

The gamma rhythms

Instructor: Mark Kramer

Today

Models of the gamma rhythms

Gamma rhythms

30-80 Hz

functions

- 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]

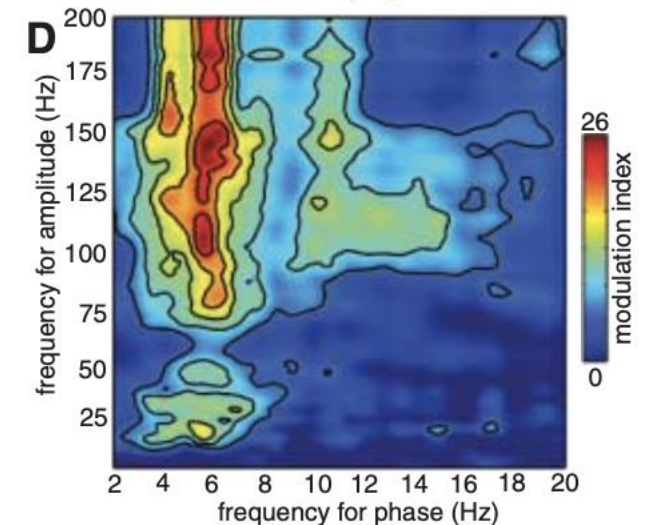
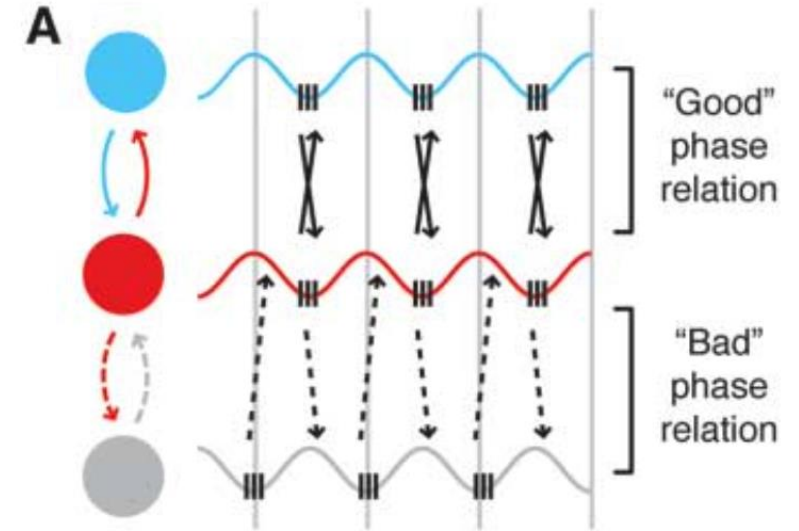
- memory

[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]

