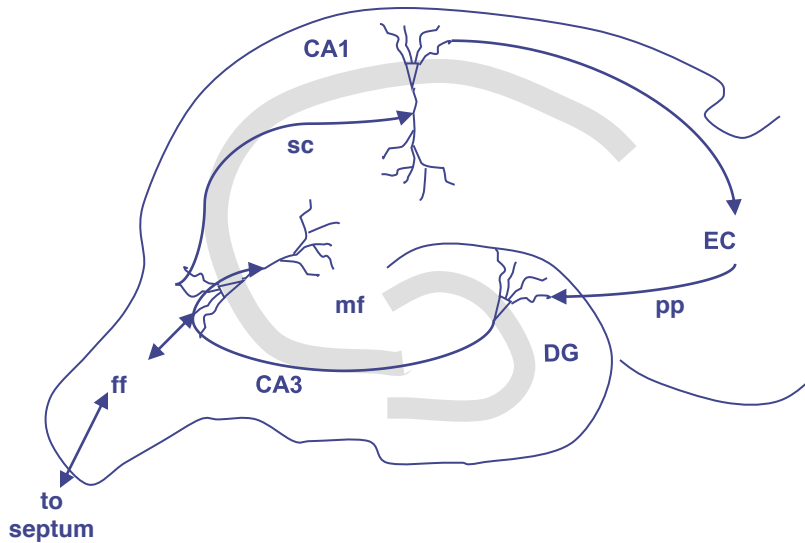




Watch online:

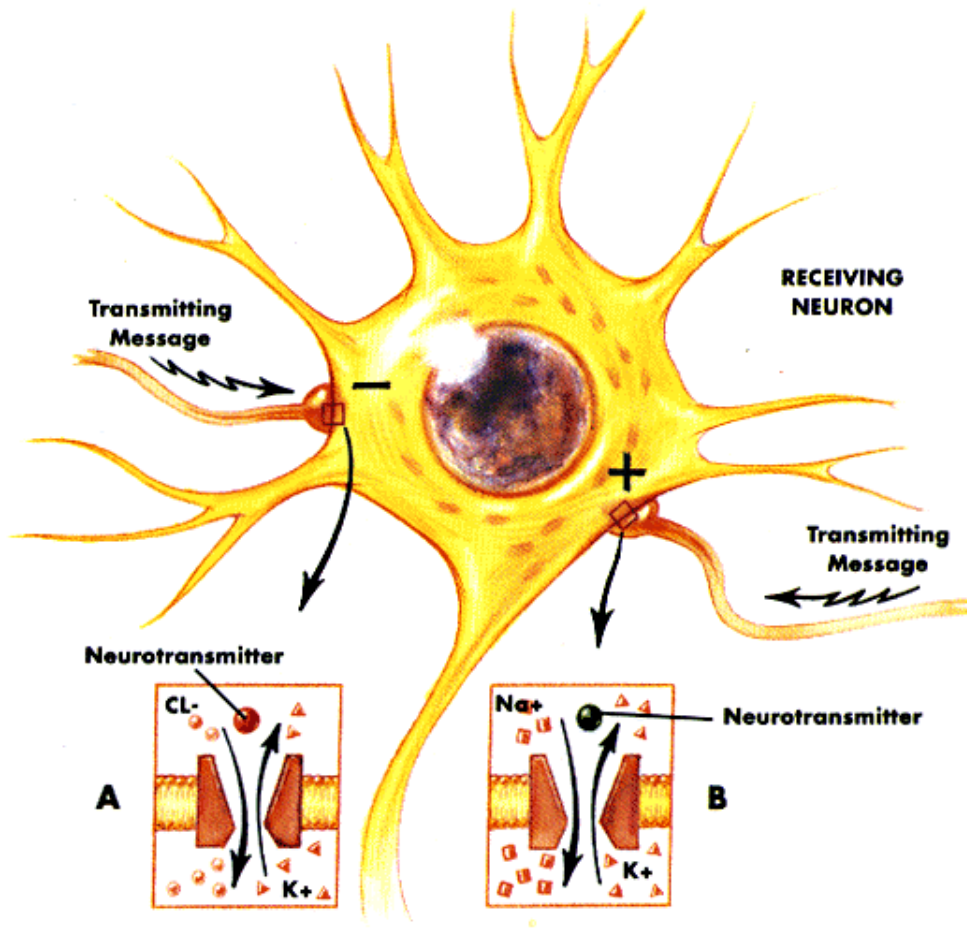
[http://www.pbs.org/saf/1402/video
/watchonline.htm](http://www.pbs.org/saf/1402/video/watchonline.htm)

Inhibitory Synaptic Plasticity in the Hippocampus



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Cell & Systems Biology
University of Toronto

