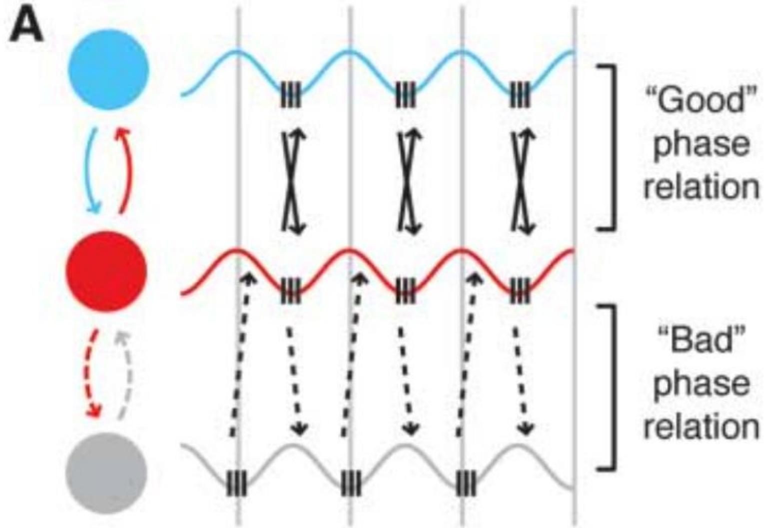
The gamma rhythms

Instructor: Mark Kramer

Today

Models of the gamma rhythms

Gamma rhythms



30-80 Hz

<u>functions</u>

- cell-assembly formation / synchronization

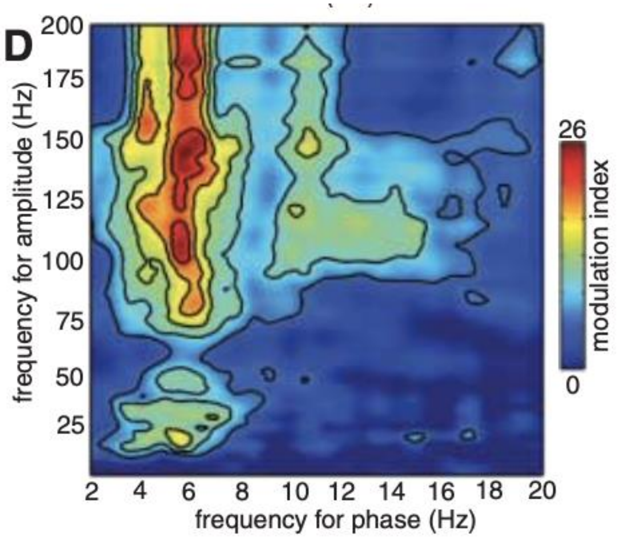
[Womelsdorf et al. "Modulation of Neuronal Interactions Through Neuronal Synchronization." Science , 2007]
[Fernández-Ruiz et al., "Gamma Rhythm Communication between Entorhinal Cortex and Dentate Gyrus Neuronal Assemblies.", Science, 2021]
[Canolty et al., "High Gamma Power Is Phase-Locked to Theta Oscillations in Human Neocortex.", Science, 2006]

- memory

[Lisman & Idiart. "Storage of 7 ± 2 Short-Term Memories in Oscillatory Subcycles." Science, 1995]
[Lundqvist et al., "Gamma and Beta Bursts Underlie Working Memory." Neuron, 2016]

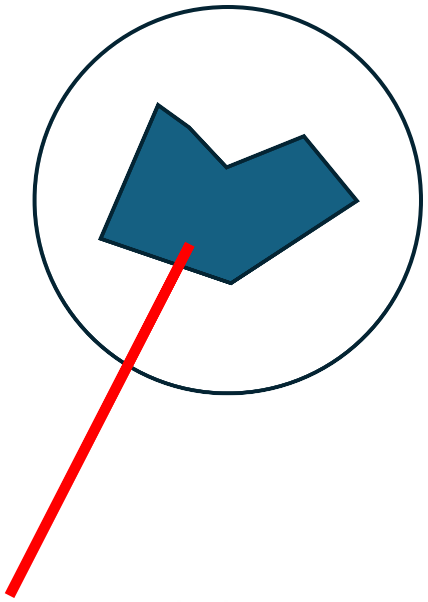
- plasticity

[Hadler et al, "Gamma Oscillation Plasticity Is Mediated via Parvalbumin Interneurons." Science Advances, 2024]



Gamma rhythms

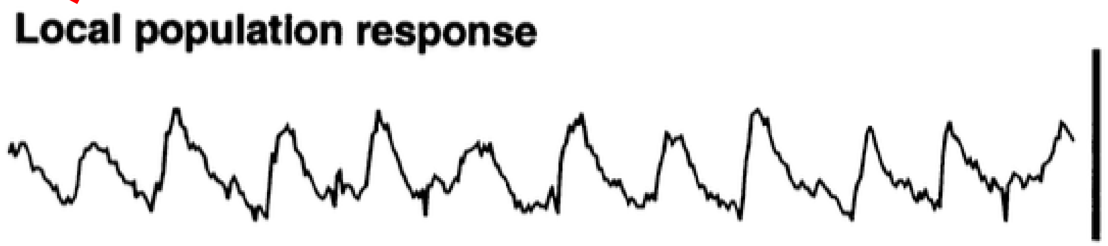
Mechanisms (via experimental models)



in vitro preparation

apply drugs (e.g., carbachol to increase excitability)

