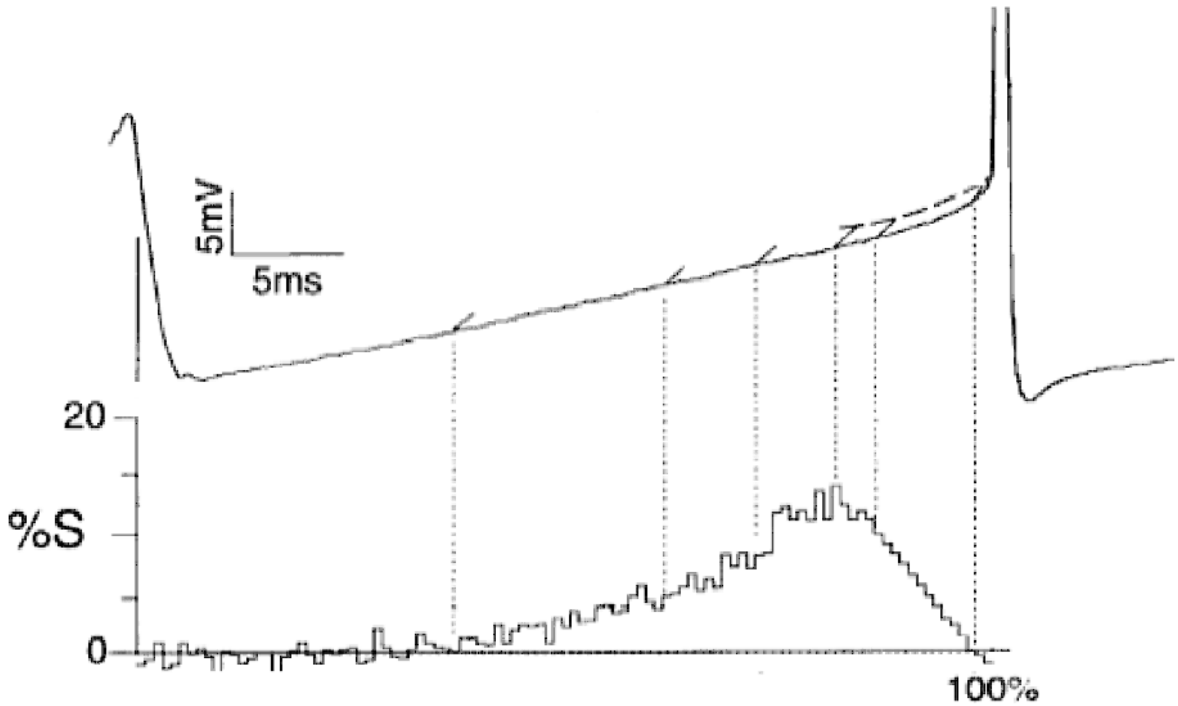
Phase Response



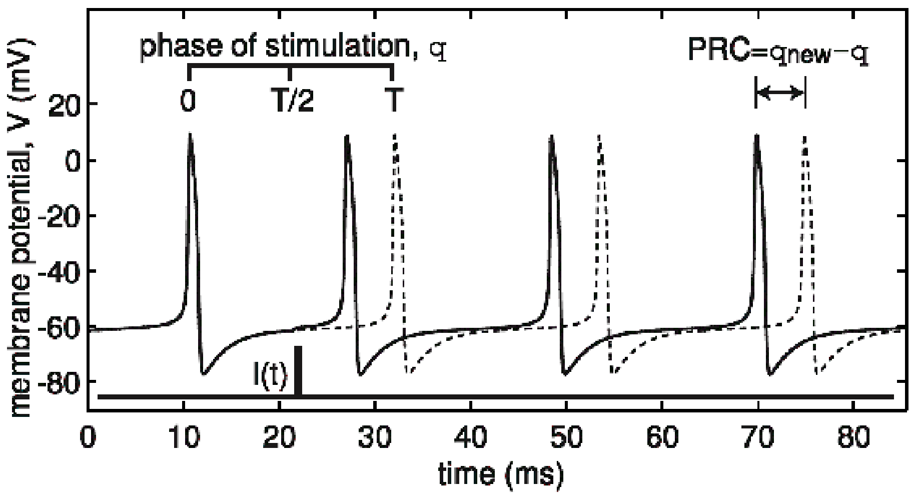
Inward current-pulses decrease a cortical neuron's period (Cat, Layer V) by up to 15% [Fetz93].