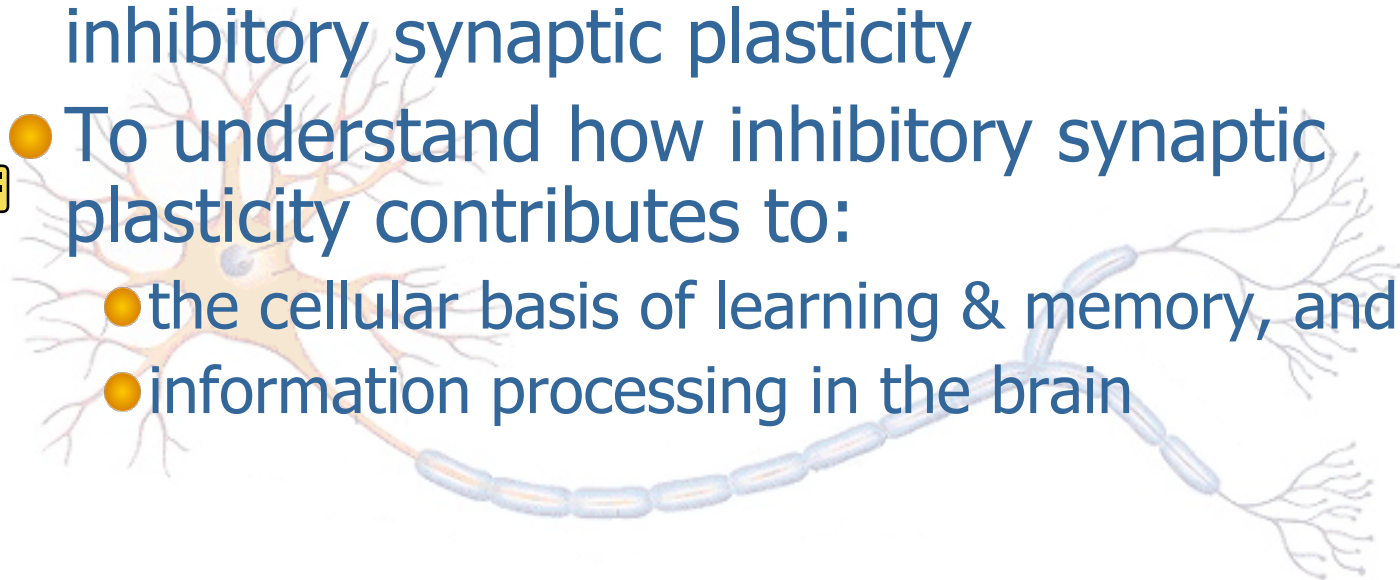
Synaptic plasticity occurs at both excitatory and inhibitory synapses



- Classic excitatory glutamatergic long-term potentiation has been well-characterized in numerous systems
- Inhibitory synaptic plasticity has been less well-characterized despite its known roles in regulating neuronal network activity

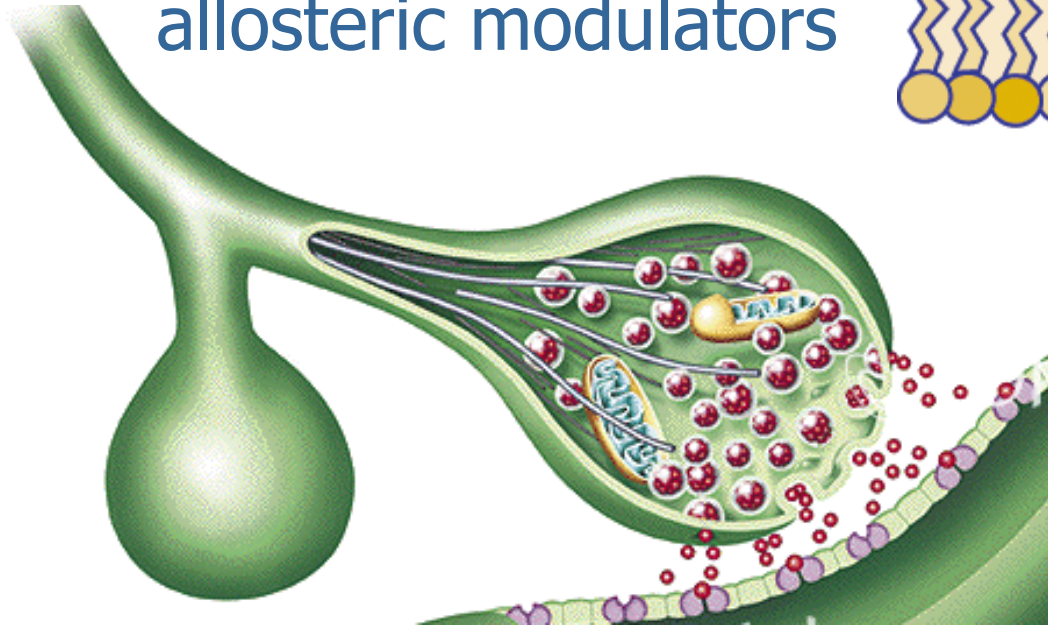
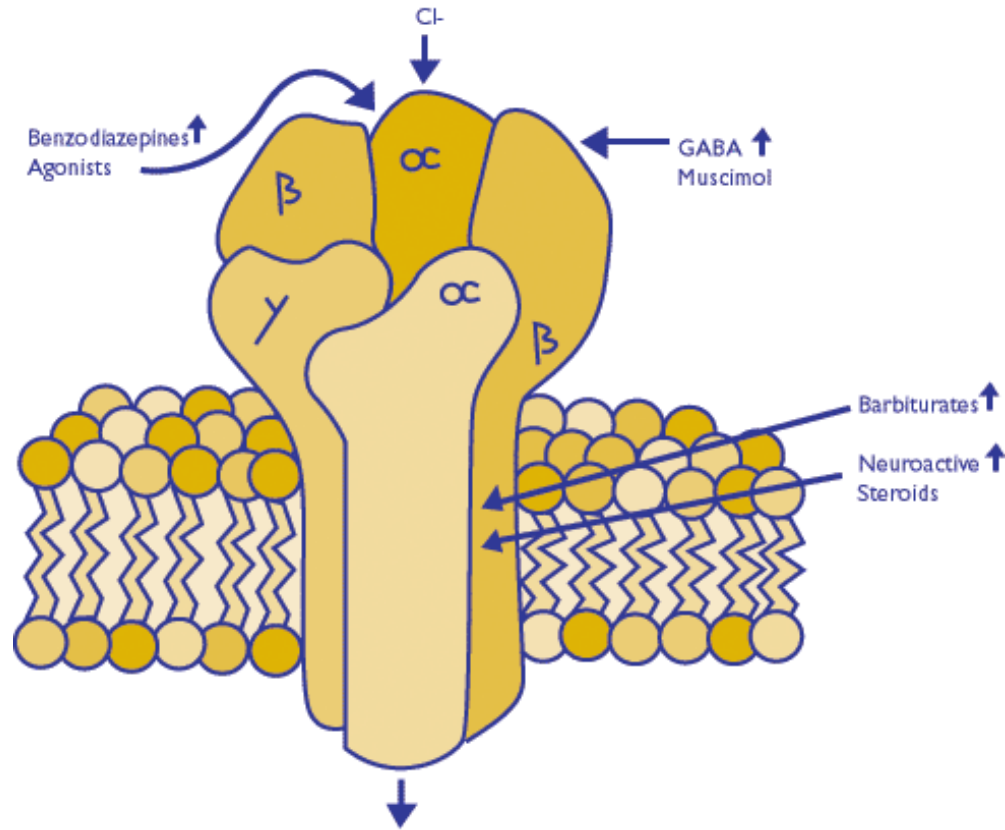
Long-Term Objectives of the Woodin Lab