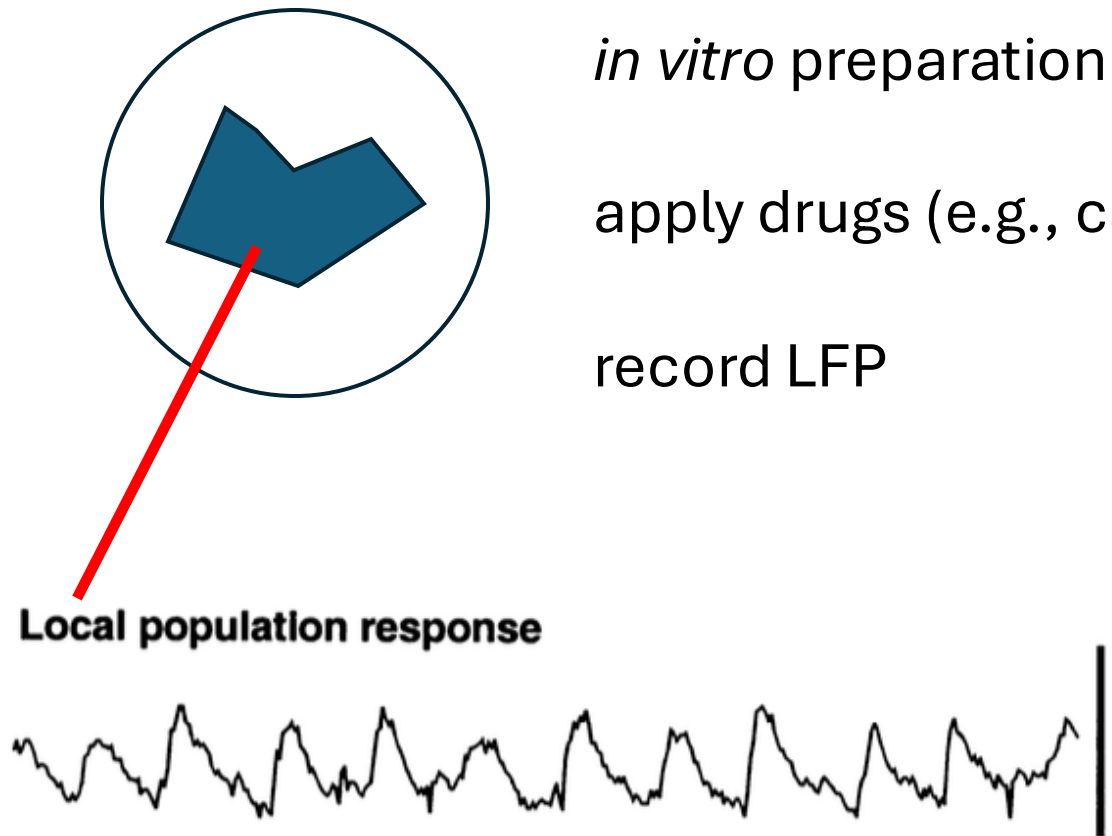
- plasticity

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



Gamma rhythms

Mechanisms (via experimental models)



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

Facts

- Block GABA_A → eliminate gamma
- Block AMPA → eliminate gamma

involves ex & inh cells + synaptic interactions

Gamma rhythms

Mechanisms (via experimental models)

More Facts

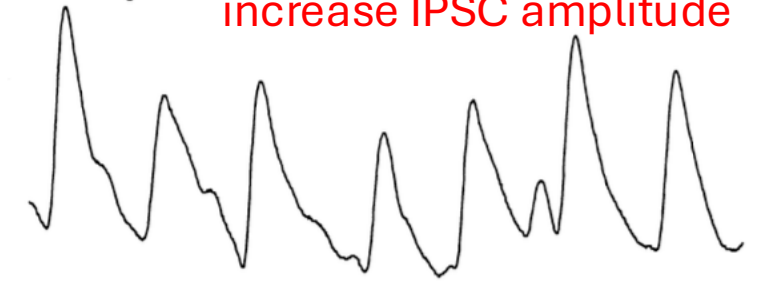
- rhythm frequency depends on GABA_A kinetics (e.g., modulate with sedatives to alter period)
- pyramidal (ex) cells can fire sparsely
- basket (inh) cells fire on most cycles

Normal



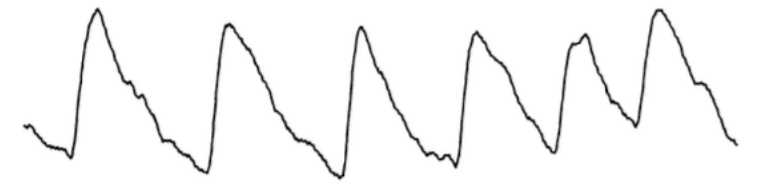
Diazepam

increase IPSC amplitude



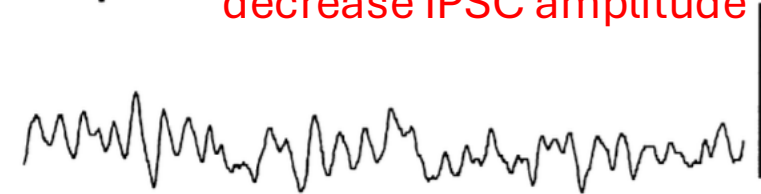
Thiopental

increase IPSC decay kinetics



morphine

decrease IPSC amplitude



100 ms

Gamma rhythms

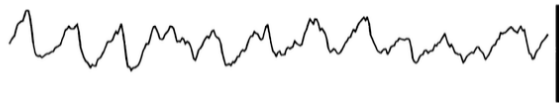
Mechanisms (via experimental models)