Synaptic input advances (excitatory) or delays (inhibitory) spiking

It is most effective at a particular point in the interspike interval

The phase response curve (PRC) describes this dependence

Measuring the phase-response curve (PRC)



A inward current-pulse ($I(t)$) advances the spike; dashed line shows default.

Synaptic input—a brief current-pulse in this case—is applied at various points in the interspike interval.

The amount by which the input advances (or delays) spiking is measured.

Plotting this advance (or delay) versus the time relative to the last spike—called the phase—yields the PRC.

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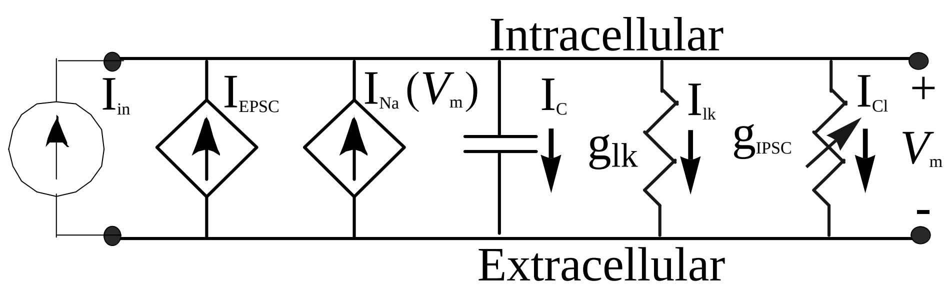
Excitation and inhibition



Positive-feedback neuron with excitatory (I_{EPSC}) and inhibitory synaptic input (g_{IPSC}).

Neurotransmitter binds to receptors, opening channels that produce an excitatory or inhibitory postsynaptic conductance or current (E/IPSC):

$$C_m \frac{dV_m}{dt} + g_{lk} V_m + g_{IPSC} V_m = I_{EPSC} + I_{Na}$$

The current flows outward when Cl^-(or K^+) channels open, resulting in inhibition, which we model as a conductance, g_{IPSC}, in parallel with g_{lk}.

The current flows inward when Na^{+}channels open, resulting in excitation, which we model as an inward current, I_{EPSC}, similar to I_{Na}.

The time-courses of both are determined by our synapse model—linear rise and exponential decay.

Excitation's rise-time and decay-constant are faster than inhibition's.

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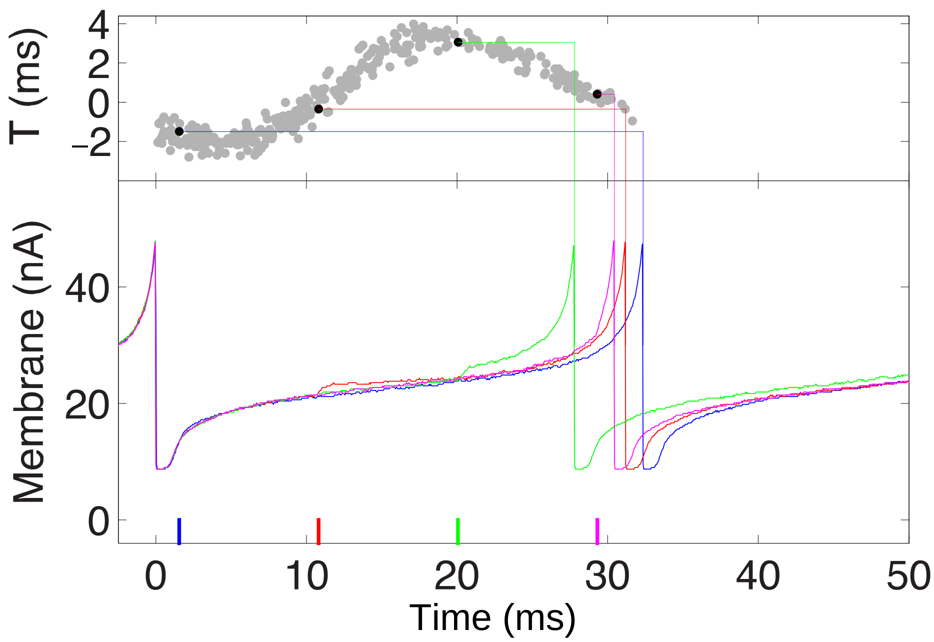
PRC for excitation



Excitation applied at various phases—around 18ms is most effective.