- To determine how electrical activity in the brain modifies inhibitory synapses (termed inhibitory synaptic plasticity)
- What are the mechanisms underlying inhibitory synaptic plasticity
- To understand how inhibitory synaptic plasticity contributes to:
 - the cellular basis of learning & memory, and
 - information processing in the brain



GABA_A Receptor

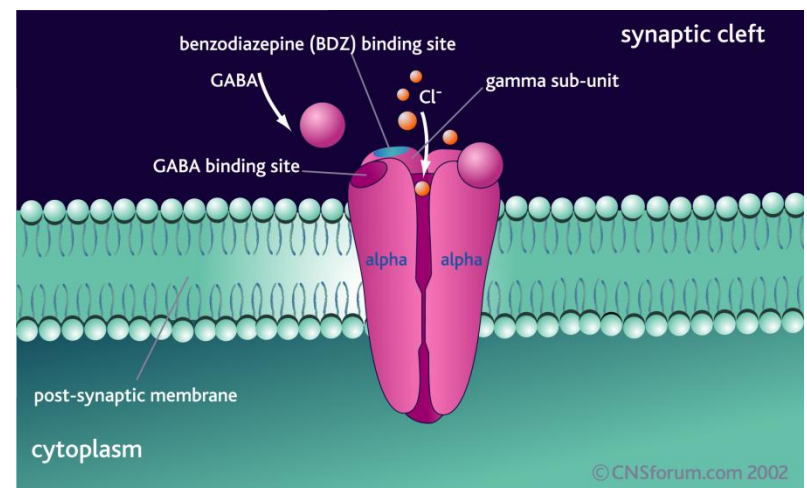
- Ligand-gated ion channel
- Largely permeable to Cl⁻
- Contains numerous binding sites for allosteric modulators

