For Discussion 5…

- Synaptic Release (Ch. 5)
- Neurotransmitter’s and receptors (Ch. 6, pg. 131 good table)
- Synaptic Plasticity (Ch. 24)
  - Short-term changes: Facilitation, summation (temporal, spatial) etc…
  - Long-term changes: LTP, LTD
**Synaptic Release**

1) AP comes from axon
2) Ca\(^{++}\) enters through V-Ca cells
3) Ca\(^{++}\) binds to proteins causing vesicle fusion
4) Vesicles release Neurotransmitters (NTs)
5) NTs bind to receptors
   1) Ionotropic - ion channels; fast response
   2) Metabotropic - G-protein coupled; slow long-lasting response
6) NTs are degraded in synapse or taken up by nearby cells

**NTs (excitatory)**

- Acetylcholine (Ach)
  - Where: NMJ, PNS & CNS
  - Receptors:
    - NMJ - ligand-gated ion channel receptors (aka ionotropic, nicotinic)
    - Brain, Heart etc - G-protein coupled receptor (aka metabotropic, muscarinic)
  - Limits of Action:
    - Degraded by acetylcholinesterase
  - Disease - myasthenia gravis (nicotinic Ach receptors targeted by immune system)
NTs (excitatory)

- Glutamate (amino acid)
  - Where (as a NT): CNS
  - Receptors:
    - hippocampus - ionotropic
      - AMPA/Kainate (monovalent channels) and NMDA (divalent channels)
    - brain - G-protein coupled receptor (metabotropic)
  - Limits of Action:
    - Synthesized from glutamine (released from glial cells)
    - Reuptake in the synapse by presynaptic glial cells
    - Elevated levels of glutamate can cause neurotoxicity

NTs (inhibitory)

- GABA (synthesized from glutamate)
  - Where: CNS in interneurons
  - Receptors:
    - Ionotropic (GABA\_A)
      - Open Cl\(^-\) channels causing hyperpolarization
      - Site of action of lots of drugs (e.g. benzodiazepines)
    - Metabotropic (GABA\_B)
      - GPCR opens K\(^+\) channel or blocks Ca\(^{++}\) channels
  - Limits of Action:
    - Synthesized from glutamate by GAD (glutamic acid decarboxylase)
    - Reuptake in the synapse by presynaptic & glial cells
- Glycine (amino acid)
NTs (other)

- NTs from Tyrosine (amino acid)
  - DOPA (precursor to Dopamine; used in treatment of Parkinson’s disease)
  - Dopamine (DA)
    - Coordination of movements; cells die in Parkinson’s disease; role in addition/reward
    - Coupled to metabotropic receptors
    - Action limited by: MAO (monoamine oxidase) (found in neurons and glia)
  - Norepinephrine/Epinephrine
    - Found in CNS and periphery
    - Act on alpha/beta adrenergic receptors (metabotropic)
      - Receptors can depolarize or hyperpolarize

Fig 6.10

NTs (other)

- NT from Tryptophan (amino acid)
  - Serotonin (aka 5HT)
    - CNS - Raphe nucleus
    - Involved in sleep, wakefulness
    - Action limited by:
      - Reuptake
        - Selective-serotonin reuptake inhibitors (SSRI) target reuptake to treat Depression

Cell bodies in raphe nucleus but the cells’ projections go throughout brain
Synaptic Plasticity

- Definition
  - Idea that a post-synaptic response can change based on timing, type and location of input

- Why do we need synaptic plasticity?
  - Synaptic changes underlie learning/memory, adaptation etc...

- Short-term - facilitation, depression, summation

- Long-term - LTP and LTD
  - Molecular memory or red herring?

Short-term (Facilitation)

- Second AP causes an increase in post response

  Why: Ca++ builds up in presynapse (b/c Ca++ removal mechanisms are slow) causing an increase in vesicle release in response to the 2nd AP
Short-term (Presynaptic Facilitation)

- Prepresynaptic cell causes a presynaptic cell to release more vesicles onto the postsynaptic cell than how much is normally released by the presynapse.
- Why: Ca++ builds up in presynapse (b/c presynapse depolarizes for a longer amount of time with causes more voltage-Ca++ channels to open) causing an increase in vesicle release in response to an AP in the presynaptic cell and the prepresynaptic cell.

Short-term (Depression)

- Second AP causes a decrease in post response.
- Why:
  - Vesicle pool depletion; removal of receptor from PM.
Short-term (Temp Summation)

- Nearly overlapping APs cause increase in EPSP
- Why:
  - Lots of Ca++ in presynapse (lots NTs)

Short-term (Spatial Summation)

- Overlapping APs (from 2 similar cells) cause combinatory change in PSP
- Why: Multiple cells each release NT at synapse
Short-term (Spatial Summation)

- Overlapping APs cancel each other’s effects
- Why: 2 Cells (1 excitatory and 1 inhibitory) each release NTs at synapse

Long-Term (LTP)

- High freq stimulation causes long-term change in EPSP (EPSP increases in response to the same amount of NT release)
- Causes: Insertion of AMPA receptors...
Long-Term (LTD)

Low freq stimulation causes long-term change in EPSP (EPSP decreases in response to the same amount of NT release)

Causes: Removal of AMPA receptors...

Assignments...
- Problem Set 5 (due next Friday)
- Read Chapters 7 & 8 (total Ch. 1-8, 23-24)