record LFP



<u>Facts</u>

- Block $GABA_A$ ➔ eliminate gamma
- Block AMPA ➔ eliminate gamma

involves ex & inh cells + synaptic interactions

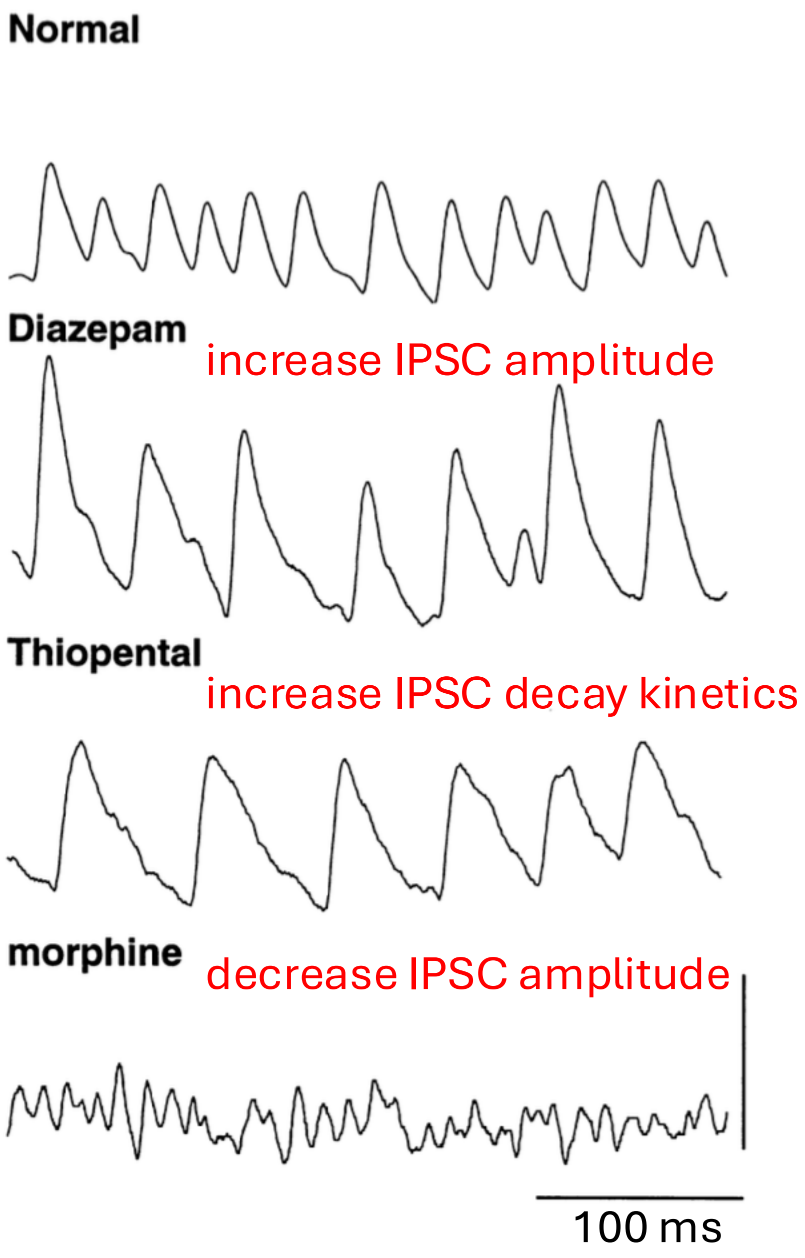
[Whittington et al., *Inhibition-Based Rhythms*, Int J Psychophysiol, 2000]

Gamma rhythms

Mechanisms (via experimental models)

<u>More Facts</u>

- rhythm frequency depends on $GABA_A$ kinetics (e.g., modulate with sedatives to alter period)
- pyramidal (ex) cells can fire <u>sparsely</u>
- basket (inh) cells fire on most cycles

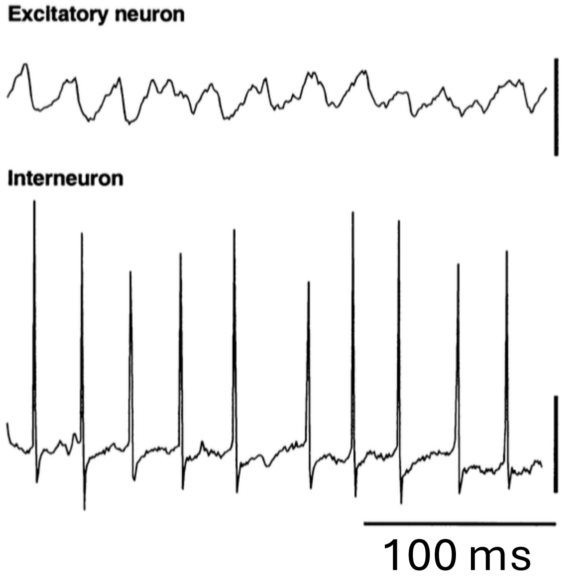


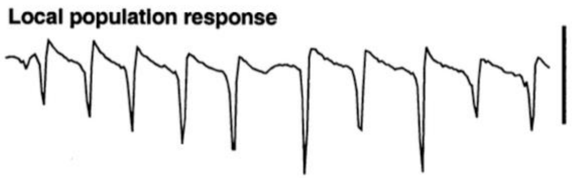
[Whittington et al., *Inhibition-Based Rhythms*, Int J Psychophysiol, 2000]