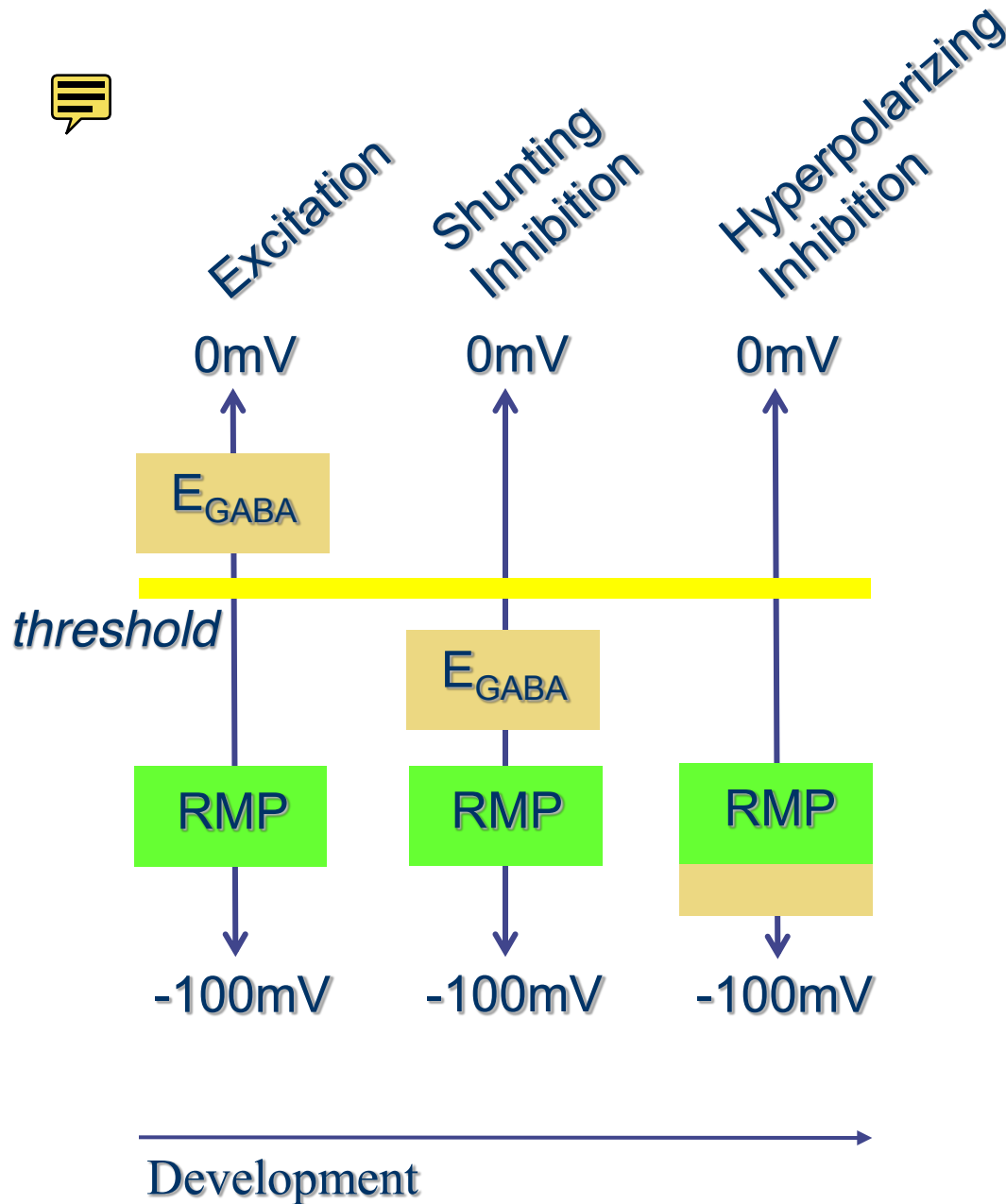




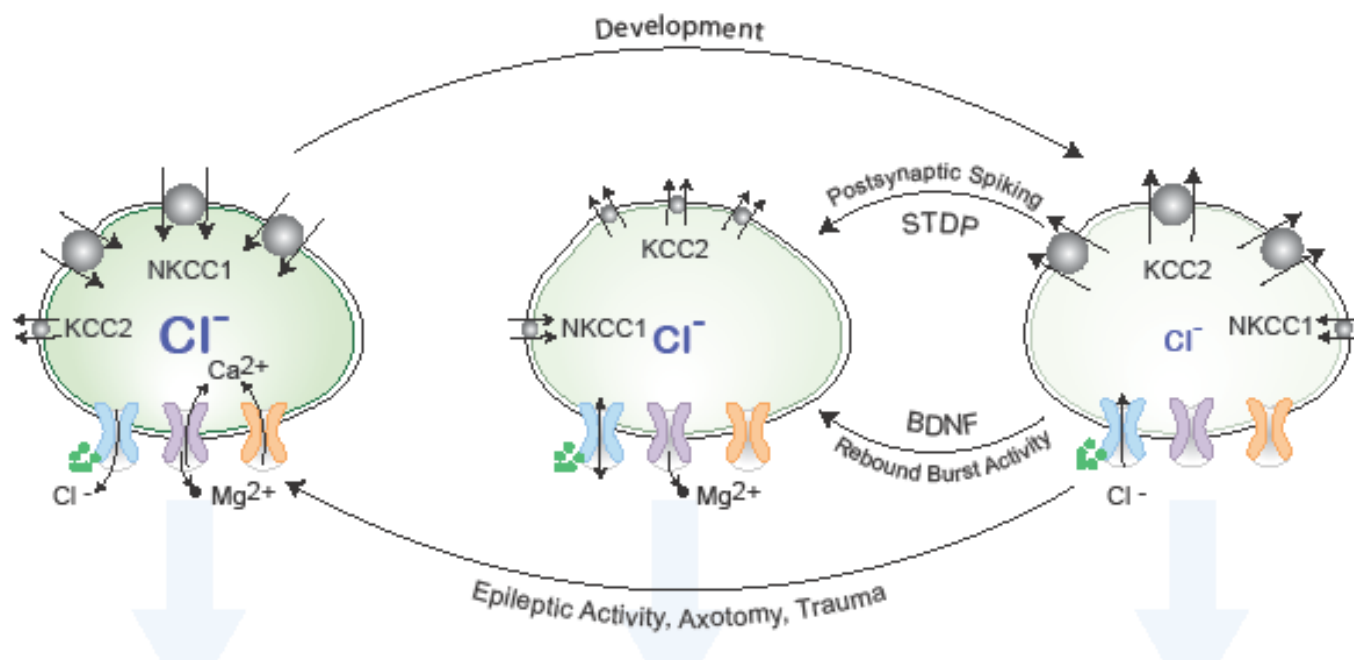
What determines the strength of inhibitory synapses?

- Synaptic conductance:
 - *amount of transmitter release*
 - *# and conductance of postsynaptic transmitter receptors*
- Driving force for Cl^- driving force (E_{GPSC} or E_{Cl})





- We determine the strength of GABA_A-mediated synaptic transmission by measuring the reversal potential for GABA (E_{GABA}); E_{GABA} is the value of the membrane potential where there is no net flow of Cl⁻ ions through the GABA_A receptor



Schematic Legend:

