⁺ and K⁺
Channel gating

Single-channel record \[ \rightarrow \text{inward current} \]

- Channel opens when ACh binds to receptor site
- Channel closes when ACh dissociates

Increasing [ACh] increases frequency of channel openings; not duration of opening or size of current through channel.

Low [ACh] \[ \rightarrow \]

High [ACh] \[ \rightarrow \]

Overall current at endplate increases with increasing [ACh] because more channels are open at any instant of time.
Channel opening requires binding of 2 ACh Molecules

ACh-activated channel formed from 5 subunits

ACH-binding sites are on 2 subunits. There are 2 of these in each channel.

ACh must bind to both sites before channel opens. Thus, channel opening increases as the square of [ACh].

[eg. if double [ACh], probability that a single site will bind ACh doubles. Thus, probability that both sites bind ACh quadruples]
Time course of channel openings during e.p.p.

ACh released into synaptic cleft is very quickly broken down by enzyme, acetylcholinesterase. [hydrolyzed to choline and acetic acid; choline is recycled by nerve to make more ACh]

[ACH] in synaptic cleft

inward current through end-plate channels

e.p.p. (end-plate potential)

rapid 'spike' of ACh because quickly broken down

decline of current as channels close because ACh dissociates from receptor sites

slow depolarization because of charging of membrane capacitance
Ionic basis of the end-plate potential

End-plate channels let through Na\(^+\) and K\(^+\) ions. Equilibrium potential is thus midway between equilibrium potentials for Na\(^+\) (+60mV) and K\(^+\) (-90mV).

Voltage-clamp muscle and record end-plate current that flows when clamp at different potentials.

\[
\begin{align*}
\text{outward} & \quad \uparrow \quad +10 \text{ mV} \\
\text{current} & \quad \quad \quad \quad \quad -10 \text{ mV} \\
\text{inward} & \quad \downarrow \quad -20 \text{ mV} \\
\text{stimulate} & \quad \uparrow \quad -60 \text{ mV} \\
\text{nerve} & 
\end{align*}
\]

No matter how much ACh is released, the end-plate potential cannot depolarize a muscle fibre beyond -10mV.
However - depolarization to -10 mV is more than enough to trigger an action potential.

---

The graph shows the change in membrane potential (mV) over time. The y-axis represents the membrane potential, ranging from -100 mV to +50 mV. The x-axis represents time, not explicitly shown in the image. The graph indicates that depolarization to -10 mV is sufficient to trigger an action potential (marked by the green arrow). The threshold for triggering an action potential is also indicated (marked by the dashed line). The end-plate potential if the action potential was blocked is also shown (marked by the dotted line).
Equivalent electrical circuit for endplate

Resting potential tends to hold muscle fibre at \(-90\text{mV}\).

Current through end-plate channels tends to depolarize to \(-10\text{mV}\).

Resulting potential depends on relative conductance of end-plate (how many channels open).

\[
\text{final voltage of muscle } E = \frac{9_{\text{ACH}} \times E_{\text{ACH}} + 9_{\text{rest}} \times E_{\text{rest}}}{9_{\text{ACH}} + 9_{\text{rest}}}
\]