Gamma rhythms

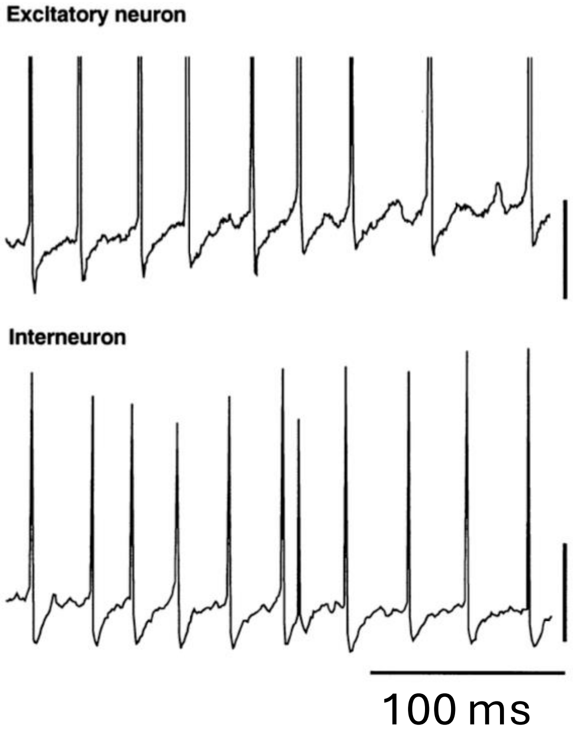
Mechanisms (via experimental models)

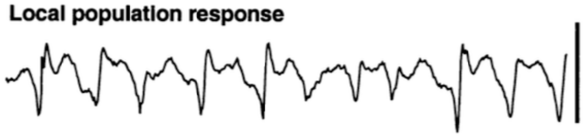
pyramidal (ex) cells don’t spike



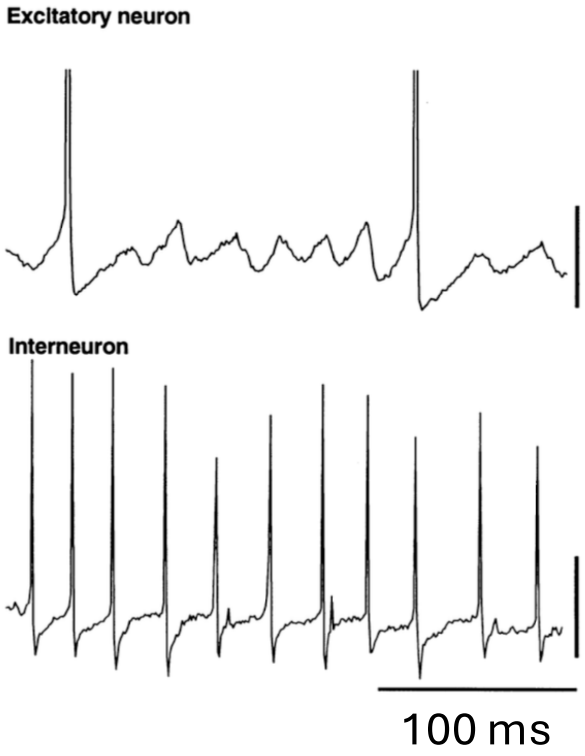


pyramidal (ex) cells always spike





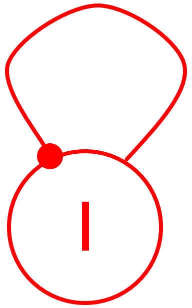
pyramidal (ex) cells sometimes spike



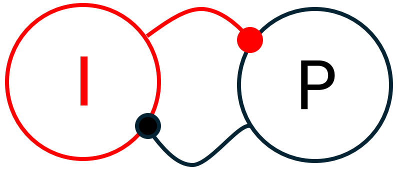
Models

Three types

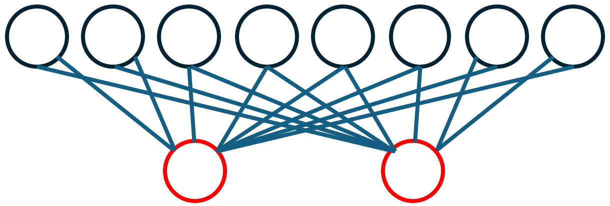
ING



PING



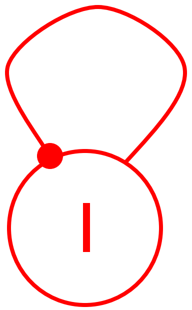
sparse
PING



ING

Interneuron **N**etwork **G**amma

ING



ING

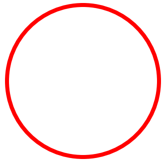
Interneuron Network Gamma

Experimental observations

(1) Excitation (driven cells)
(2) $GABA_A$ critical
(3) Altering $GABA_A$ kinetics changes frequency

Model

1 cell



Load with standard HH currents

$$\frac{dV}{dt} = I_{Na} + I_K + I_L + I_{inj}$$

To mimic (1) make I_{inj} large ➔ depolarize neuron ➔ fast spiking

ING

Interneuron Network Gamma

Experimental observations

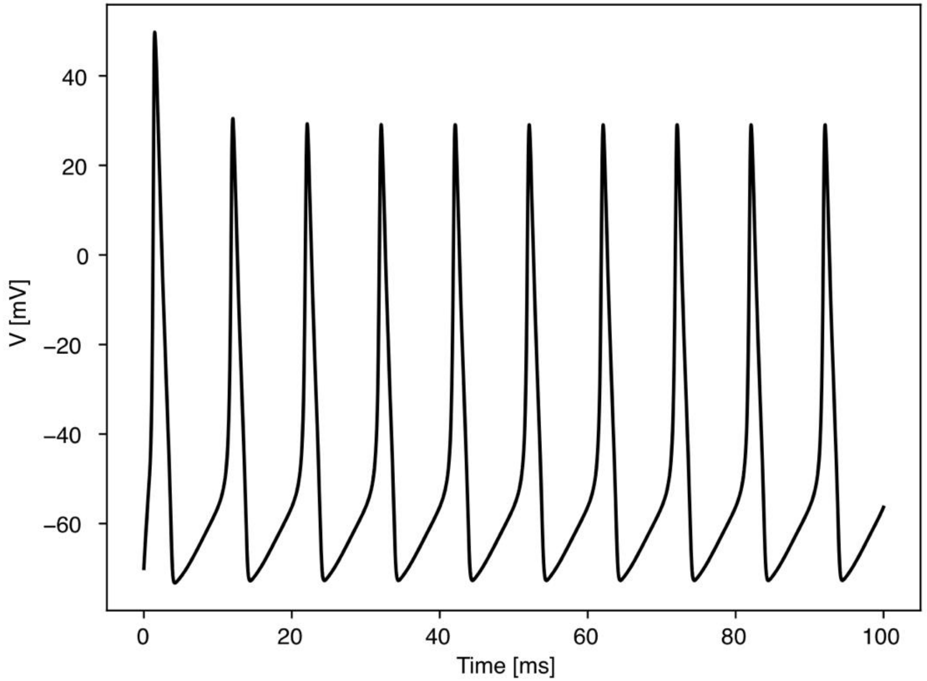
(1) Excitation (driven cells)