Local population response

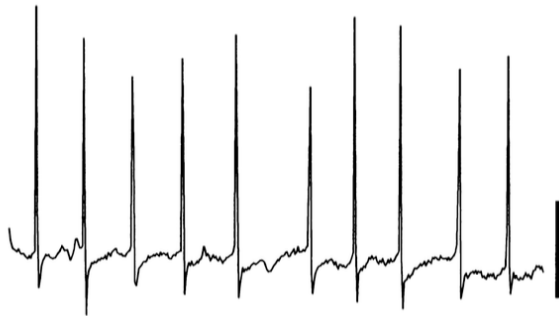


pyramidal (ex) cells don't spike

Excitatory neuron

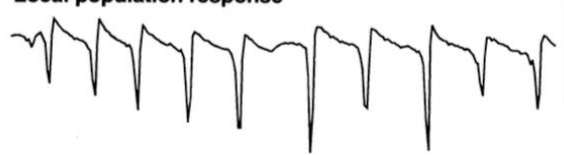


Interneuron



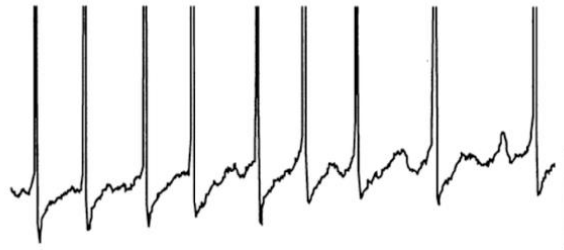
100 ms

Local population response

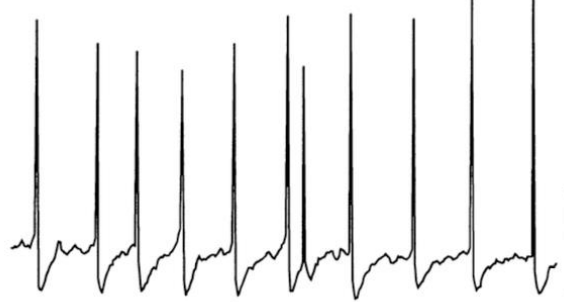


pyramidal (ex) cells always spike

Excitatory neuron



Interneuron



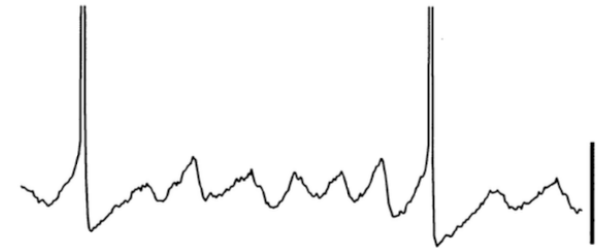
100 ms

Local population response

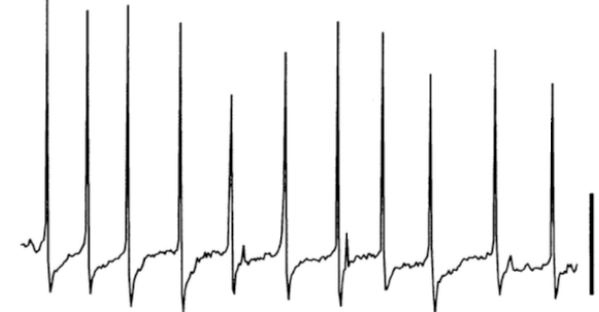


pyramidal (ex) cells sometimes spike

Excitatory neuron



Interneuron

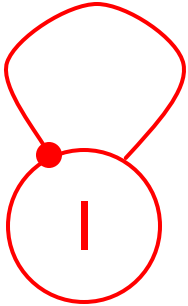


100 ms

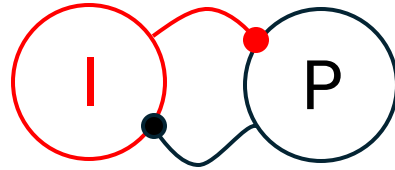
Models

Three types

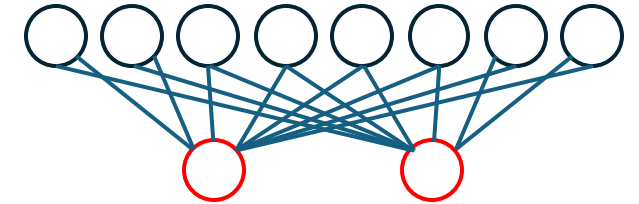
ING



PING



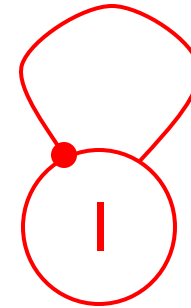
sparse
PING



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

ING



ING

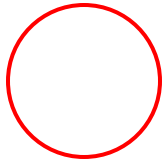
Interneuron Network Gamma

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

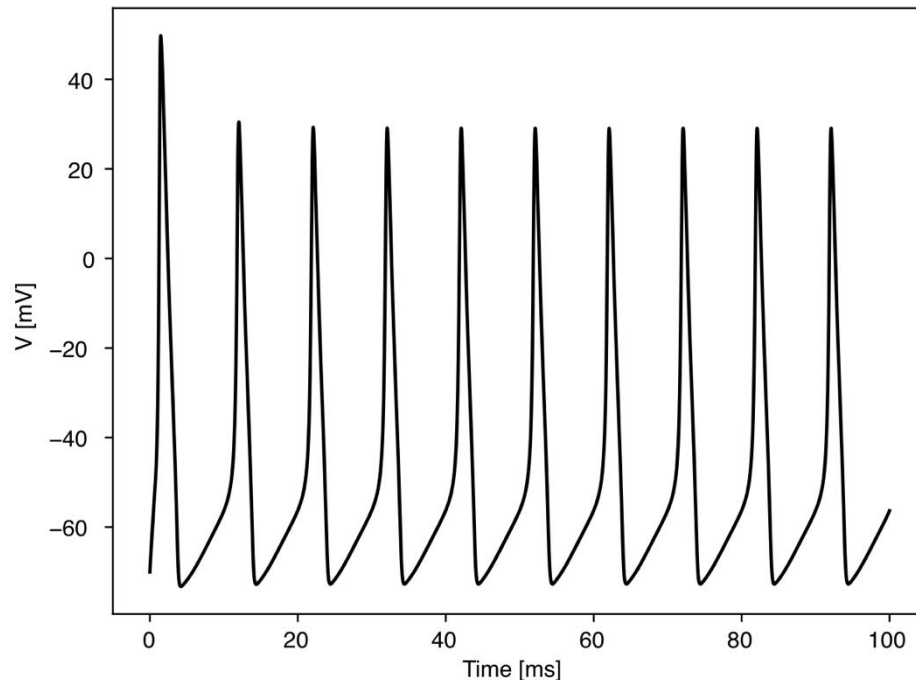
(1) Excitation (driven cells)

