February 25, 2013
Synaptic Plasticity
Due today - RP Lab

Intrinsic Synaptic Plasticity (short term)
Change in synaptic strength due to activity of synapses
Important for:
- coincidence detection
- gain control
- oscillatory networks (phase onset and offset, cycle period)
- habituation, sound localization
- learning and memory

Extrinsic Synaptic Plasticity
Change in synaptic strength due to neuromodulatory substances
Important for:
- network reconfiguration (active network members, their excitability and synaptic connections)

Synaptic changes due to disease

This week in Lab:
Intrinsic synaptic modulation
Facilitation

Intrinsic synaptic modulations:
Post-tetanic potentiation
Intrinsic synaptic modulation:
Depression

Facilitation:

- MEPP sizes do not change.
- MEPP frequency increases.
- Quanta content \((m = \text{PSP/mini})\) is increased pre or post.

Sites of synaptic change in short term plasticity?

Facilitation:

a) MEPP sizes do not change.
b) MEPP frequency increases.
Quanta content \((m = \text{PSP/mini})\) is increased pre or post.
Residual Ca hypothesis for facilitation:
Presynaptic Ca builds up with each AP

Sequestration of calcium after an action potential

Takes 100-500 msec to bring calcium levels to normal after an A.P.

Non-linear dependence of transmitter release on [Ca]_

AP brings in 5 units of Ca
5 + 5 = 525
80% uptake before Next AP
1 unit left = 1
Next AP = 1 + 5 units
6 + 12 = 1296 (twice as much NT release!)

Facilitation

BUT:
1) Simulations of expected peak and residual Ca^2+ levels not able to account for facilitation.
2) Using Ca^2+ sensitive dyes, presynaptic [Ca^2+] was not raised enough to account for enhanced synaptic transmission.
3) The time course of I_{Ca}(Ca) is too fast. The decay of this current should reflect the decay of residual Ca^2+.

Ca may be acting at multiple sites of the synaptic machinery.
PTP:
1) Correlates with decay of Ca²⁺ image in whole terminal, not just at release sites, and reduced by Ca²⁺-chelators.

2) In crustacean motor neurons, Na⁺ has a role, perhaps through the Ca/Na pump. Entry of Na⁺ during AP firing may reduce the efficiency of the Na/Ca exchanger to get rid of Ca²⁺.

3) Ca²⁺ unloading from mitochondria or other internal stores.

3) In Aplysia- MEPP frequency up with PTP, but not amplitude. Both pre- and post- synaptic Ca²⁺-chelators reduce PTP, as well as postsynaptic hyperpolarization.

Other mechanisms for depression:
1) Inactivation of I_Ca during repetitive activity
2) Activation of inhibitory currents (IK(Ca) and ICl(Ca))
3) Transmitter release controlled by autoreceptors
   GABA responses are blocked by antagonists of presynaptic GABAa receptors.
4) Desensitization of post-synaptic receptors.
Overlapping Stages of Intrinsic Plasticity

Example: Disease as a synaptic modulator
Pre (and) or post-synaptic sites of action?

Myasthenia gravis