Excitation is most effective at 18ms (0.55 T), advancing spiking by 3.9ms (0.12 T) .

Excitation is ineffective immediately after and before spiking:

Immediately after, it is overwhelmed by the outward current that terminates a spike.

Immediately before, it is swamped by the inward current that initiates a spike.

The rise-time was 0.7ms; the decay constant was 1.7ms.

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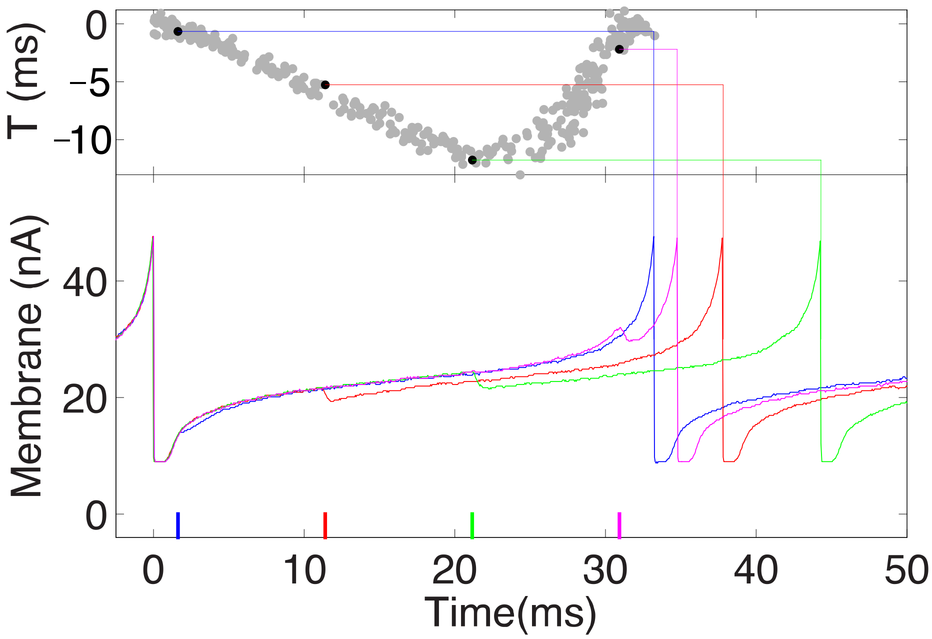
PRC for inhibition



Inhibition applied at various phases—around 22ms is most effective.

Inhibition is most effective at 22ms (0.65 T), delaying spiking by 12ms (0.36 T) .

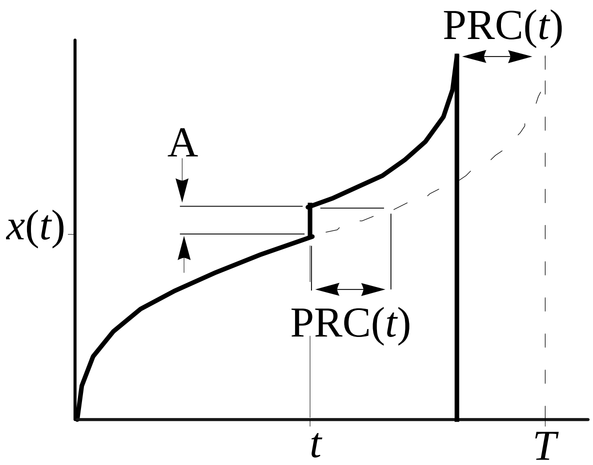
Inhibition is also ineffective immediately after and before spiking:

Immediately after, the driving force across the conductance (i.e., V_m) is small.

Immediately before, it is overwhelmed by the inward current that initiates a spike.

The rise-time was 0.4ms; the decay constant was 0.6ms.