(2) $GABA_A$ critical

(3) Altering $GABA_A$ kinetics changes frequency

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

Ex. $I_{inj} = 30$



Q. What sets the timescale of spiking?

A. Dynamics of intrinsic currents (Na, K)

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Interneuron Network Gamma

Experimental observations

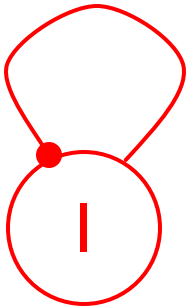
(1) Excitation (driven cells)

(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

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

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Interneuron Network Gamma

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

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

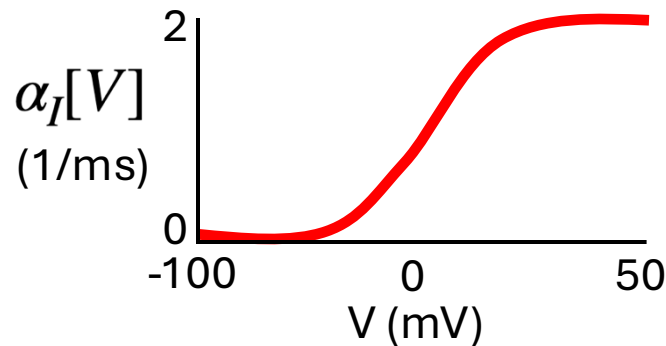
(3) Altering GABA_A kinetics changes frequency

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 ≈ 10 ms

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Interneuron Network Gamma

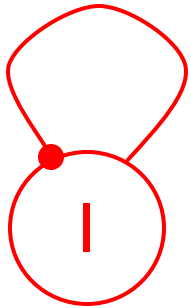
Experimental observations

(1) Excitation (driven cells)