GABA

GABA_AR

NMDAR

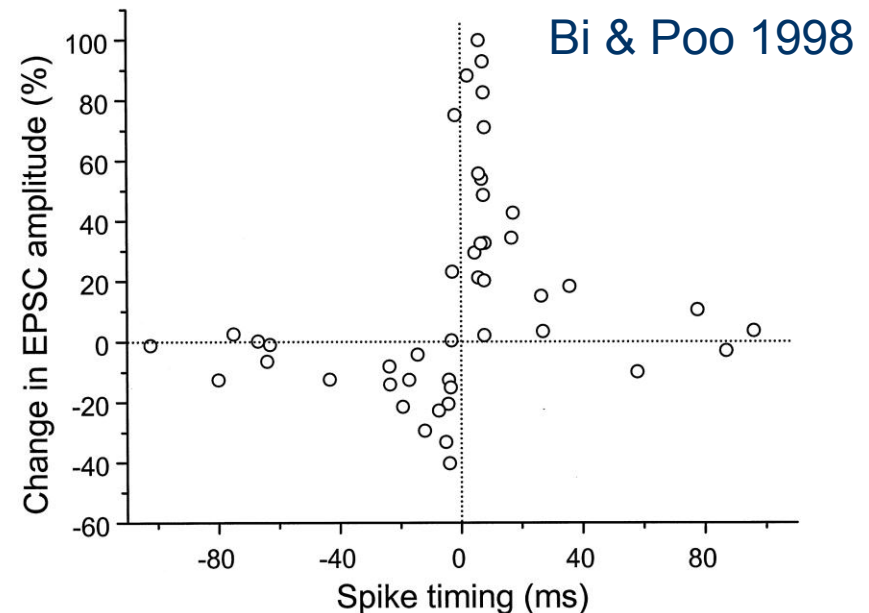
VDCC

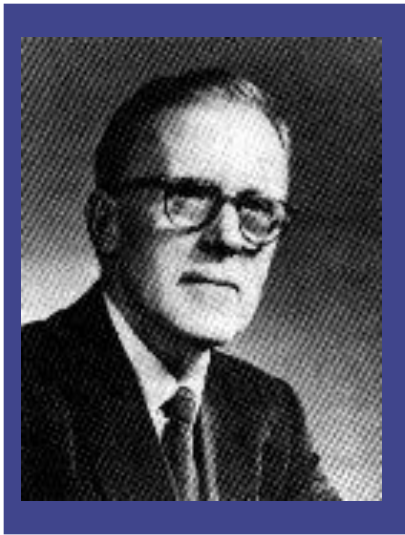
K⁺
Cl⁻ KCC2

Na⁺/K⁺
2Cl⁻ NKCC1

Spike-timing Dependent Plasticity

- STDP; induced by low-frequency coordinated pre- and postsynaptic activity
- An extension of Hebb's Rule and the statement "cells that fire together wire together"
- Well characterized at excitatory glutamatergic synapses in the CA1





“When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A’s efficiency, as one of the cells firing B, is increased.”

— Donald O. Hebb

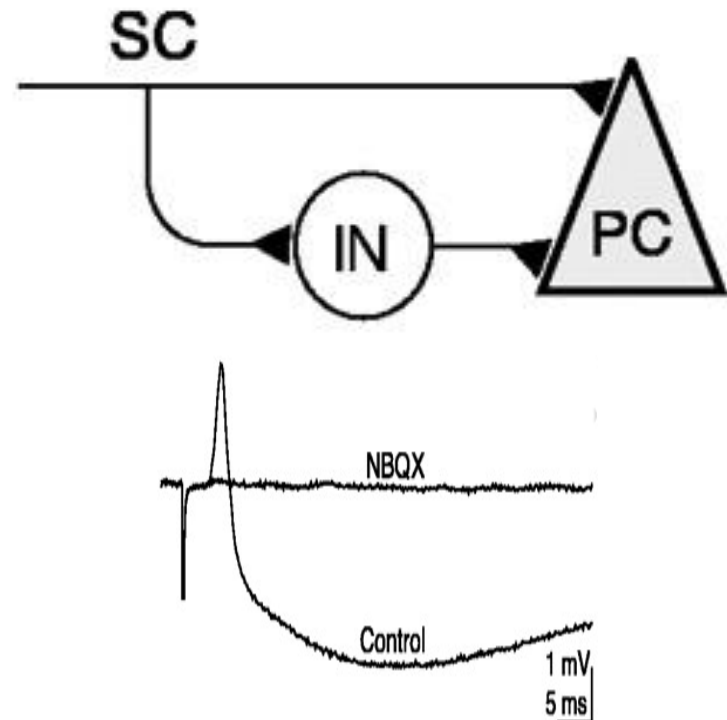
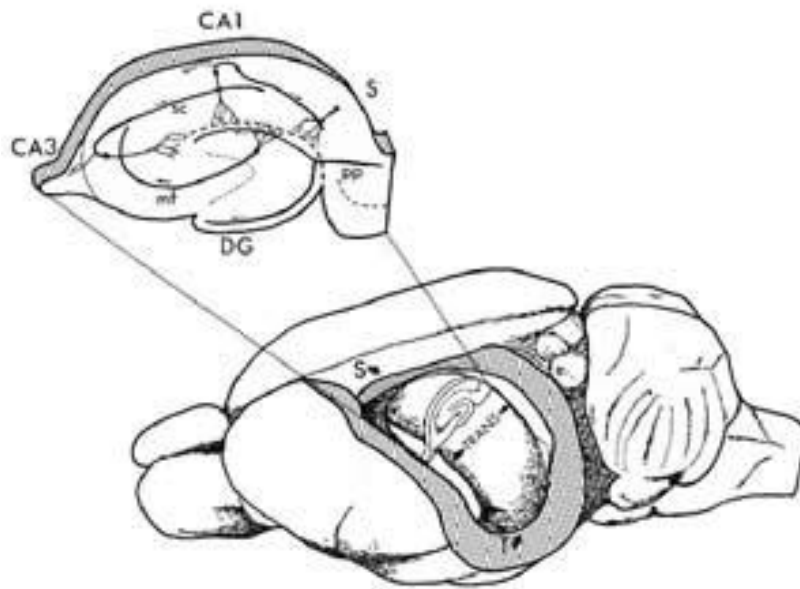
The Organization of Behavior, 1949