Calculating the PRC



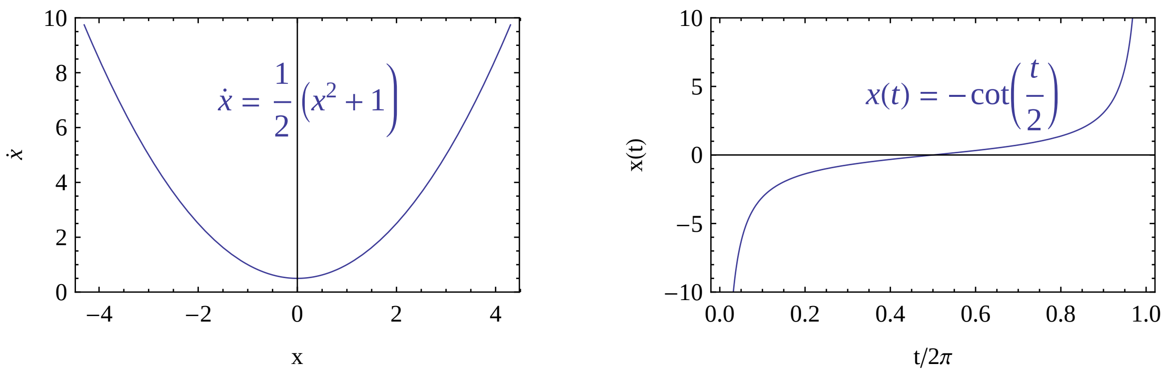
PRC(t) tells us how much a perturbation A (due to a current pulse) shifts $x(t)$.

The PRC gives the point on the membrane-voltage's old (default) trajectory that corresponds to its new (perturbed) value:

```
  x[t + PRC[t]] = x[t] + A
⟺ PRC[t] = x^-1[x[t] + A] - t
```

Thus, we must find the solution ($x(t)$) to the membrane-voltage's ODE and invert it. Not fun!

Quadratic integrate-and-fire neuron



Phase plot (left) and membrane voltage (right); inflexion point is at $x = 0$ (due to offset).

This model can be solved analytically:

```
  x[t] = -Cot[t / 2]  with  T = 2 π
⟹ PRC[t] = 2 Cot^-1[Cot[t / 2] - A] - t
```

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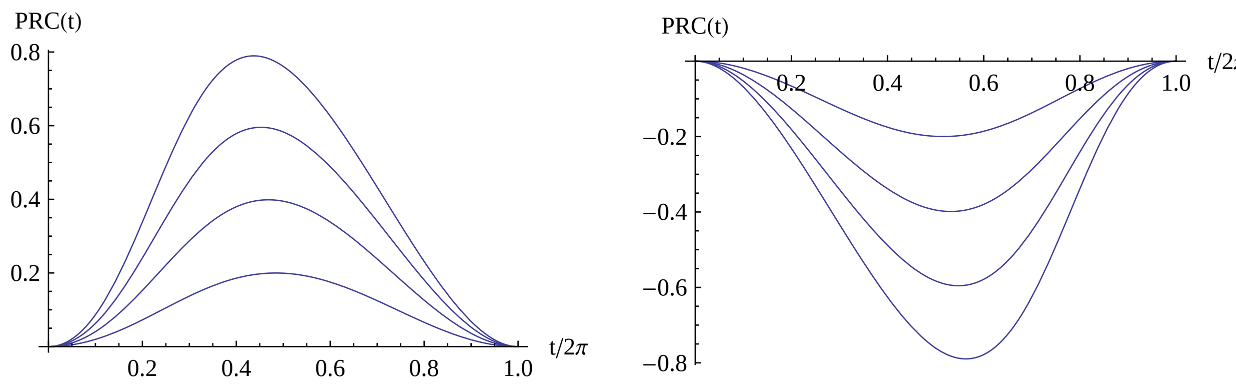
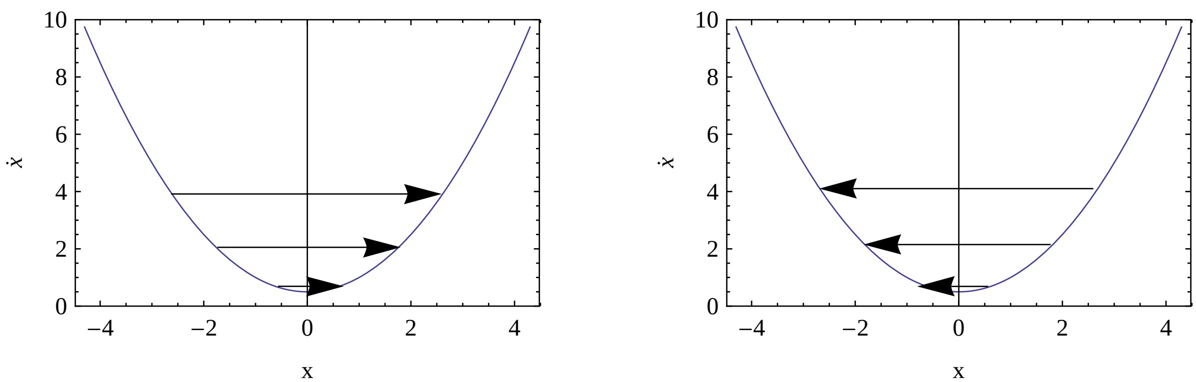
Quadratic I&F neuron's PFC