(2) $GABA_A$ critical

(3) Altering $GABA_A$ kinetics changes frequency

To mimic (1) make I_{inj} large ➔ depolarize neuron ➔ fast spiking

Ex. $I_{inj} = 30$



Q. What sets the timescale of spiking?

A. Dynamics of intrinsic currents (Na, K)

ING

Interneuron Network Gamma

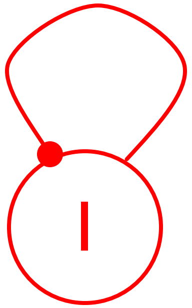
Experimental observations

(1) Excitation (driven cells)

(2) GABA_A critical

(3) Altering GABA_A kinetics changes frequency

To mimic (2) add an inhibitory synapse



autapse (presynaptic neuron = postsynaptic neuron)

Q. Realistic?

Then

$$\frac{dV}{dt} = I_{Na} + I_K + I_L + I_{inj} + \boxed{I_{synapse}}$$

ING

Interneuron Network Gamma

$$\frac{dV}{dt} = I_{Na} + I_K + I_L + I_{inj} + \boxed{I_{synapse}}$$

Synaptic current

$$I_{synapse} = g_I \, s_I \, (E_I - V)$$

maximal conductance

inh. synapse gate

equilibrium voltage for inh. synapse (-80 mV)

neuron voltage

Experimental observations

(1) Excitation (driven cells)

(2) $GABA_A$ critical

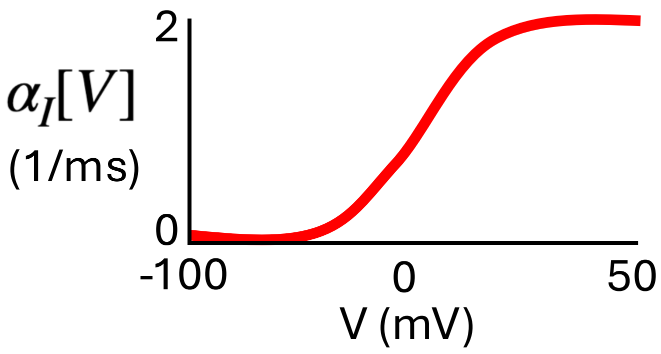
(3) Altering $GABA_A$ kinetics changes frequency

Synaptic gate dynamics

$$\frac{ds_I}{dt} = \alpha_I[V](1 - s_I) - \beta_I[V]s_I$$

forward rate fxn

backward rate fxn



$$\beta_I[V] = \beta_I = \frac{1}{\tau_d}$$

constant

decay time $\approx$ 10 ms

ING

Experimental observations

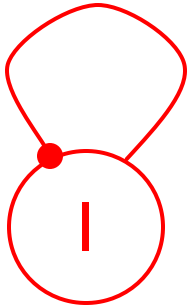
(1) Excitation (driven cells)

(2) $GABA_A$ critical

(3) Altering $GABA_A$ kinetics changes frequency

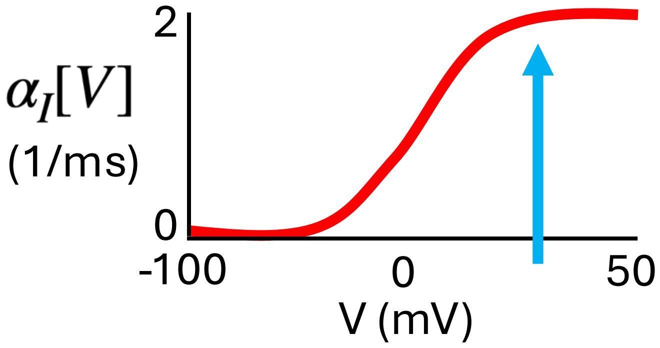
Interneuron Network Gamma

$$\frac{ds_I}{dt} = \alpha_I[V](1 - s_I) - \beta_I[V]s_I$$



Q. What happens?

- neuron spikes (V > 0)
- $\alpha_I[V] \rightarrow 2$
- $s_I \rightarrow 1$ (open)
- Chlorine (Cl^-) flows in → hyperpolarize cell (push to -80 mV)



Note: $[Cl^-]_{out} >> [Cl^-]_{in}$

ING

Interneuron Network Gamma

<u>Experimental observations</u>

(1) Excitation (driven cells)

