March 19, 2014
Snail Brain recordings
Neuromodulation

Lab 5 due today
Lab 6 Results tomorrow
Midterm due Thursday, March 27
Disease Presentations next week!

Example: Disease presentation Slide- 2 slide limit

Parkinson’s Disease

- Symptoms
  - Tremor
  - Bradykinesia
  - Impaired posture

- Cause
  - Degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc) results in dopamine (DA) imbalance
  - DA imbalance causes reduced excitation of striatum and eventually motor cortex
  - Reduced activity of motor cortex causes the symptoms of Parkinson’s Disease

- Treatment
  - Dopamine supplement
    - L-DOPA, a dopamine precursor
  - Dopamine agonist
  - AChE inhibitors
  - Deep brain stimulation
    - Use a pacemaker-like device to deliver periodic shocks to select parts of the brain
    - The shocks reduce symptoms of Parkinson’s Disease such as tremors


Example: Disease as a synaptic modulator

Pre (and) or post-synaptic sites of action?

Myasthenia gravis

Example: Disease as a synaptic modulator

Pre (and) or post-synaptic sites of action?

Lambert-Eaton Syndrome
Neuromodulation: altering of electrical properties through intracellular biochemical changes caused by extrinsic chemicals.

not usually rapid, not point to point, not simple excitation or inhibition

Types of chemical synapses

Extrinsic Synaptic Modulation

Sites of Synaptic Change by Neuromodulators (diseases too)
Modulatory control of intrinsic electrical activity as well as synaptic strength

Modulation of voltage sensitive channels orchestrated channel activity

What are other neuroactive compounds that can change synapses/excitability?
Brain neuromodulatory pathways “sprinkler system”

Two main ways to generate second messengers

1) G protein activation of subunits leading to cAMP

Some tools to study g-protein action:
- Cholera toxin - activates g-proteins
- Pertussis toxin - inhibits g-proteins

2) Membrane lipid pathway

Membrane lipid pathway
Blood clotting, sleep, inflammation, pain

Constrict bronchial airways (asthma)

Link to other physiological systems!

Many different types of G proteins

Amplification in signal transduction pathways

What’s the big deal about protein phosphorylation?
Protein Kinase A
Protein Kinase C

Kinase phosphorylation sites on Na channel

Effects of phosphorylation on Na channel

Protein Kinase A
Protein Kinase C
V-gated channel modulation

Fight or Flight: Epinephrine (adrenaline) rush
Heart I_{Ca}

Neuromodulation enhancing transmitter release through AP broadening