PRCs for excitation and inhibition (A = ±0.1, 0.2, 0.3, 0.4).

The PRC becomes more asymmetrical as the kick (*A*) gets larger because, to be most effective, it must take the neuron across its inflexion point, where the membrane voltage changes at its slowest rate.



Excitatory (⟶) or inhibitory (⟵) kicks are most effective when they straddles the trajectory's slowest part.

For excitation, larger kicks must happen earlier to advance the neuron past the inflexion point.

For inhibition, larger kicks must happen latter to retard the neuron past the inflexion point.

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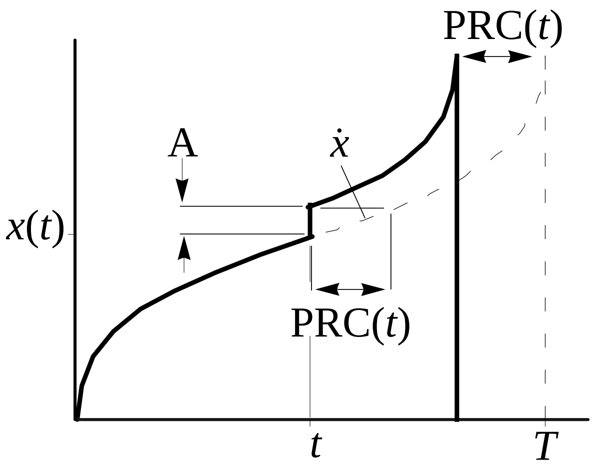
Weak coupling: A ≪ 1



For small A, linear interpolation yields a good approximation for PRC(t).

Extrapolating $x(t)$ linearly yields:

$$\dot{x}[t]\ \mathrm{PRC}[t] \approx A \Longleftrightarrow \mathrm{PRC}[t] \approx A / \dot{x}[t]$$

Makes the intuitive prediction that the kick is most effective when $\dot{x}$ is minimum—at the inflection point.