(2) GABA_A critical

(3) Altering GABA_A kinetics changes frequency

<u>Model</u>

$$C\,\frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_{\text{K}}n^4(V - V_{\text{K}}) - \bar{g}_{\text{Na}}m^3h(V - V_{\text{Na}}) - \bar{g}_{\text{L}}(V - V_{\text{L}}) \boxed{-g_I\, s_I\,(V - E_I)}$$

$$\frac{dn}{dt} = -\frac{n - n_\infty(V)}{\tau_n(V)}$$

$$\frac{dm}{dt} = -\frac{m - m_\infty(V)}{\tau_m(V)}$$

$$\frac{dh}{dt} = -\frac{h - h_\infty(V)}{\tau_h(V)}$$

$$\boxed{\frac{ds_I}{dt} = \alpha_I[V](1 - s_I) - \beta_I[V]s_I}$$

5 variables

5 differential equations

ING

Interneuron Network Gamma

Experimental observations

(1) Excitation (driven cells)

(2) $GABA_A$ critical

(3) Altering $GABA_A$ kinetics changes frequency

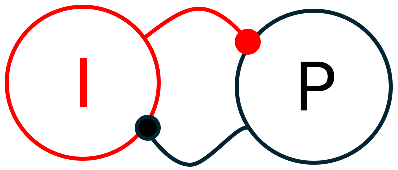
Q. How does it work?

Python

PING

START ZOOM

Pyramidal **I**nterneuron **N**etwork **G**amma

PING 

PING

Using ING

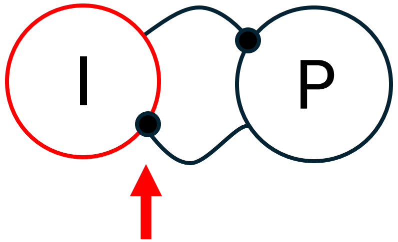
<u>Experimental observations</u>

- ✅ (1) Excitation (driven cells)
- ✅ (2) $GABA_A$ critical
- ✅ (3) Altering $GABA_A$ kinetics changes frequency
- ❌ (4) AMPA critical

New model

+ include excitatory (pyramidal) cell

PING



include AMPA synapse

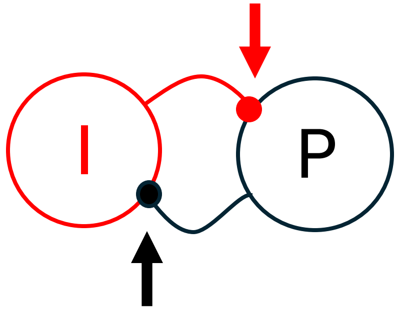
<u>Idea</u>: cells collaborate to produce gamma

PING

Connect cells with synapses

when I-cell spikes → hyperpolarize P-cell
inhibitory (GABA) synapse

PING

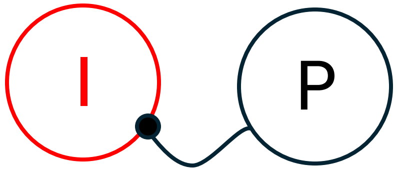


excitatory (AMPA) synapse
when P-cell spikes → depolarize I-cell

Build the model: HH + synapses

PING

Include synapses



$$\frac{dV_I}{dt} = I_{Na} + I_K + I_L + I_{inj} + \boxed{I_{synapse\,P\to I}}$$

I-cell voltage

Synaptic current

$$I_{synapse\,P\to I} = g_P\, s_P\, (E_P - V_I)$$

maximal conductance

ex. synapse gate

equilibrium voltage for ex. synapse (0 mV)

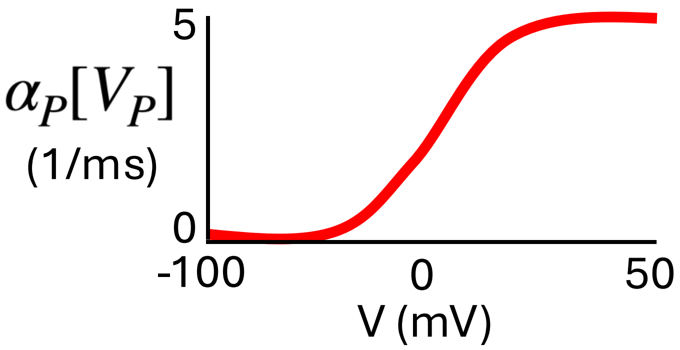
I-cell voltage **post-synaptic** cell

Synaptic gate dynamics

$$\frac{ds_P}{dt} = \alpha_P[V_P](1 - s_P) - \beta_P[V_P]s_P$$

forward rate fxn, **pre-synaptic** V

backward rate fxn



$$\beta_P[V_P] = \beta_P = \frac{1}{\tau_d}$$

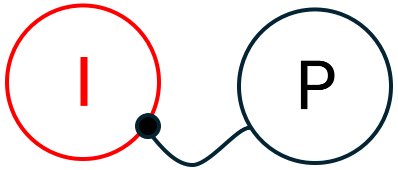
constant

decay time $\approx$ 2 ms

Note: faster than inh. synapse

PING

Include synapses



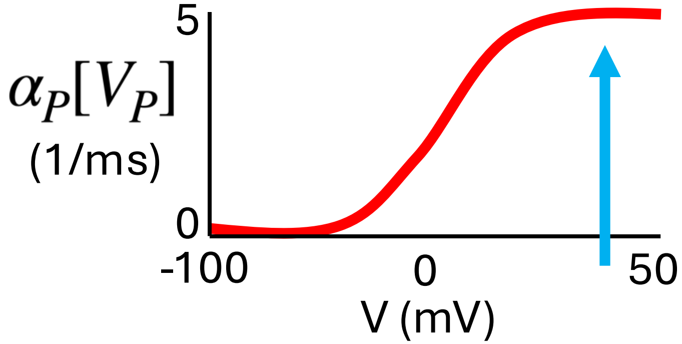
$$\frac{dV_I}{dt} = I_{Na} + I_K + I_L + I_{inj} + I_{synapse\, P \to I}$$

$$\frac{ds_P}{dt} = \alpha_P[V_P](1 - s_P) - \beta_P[V_P]s_P$$

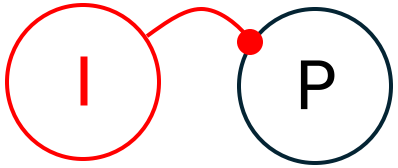
Q. What happens?