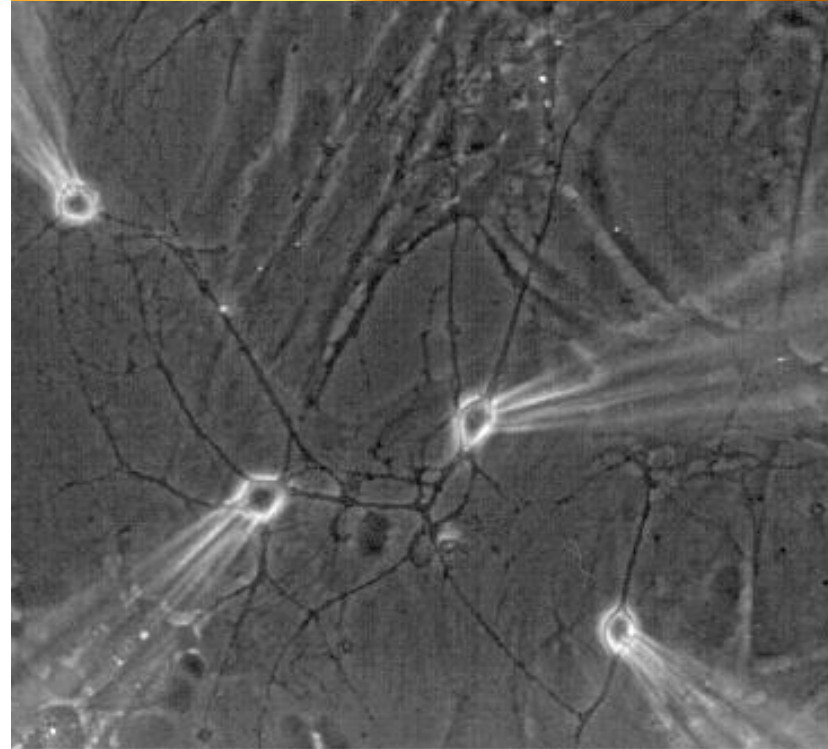
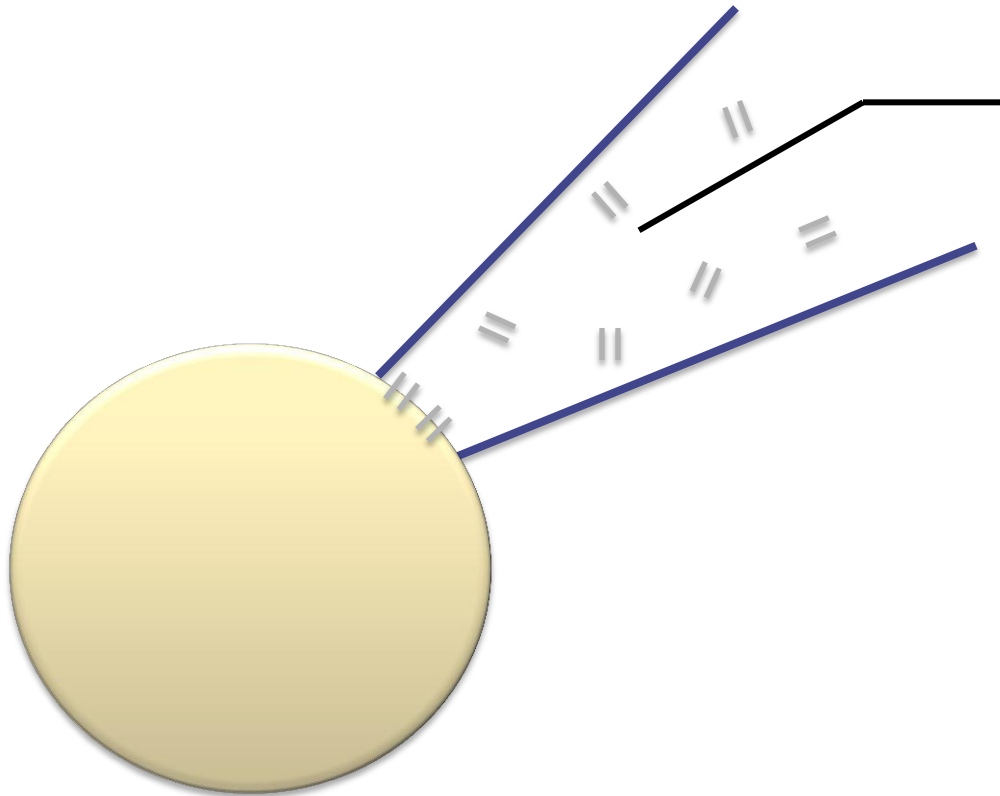


Rational for GABAergic STDP

- Inhibitory GABAergic synapses are embedded in neuronal circuits with precise timing