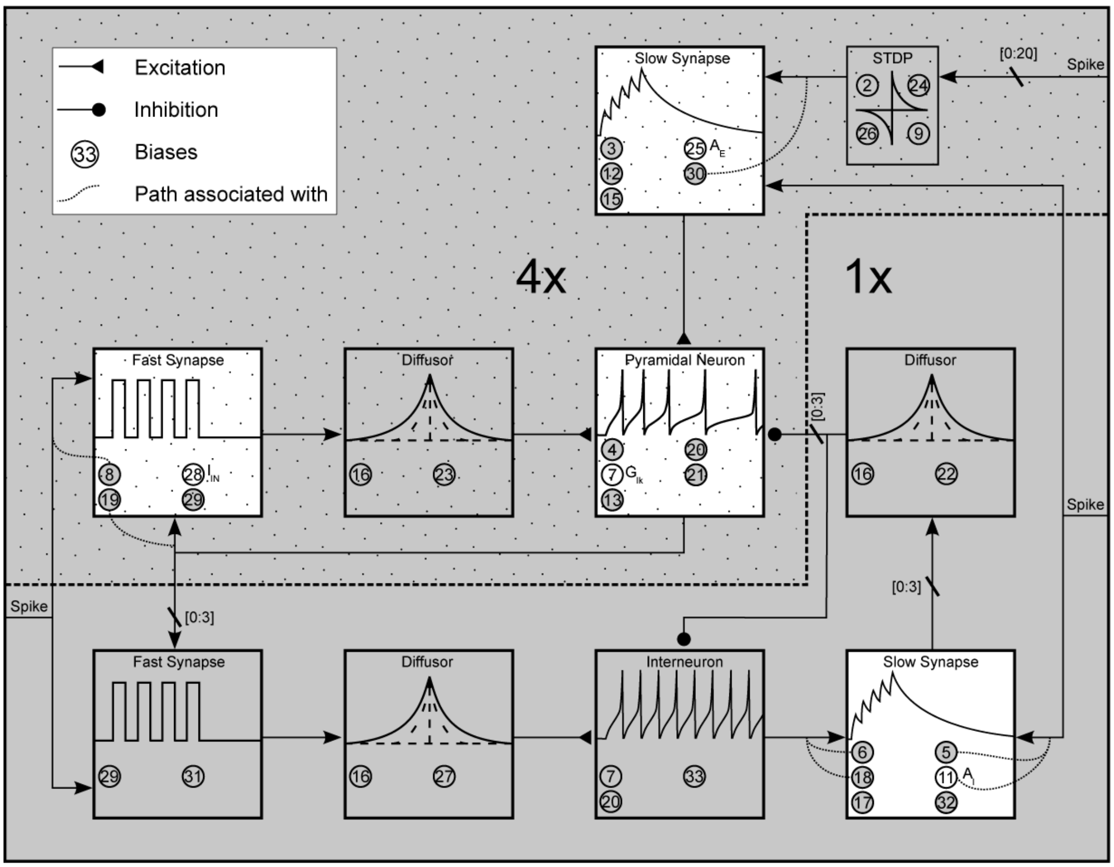
For the quadratic I&F-neuron, we get :

$$\dot{x}[t] = 1 / \mathrm{Sin}^2[t] \Longrightarrow \mathrm{PRC}[t] \approx A\ \mathrm{Sin}^2[t]$$

This matches the $A = 0.1$ curve in the previous slide.