- P-cell spikes (V_P > 0)
- $\alpha_P[V_P]$ → 5
- s_P → 1 (open)
- charge (Na^+) flows in → depolarize I-cell (push to 0 mV)

<u>Note</u>: $[Na^+]_{out} >> [Na^+]_{in}$



PING

Include synapses 

$$\frac{dV_P}{dt} = I_{Na} + I_K + I_L + I_{inj} + \boxed{I_{synapse\, I\to P}}$$

P-cell voltage

Synaptic current

$$I_{synapse\, I\to P} = g_I\, s_I\,(E_I - V_P)$$

maximal conductance

inh. synapse gate

equilibrium voltage for inh. synapse (-80 mV)

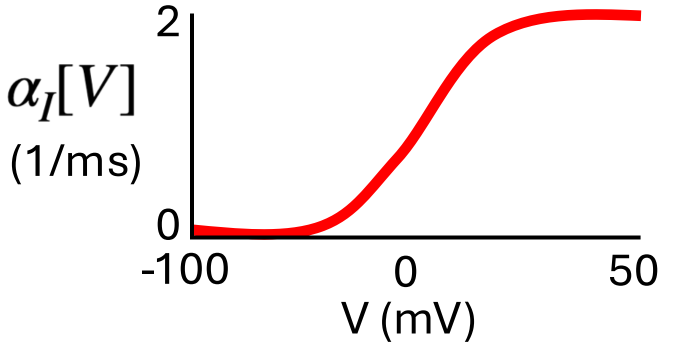
P-cell voltage **post-synaptic** cell

Synaptic gate dynamics

$$\frac{ds_I}{dt} = \alpha_I[V_I](1 - s_I) - \beta_I[V_I]s_I$$

forward rate fxn, **pre-synaptic** V

backward rate fxn



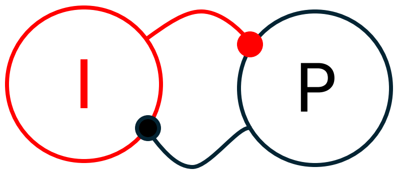
$$\beta_I[V] = \beta_I = \frac{1}{\tau_d}$$

constant

decay time $\approx$ 10 ms

PING

Put it all together



10 variables

$$\frac{dV_P}{dt} = I_{Na} + I_K + I_\ell + I_{inj,P} + \overbrace{g_I s_I (E_I - V_P)}^{\text{inh. synaptic input}}$$

$$\frac{dm_P}{dt} = \quad \frac{dh_P}{dt} = \quad \frac{dn_P}{dt} = \quad \text{HH}$$

$$\frac{ds_P}{dt} = \alpha_P[V_P](1-s_P) - \beta_P[V_P]\, s_P \qquad \text{(ex. gate dynamics).}$$

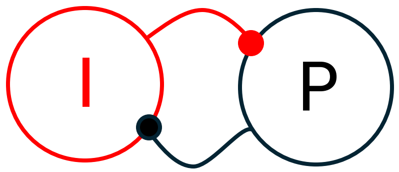
$$\frac{dV_I}{dt} = I_{Na} + I_K + I_\ell + I_{inj,I} + \underbrace{g_P s_P (E_P - V_I)}_{\text{ex. synaptic input}}$$

$$\frac{dm_I}{dt} = \quad \frac{dh_I}{dt} = \quad \frac{dn_I}{dt} = \quad \text{HH}$$

$$\frac{ds_I}{dt} = \alpha_I[V_I](1-s_I) - \beta_I[V_I]\, s_I \qquad \text{(inh. gate dynamics)}$$

PING

Q. How does this generate a gamma rhythm?



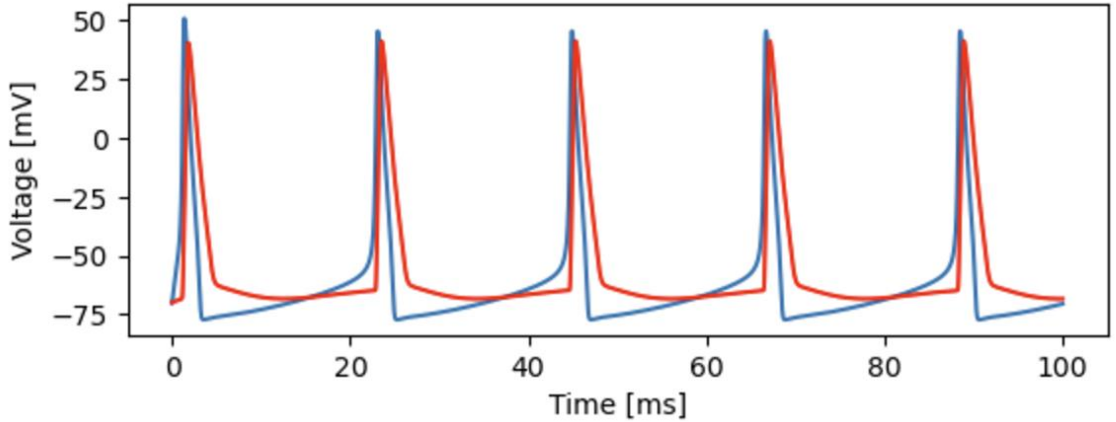
Assume P-cell has $I_{inj,P}$ big enough to spike repeatedly in isolation

t=0 P-cell spikes → excitation to I-cell → I-cell spikes

t≈0 I-cell spikes → inhibition to P-cell

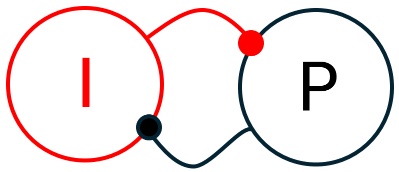
t=25 P-cell recovers → P-cell spikes

Repeat …



PING

Q. Consistent with experimental observations?



<u>Experimental observations</u>

? (1) Excitation (driven cells)

