Harvard-MIT Division of Health Sciences and Technology
HST.131: Introduction to Neuroscience
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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

Ionotropic vs Metabotropic

- Ionotropic R - linked directly to ion channel
  - Fast and localized

- Metabotropic 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

$GABA_A$ Receptors

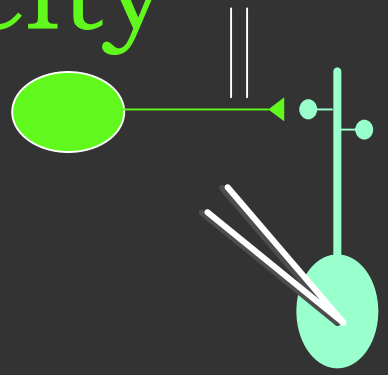
- Anion Selective
- Structurally similar to AChR
- Site for many sedatives
  - Barbiturates, benzodiazepines potentiate response
- Typically inhibitory, but can be excitatory at times
  - Due to changes in Nernst potential

Synaptic Plasticity

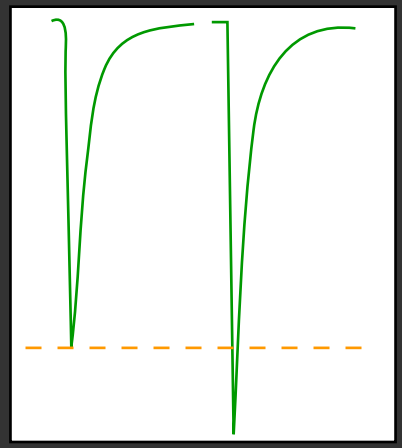
- Short Term → msec - sec
- Synaptic Modulation → sec – min
- Long term modifications → min - hours
  - Spike Time Dependent Plasticity
  - Long Term Potentiation
  - Long Term Depression

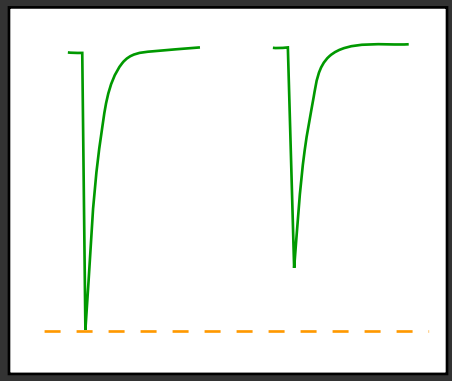
- Homeostatic plasticity - days

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

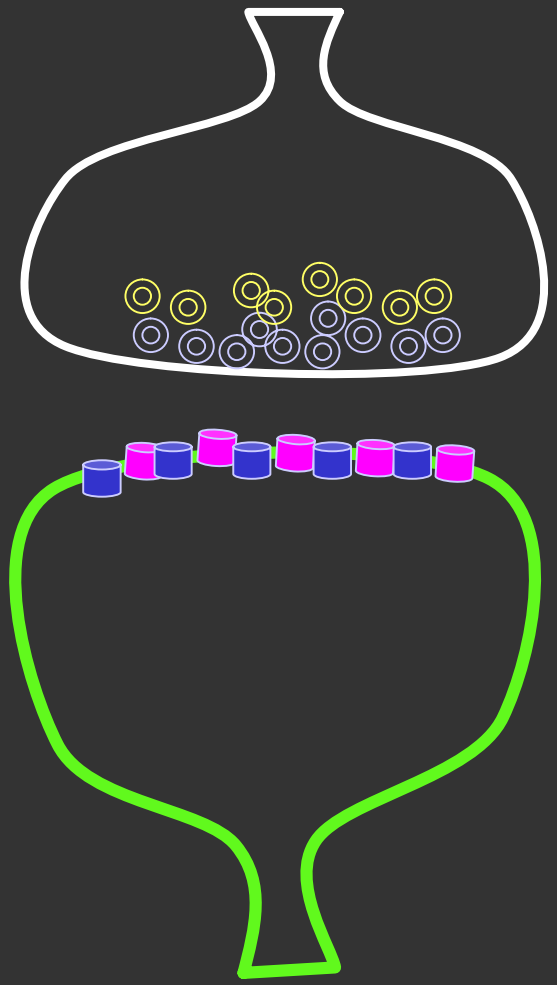




Figures courtesy of MIT OCW.

