Synapses are densely packed in the neuropil

Ventura & Harris (1999)
glutamate

\[
\begin{align*}
\text{COO}^- \\
\text{CH} - \text{CH}_2 - \text{CH}_2 - & \text{COO}^- \\
\text{NH}_3^+ 
\end{align*}
\]
The EPSP

Action Potential in “Presynaptic” CA3 pyramidal cell

Excitatory Postsynaptic Potential in “Postsynaptic” CA1 pyramidal cell

Both pre- and postsynaptic neurons are recorded in the Current Clamp configuration
The EPSC

Presynaptic neuron is recorded in the Current Clamp configuration: measure the membrane potential ($V_m$).

Postsynaptic neuron is recorded in the Voltage Clamp configuration: measure the membrane current ($I_m$).
Excitatory Glutamatergic Synaptic Transmission

Metabotropic
- mGLURs
  - G-protein coupled

Ionotropic
- AMPAR
  - Ligand gated Na+/K+
    - (some also Ca2+)
- NMDAR
  - Ligand gated Na+/K+/Ca2+
- KainateR
  - Ligand gated Na+/K+
The Ionotropic Glutamate Receptor Family

- AMPA R
- Kainate R
- NMDA R
Domains of the AMPAR subunit

Amino Terminal Domain
S2
Domain 2
agostist
Domain 1
S1

out
membrane
in
AMPA Receptors form Tetramers

Top view

Side view

Resting → Glu → Open
The AMPAR opens a non-selective cationic conductance
The Reversal Potential

AMPAR mediated EPSC in a Voltage Clamped pyramidal cell

Synaptic current reflecting movement of Na⁺ and K⁺

The Reversal Potential

At negative potentials:

$I_{Na}$ inward > $I_K$ outward

$E_{rev} = 0 \text{ mV}$. @ 0 mV: $I_{Na} = -I_K$

The I/V plot

Ohms law:

$I = (1/R)V$

$G = 1/R$

$I = G*V$

$G$: Synaptic conductance (slope of I/V plot)
AMPAR containing the GLUR2 Subunit are permeable to K$^+$ and Na$^+$

AMPAR lacking the GLUR2 subunit are also permeable to Ca$^{++}$
AMPAR containing the GLUR2 subunit have a linear I/V plot

AMPAR lacking the GLUR2 subunit have a rectifying I/V plot
NMDARs are permeable to K+, Na+ and Ca++

NMDARs has to bind to both glutamate and glycine in order to open
At negative potentials current through NMDARs is blocked by Mg$^{++}$ (voltage dependent block)
NMDA receptors are blocked by external Mg$^{2+}$ in a voltage dependent manner.
Gating of NMDA receptors is slow

Very brief glutamate pulse on the patch (synapse-like)

Current through NMDA receptors in an outside-out patch of a neuronal membrane
AMPAR and NMDA receptor immunogold labeling at cortical synapses.

Asymmetric synapses labeled with antibodies recognizing NMDA receptors (a–c) or AMPA receptors (d–f) or with antibodies to AMPA receptors (10-nm particles) followed by antibodies to NMDA receptors (g–i; 20-nm particles). Whereas large (c, f, i) and medium-sized (b, e, h) synapses contain both types of receptor, a subpopulation of the small synapses displays only NMDA receptors (a, d, g). Arrowheads indicate extent of postsynaptic density. Each section corresponds to the PSD diameter, as identified in serial sections. Mitochondrion designated by ‘m; terminal designated by ‘t’. Scale bar, 200 nm.
NMDARs are coincidence detectors of pre- and postsynaptic activity