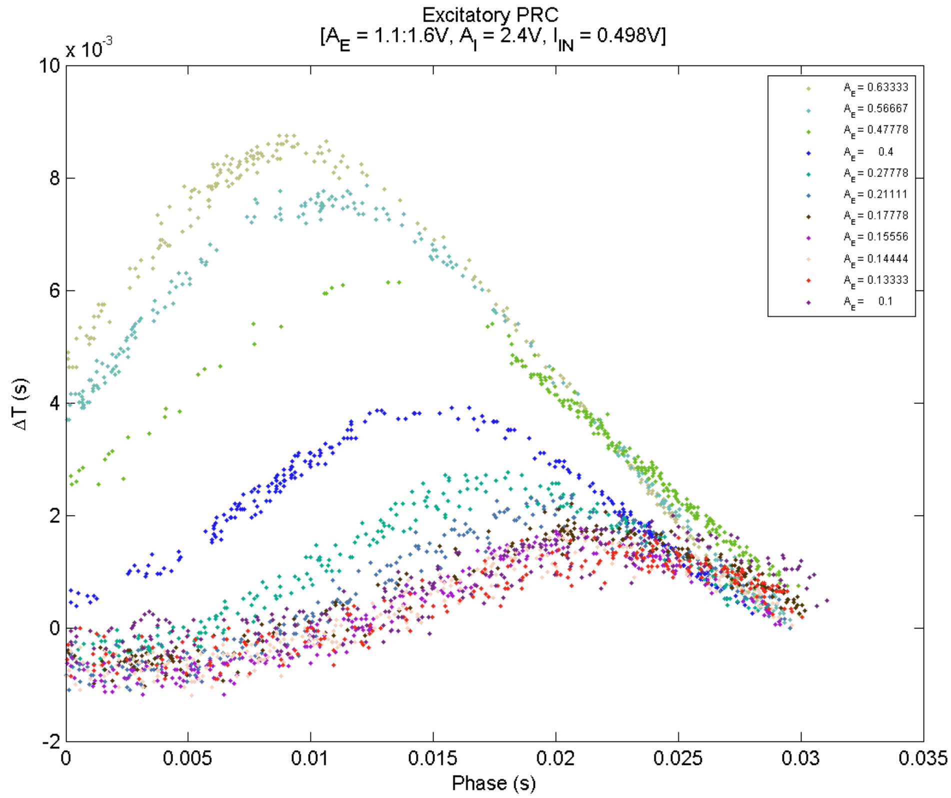
Lab4: Set-up

1	Vrefd2a	reference voltage - leave at 2.530	18	VMAGGABA	(-) increases inhibitory synapse strength (inhibitory interneuron input)
2	VQAPRE	(-) increases LTP-side of STDP curve's height	19	VQAAMPA2	(-) increases fast excitatory synapse strength pulse-width (pyramidal neuron input)
3	VLEAKDNMDA	(+) increases slow excitatory synapse rise-time	20	VLEAKREFRACT	(+) increases absolute refractory period
4	VMAGK	(-) increases m-type potassium channel strength	21	VLEAKK	(+) increases m-type potassium decay-constant (and strength)
5	VLEAKDGABA2	(+) increases inhibitory synapse rise-time (external input)	22	VRI	(+) increases spread of inhibition
6	VLEAKDGABA	(+) increases inhibitory synapse rise-time (inhibitory interneuron input)	23	VRRC	(+) increases spread of fast excitation to pyramidal neurons
7	VLEAKSOMA	(+) increases somatic leak current	24	VLEAKPOST	(+) increases LTP-side of STDP curve's decay
8	VQAAMPA	(-) increases fast excitatory synapse strength pulse-width (external input)	25	VMAGNMDA	(-) increases slow excitatory synapse strength
9	VQAPOST	(-) increases LTD-side of STDP curve's height	26	VLEAKPRE	(+) increases LTD-side of STDP curve's decay
10	VLEAKLTP	not used	27	VRE	(+) increases spread of fast excitation to interneurons
11	VMAGGABA2	(-) increases inhibitory synapse strength (external input)	28	VMAGAMPARC	(+) increases fast excitatory synapse strength to pyramidal neurons
12	VQADNMDA2	(+) increases slow excitatory synapse rise-time	29	VLEAKAMPA	(-) increases fast excitatory synapse strength pulse-width
13	VANP	(+) increases pyramidal neuron sodium threshold	30	VQANMDA	(+) increases slow excitatory synapse rise-time
14	VLEAKLTD	not used	31	VMAGAMPAINT	(+) increases fast excitatory synapse strength to interneurons
15	VLEAKNMDA	(+) increases slow excitatory synapse decay-constant (and strength)	32	VQADGABA	(+) increases inhibitory synapse rise-time
16	VG	leave at 1.250	33	VANI	(+) increases interneuron sodium threshold
17	VLEAKGABA	(+) increases inhibitory synapse decay-constant (and strength)			