? (2) $\mathrm{GABA_A}$ critical

? (3) Altering $\mathrm{GABA_A}$ kinetics changes frequency

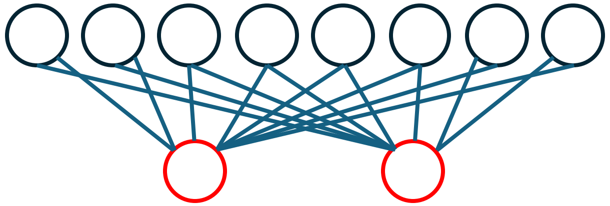
? (4) AMPA critical

Python *Homework*

Sparse PING

Sparse Pyramidal **I**nterneuron **N**etwork **G**amma

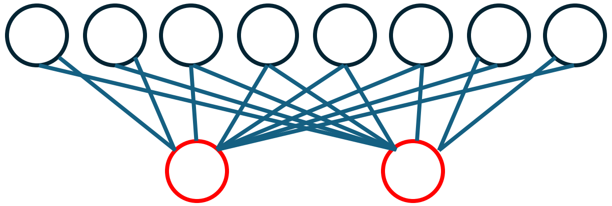
sparse
PING



Sparse PING

Idea: update the PING model to include a <u>population</u> of P&I cells.

<u>**Ex.**</u> 80 P cells & 20 I cells



Each includes HH equations

P1

$$C\frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}$$
$$\frac{dn}{dt} = -\frac{n - n_\infty(V}{\tau_n(V)}$$
$$\frac{dm}{dt} = -\frac{m - m_\infty(}{\tau_m(V)}$$
$$\frac{dh}{dt} = -\frac{h - h_\infty(V}{\tau_h(V)}$$

P2

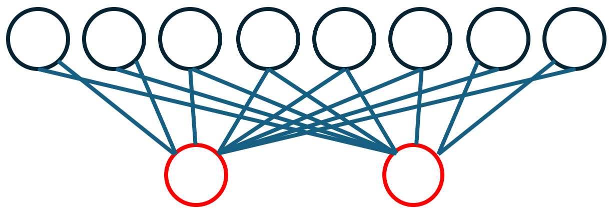
$$C\frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_{\text{K}}$$
$$\frac{dn}{dt} = -\frac{n - n_\infty(V)}{\tau_n(V)}$$
$$\frac{dm}{dt} = -\frac{m - m_\infty(V}{\tau_m(V)}$$
$$\frac{dh}{dt} = -\frac{h - h_\infty(V)}{\tau_h(V)}$$

P3

$$C\frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_{\text{K}} n^4 (V - V_{\text{K}}) - \bar{g}_{\text{Na}} m^3 h (V - V_{\text{Na}}) - \bar{g}_{\text{L}} (V - V_{\text{L}})$$
$$\frac{dn}{dt} = -\frac{n - n_\infty(V)}{\tau_n(V)}$$
$$\frac{dm}{dt} = -\frac{m - m_\infty(V)}{\tau_m(V)}$$
$$\frac{dh}{dt} = -\frac{h - h_\infty(V)}{\tau_h(V)}$$

400 differential equations

Sparse PING



Connect with synapses

Each P → all I (with ex. synapses)
Each I → all P (with inh. synapses)

Then (for P1)

$$C\frac{dV}{dt} = I_{\mathrm{input}}(t) - \bar{g}_{\mathrm{K}} n^4 (V - V_{\mathrm{K}}) - \bar{g}_{\mathrm{Na}} m^3 h (V - V_{\mathrm{Na}}) - \bar{g}_{\mathrm{L}} (V - V_{\mathrm{L}}) \boxed{+ I_{syn\ I1\to P1} + I_{syn\ I2\to P1} + \ \ldots}$$

many terms

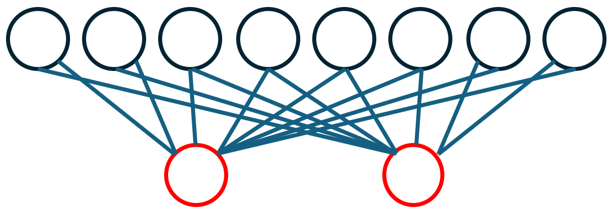
$$\frac{dn}{dt} = -\frac{n - n_\infty(V)}{\tau_n(V)}$$

$$\frac{dm}{dt} = -\frac{m - m_\infty(V)}{\tau_m(V)}$$

$$\frac{dh}{dt} = -\frac{h - h_\infty(V)}{\tau_h(V)}$$

$$\boxed{\frac{ds_{I1}}{dt} = \ldots, \frac{ds_{I2}}{dt} = \ldots, \frac{ds_{I3}}{dt} = \ldots}$$

Sparse PING

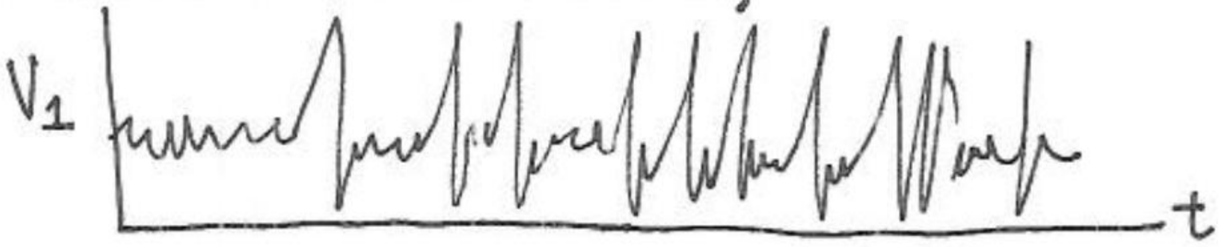


Q. How will the model work?

<u>**Idea**</u>:

- Give P cells enough depolarizing input to spike at high rate in isolation.
- Include noise in dynamics.