(2) GABA_A critical

(3) Altering GABA_A kinetics changes frequency

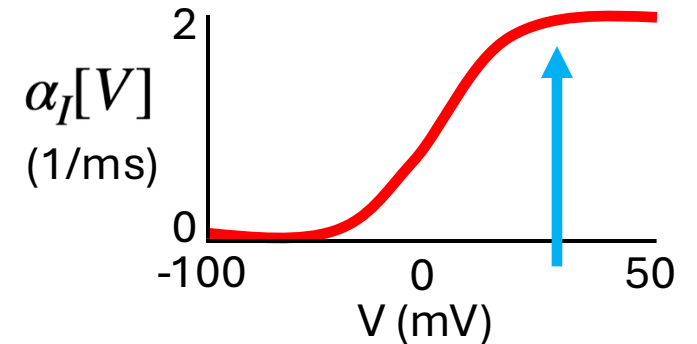
$$\frac{ds_I}{dt} = \alpha_I[V](1 - s_I) - \beta_I[V]s_I$$



Q. What happens?

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

Note: $[\text{Cl}^-]_{\text{out}} \gg [\text{Cl}^-]_{\text{in}}$



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Interneuron Network Gamma

Experimental observations

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

Model

$$C \frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_K n^4 (V - V_K) - \bar{g}_{\text{Na}} m^3 h (V - V_{\text{Na}}) - \bar{g}_L (V - V_L) - g_I s_I (V - E_I)$$

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

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

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

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

5 variables

5 differential equations

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Interneuron Network Gamma

Experimental observations

(1) Excitation (driven cells)

(2) GABA_A critical

(3) Altering GABA_A kinetics changes frequency

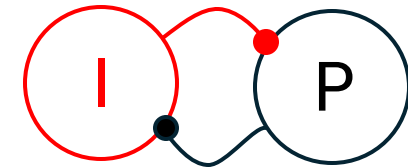
Q. How does it work?

Python

PING

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

PING



PING

Using ING

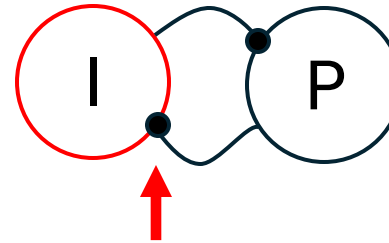
Experimental observations

- ✓ (1) Excitation (driven cells)
- ✓ (2) GABA_A critical
- ✓ (3) Altering GABA_A kinetics changes frequency
- ✗ (4) AMPA critical

New model

+ include excitatory (pyramidal) cell

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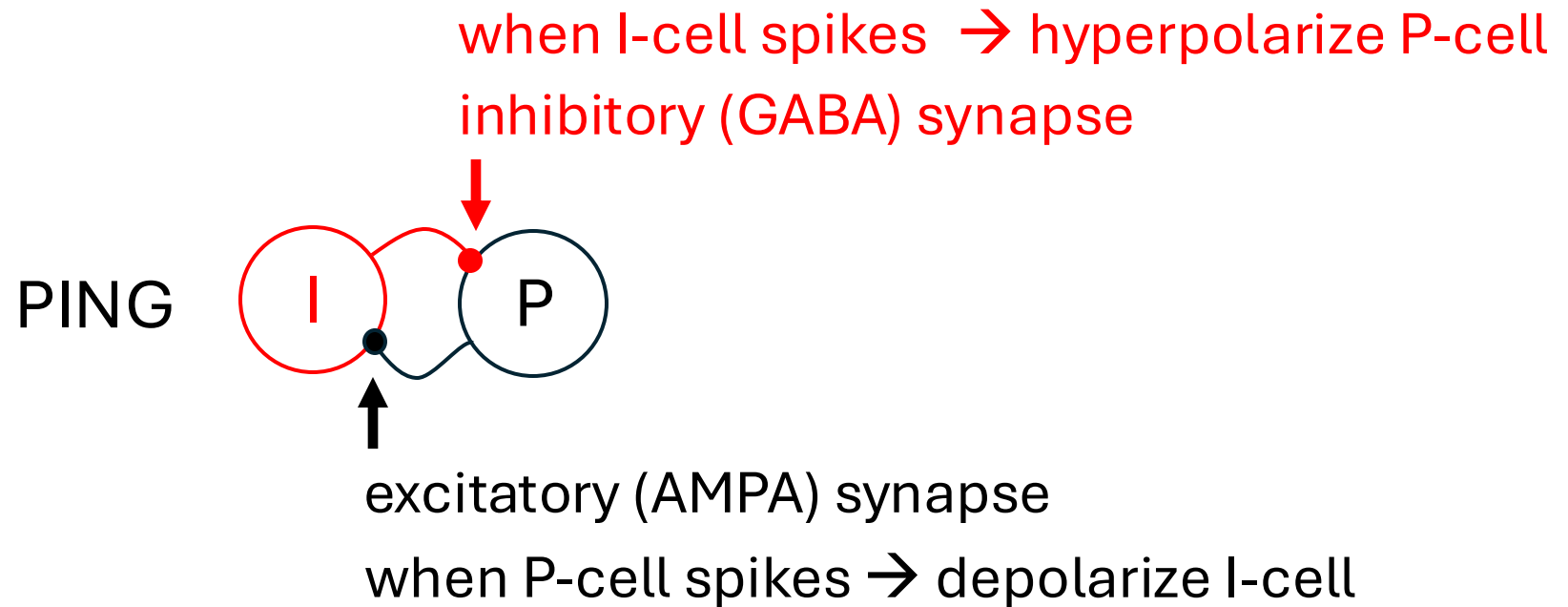