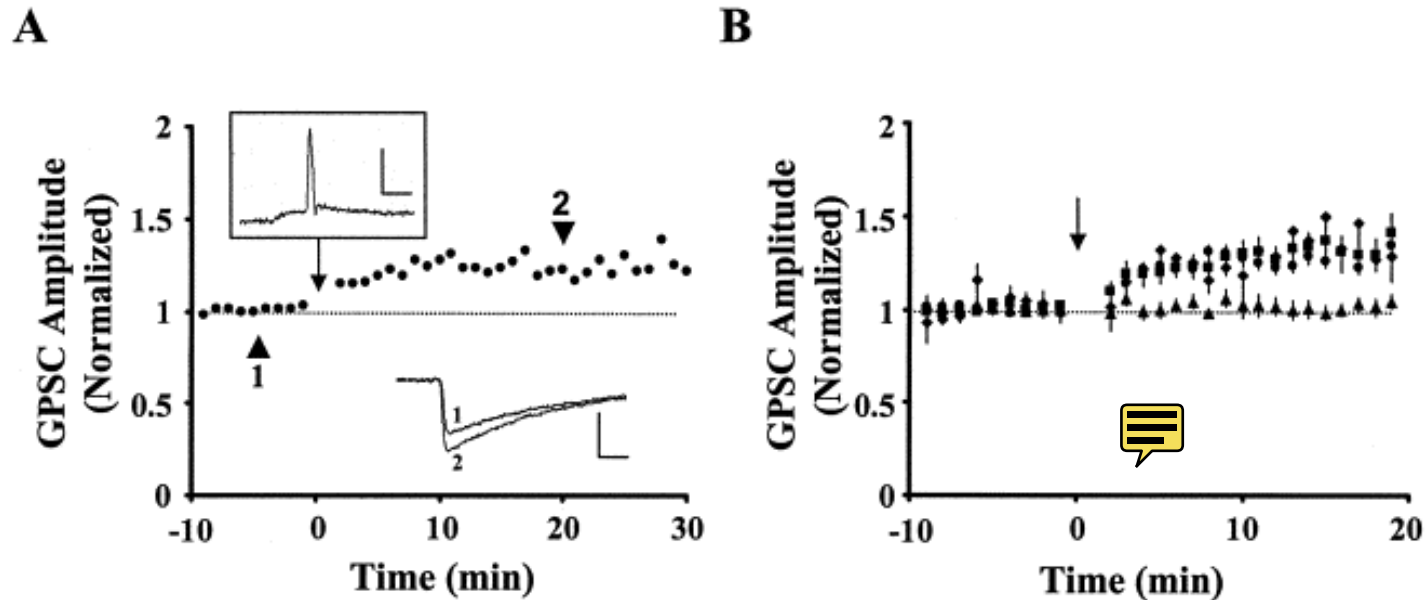
Gramicidin forms pores which are permeable to monovalent cations and small uncharged molecules but not to Cl^-