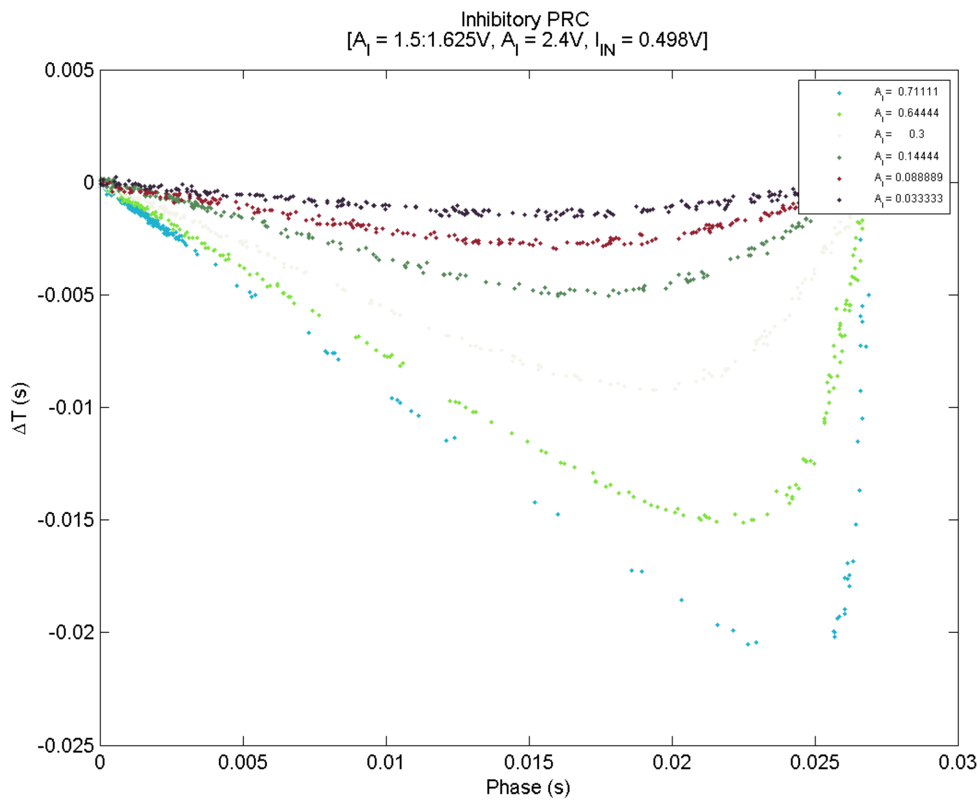


You will use the slow synapses to excite or inhibit the pyramidal neuron.

Lab4: Data



Excitatory PRC
[A_E = 1.1:1.6V, A_I = 2.4V, I_IN = 0.498V]
x 10^-3
10
8
6
4
2
0
-2
ΔT (s)
0
0.005
0.01
0.015
0.02
0.025
0.03
0.035
Phase (s)
A_E = 0.63333
A_E = 0.56667
A_E = 0.47778
A_E = 0.4
A_E = 0.27778
A_E = 0.21111
A_E = 0.17778
A_E = 0.15556
A_E = 0.14444
A_E = 0.13333
A_E = 0.1



PRCs for excitation and inhibition.

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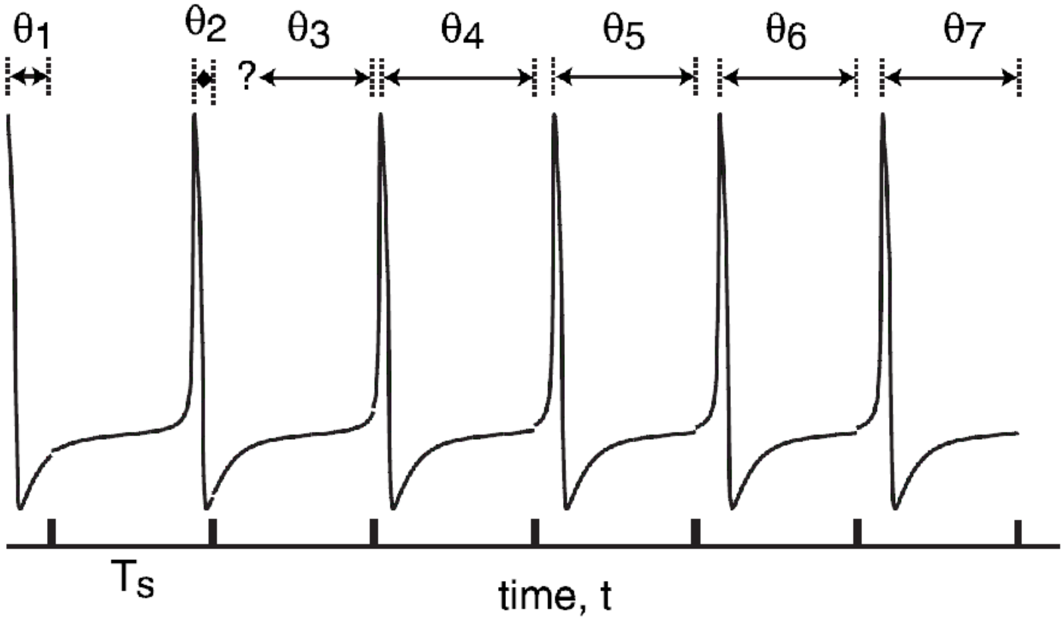
Next week: Phase-locking



Occurs when phase reset matches difference in periods