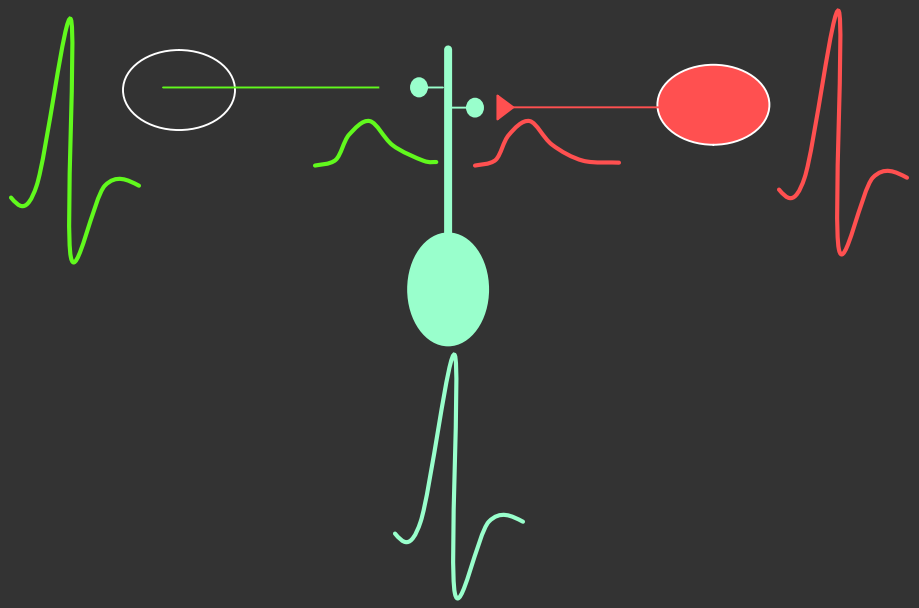
Synaptic Modulation

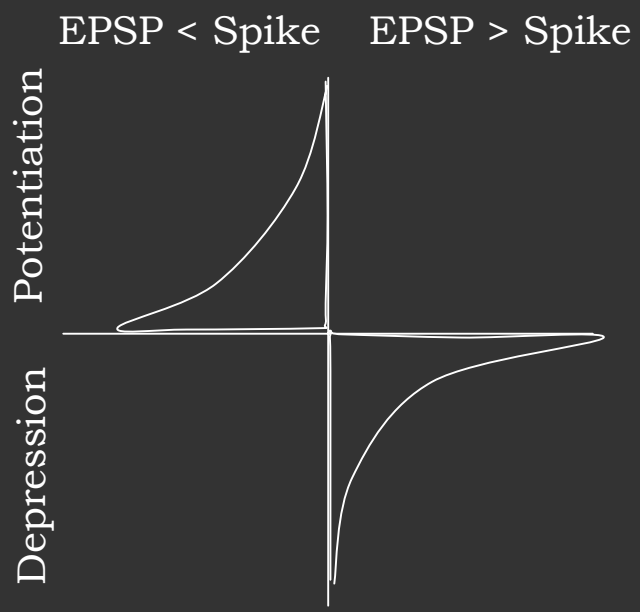
- Presynaptic:
  - Ca^{++} channels
  - K^{+} channels
  - Probability of release
  - vesicle pool size
- Postsynaptic
  - Receptor number
  - Channel Conductance
  - Nt reuptake



Potentiation & Depression

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





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)

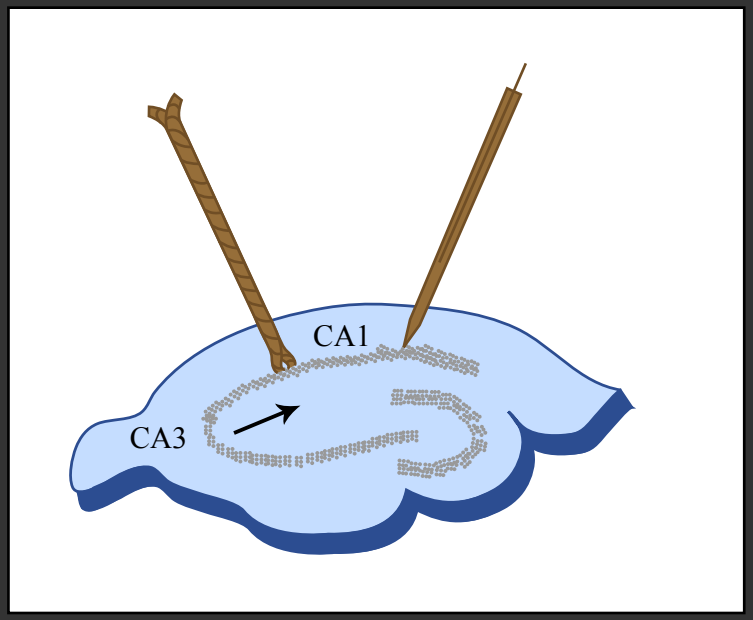
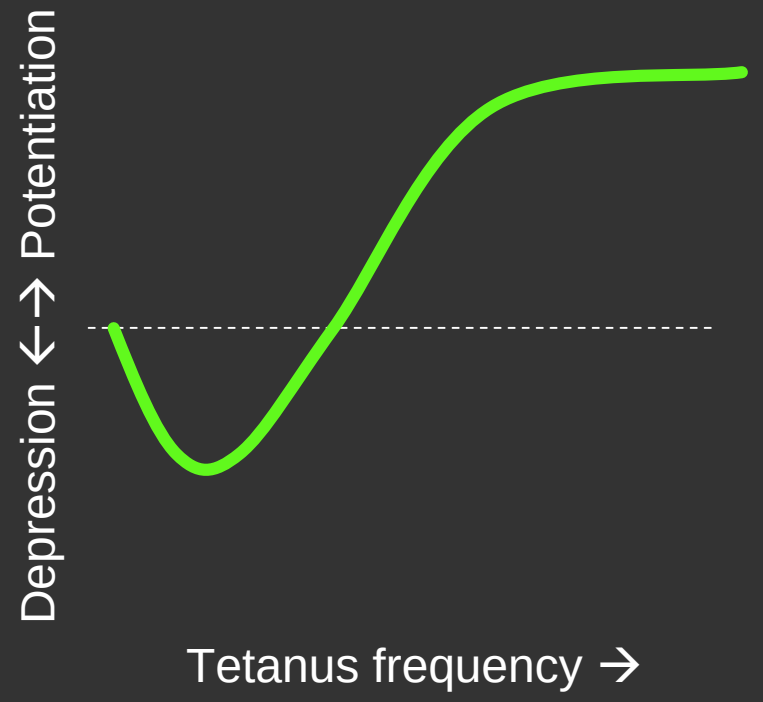


Figure courtesy of MIT OCW.

- 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

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?