GABAergic Synapses are Modified by STDP



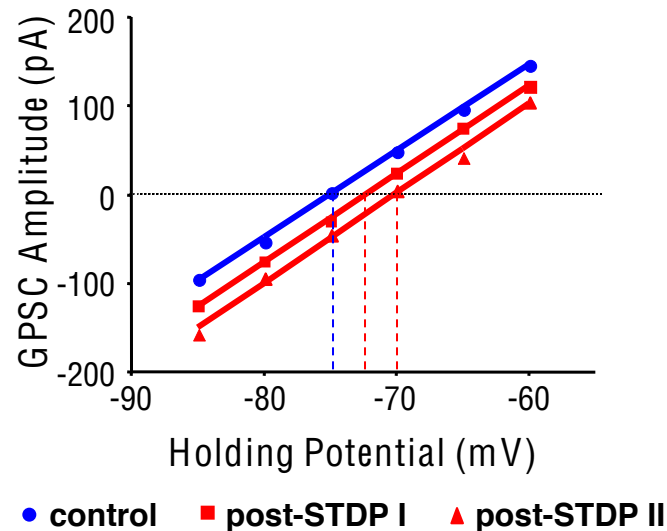
- STDP protocol: 5Hz, 30sec



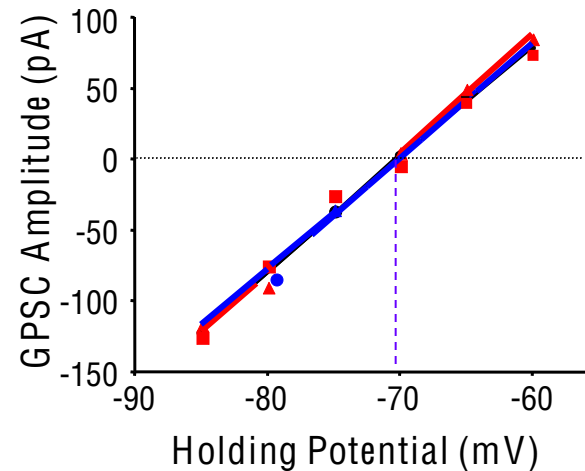
GABAergic synapses are modified by STDP



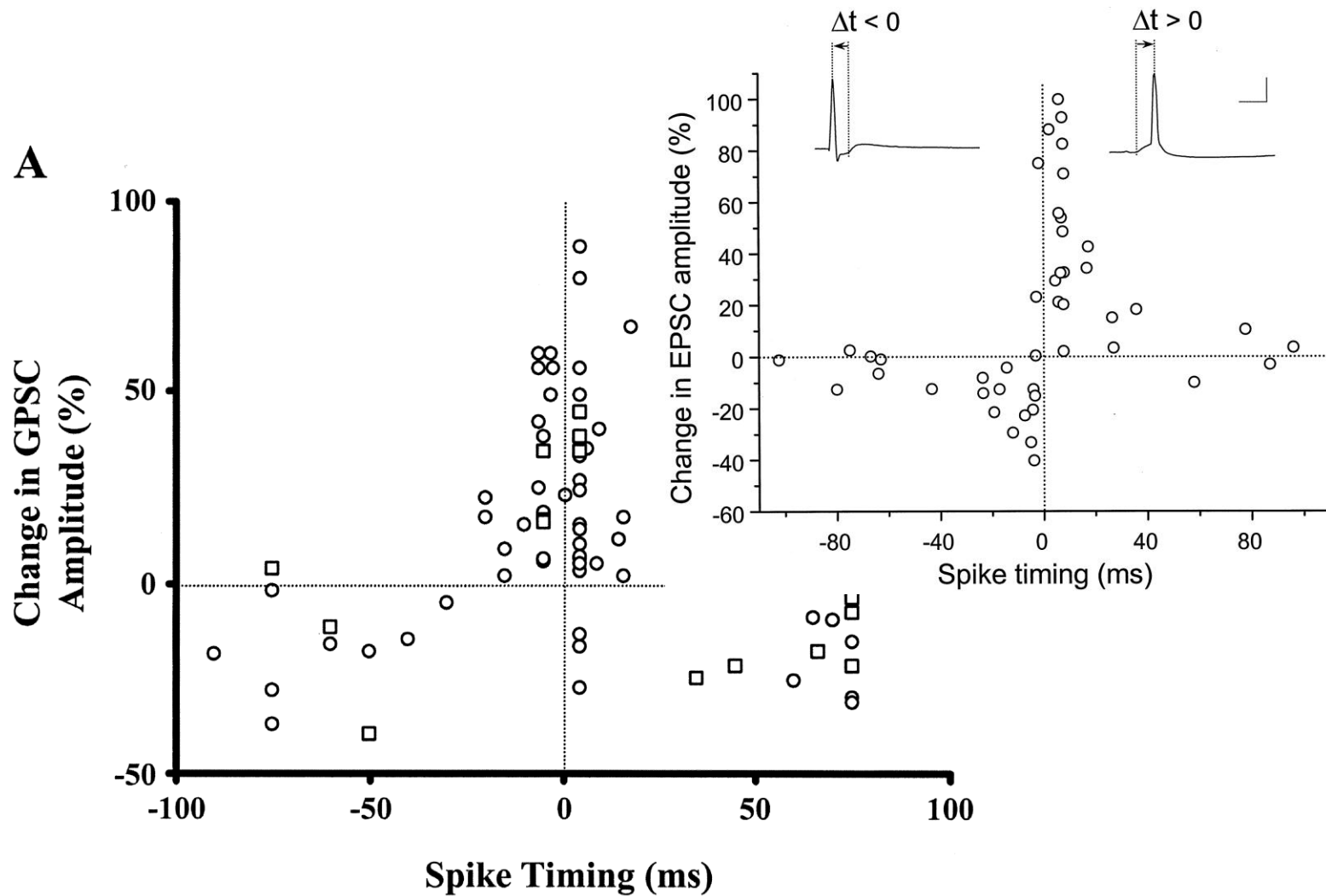
Correlated
Spike Timing +5ms



Uncorrelated
Spike Timing +75ms

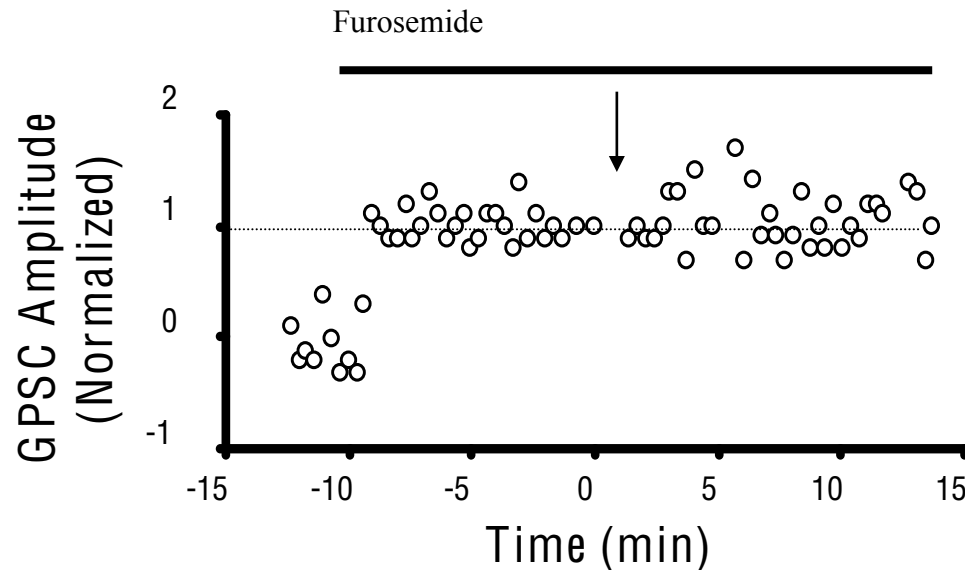


The GABAergic STDP Window is Symmetrical



Inhibitory GABAergic Synapses undergo STDP

- Correlated activity weakens inhibition through a depolarization of E_{GABA}
- The mechanism is a Ca^{2+} dependent decrease in KCC2 activity



- Is inhibitory synaptic plasticity restricted to a developmental stage?
- What mechanisms mediate inhibitory synaptic plasticity?