Then, for some P-cell. in isolation,

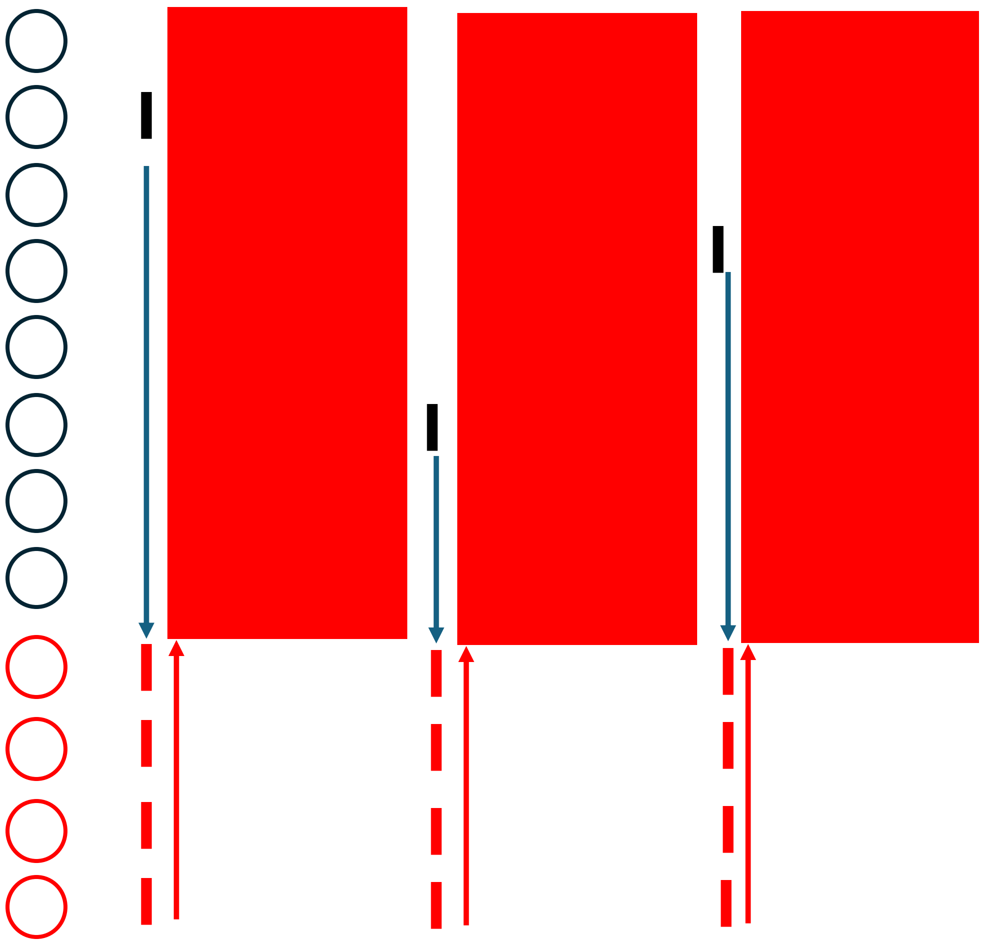


P-cell spikes.

Time between spikes varies due to noise.

- Make synapses strong

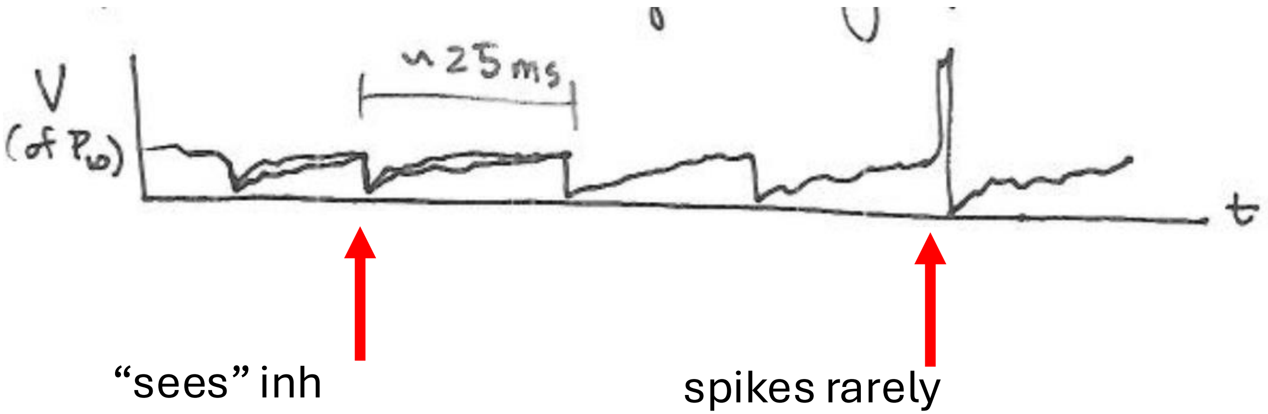
Sparse PING



inh window
depends on decay time
of inh. synapse

<u>Note</u>: a different P-cell can spike on each cycle

Plot V for a P-cell



Each P-cell fires sparsely ... "sparse PING"

Match experimental observation

<u>Cost</u>: more complexity.