Synapses and plasticity
Outline

• Chemical synapses
• Presynaptic function
• Postsynaptic function – Receptor types
• Synaptic Plasticity
Chemical Synapses

- Have synaptic delay
  - 200 μs – non-enzymatic reaction
  - Neurotransmitter release mediated through local, transient Ca++
    - Binds SNARE complex

- Are Unidirectional

- Release amino acids, small molecules, peptides

- CNS synapses less reliable than NMJ
Types of Receptors

- Receptor dictates whether excitatory or inhibitory

- **Excitatory**
  - Non-selective cation (Na\(^+\), K\(^+\)) channels will depolarize
    - Driving force of Na\(^+\) dominates
  - Glutamate R, AChR

- **Inhibitory**
  - K\(^+\) and Cl\(^-\) channels will hyperpolarize or **shunt** depolarizing responses
    - Do not take \(V_m\) past threshold
  - GABAR, glycine R, 5-HT R
Ionotropics vs Metabotropics

- **Ionotropics R** - linked directly to ion channel
  - Fast and localized

- **Metabotropics R** – Linked to G proteins
  - Slow and more widespread effects
  - Can open K+ channels, inhibit Ca++ entry
  - Impinge on various signaling pathways
    - cAMP, cGMP, PLC
  - Are hijacked by cholera toxin and pertussis toxin
Glutamate receptors

- AMPA Receptor
  - Fast, desensitizing
  - Most often Na+/K+, but some can pass Ca++ (RNA editing)
  - Voltage independent

- NMDA Receptor
  - Slower time course - increased Glutamate affinity
  - Voltage-dependent – Mg++ blockade
  - Highly Ca++ permeable
GABA<sub>A</sub> Receptors

- Anion Selective
- Structurally similar to AChR
- Site for many sedatives
  - Barbiturates, benzodiazepines potentiate response

- Typically inhibitory, but can be excitatory at times
  - Due to changes in Nernst potential
Synaptic Plasticity

- Short Term $\rightarrow$ msec - sec
- Synaptic Modulation $\rightarrow$ sec – min
- Long term modifications $\rightarrow$ min - hours
  - Spike Time Dependent Plasticity
  - Long Term Potentiation
  - Long Term Depression

- Homeostatic plasticity - days
Short term plasticity

- Presynaptic cell stimulated twice, in rapid succession

- Facilitation
  - Second response is larger than first
  - Due to residual Ca^{++} in presynaptic terminal

- Depression
  - Second response is smaller than first
  - Depletion of vesicle pool or receptor desensitization

Figures courtesy of MIT OCW.
**Synaptic Modulation**

- **Presynaptic:**
  - Ca^{++} channels
  - K^{+} channels
  - Probability of release
  - Vesicle pool size

- **Postsynaptic**
  - Receptor number
  - Channel Conductance
  - Nt reuptake
Potentiation & Depression

- Spike time dependent plasticity
  - Reward synapses that lead to spiking
  - Punish those that do not

EPSP < Spike EPSP > Spike

Potentiation

Depression
CA3-CA1 LTP

- LTP: A long-lasting increase in synaptic strength (AMPA-R currents)
  - First studied in the hippocampus

- Tetanus-
  - Many stimulus presented in short time (100 Hz)

- Like multiple pairings of STDP in a very short time

- Requires Ca++ influx via NMDA-R activation
  - So it requires glutamate AND postsynaptic Depolarization

- Mechanism: insertion of postsynaptic AMPARs
  - Though some evidence for presynaptic changes exist

Figure courtesy of MIT OCW.
Long Term Depression

- The opposite of LTP
- Long lasting reduction in synaptic sensitivity
  - Removal of AMPARs
- Induced by low frequency tetanus
  - Not enough stimulation to consistently drive the cell
- Requires Ca^{++} entry, but much lower levels than LTP
Other plasticity

- Mossy fiber-CA3 LTP: presynaptic expression
  - Decreased facilitation post LTP

- Homeostasis
  - Keeps average activity at a constant level in a cell
  - Long term disuse causes global increase in synaptic strength
Questions

• What is the evidence that neurotransmitter release is not an enzymatic process?

• If a glutamate receptor fluxed only K+, would it be considered excitatory or inhibitory?

• A high frequency tetanus given in the presence of APV will lead to what kind of change in postsynaptic response?