include AMPA synapse

Idea: cells collaborate to produce gamma

PING

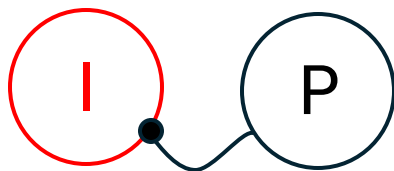
Connect cells with synapses



Build the model: HH + synapses

PING

Include synapses



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

I-cell voltage

Synaptic current

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

maximal
conductance

ex. synapse gate

equilibrium voltage
for ex. synapse (0 mV)

I-cell voltage

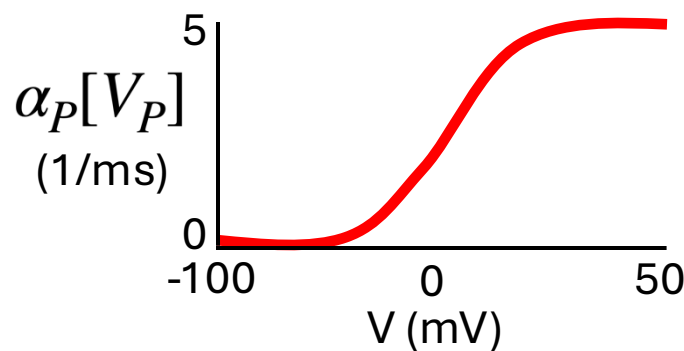
post-synaptic cell

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



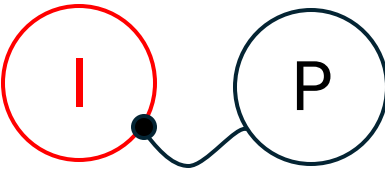
$$\beta_P[V_P] = \beta_P = \frac{1}{\tau_d}$$

constant

decay time ≈ 2 ms

Note: faster than inh. synapse

PING

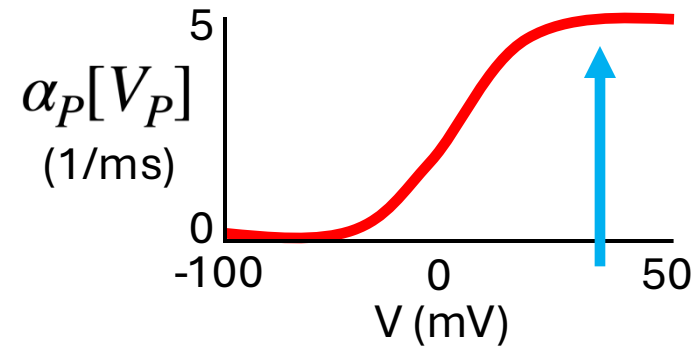
Include synapses  $\frac{dV_I}{dt} = I_{Na} + I_K + I_L + I_{inj} + I_{synapse\ P \rightarrow I}$

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

Q. What happens?

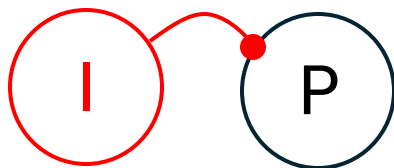
- P-cell spikes ($V_P > 0$)
- $\alpha_P[V_P] \rightarrow 5$
- $s_P \rightarrow 1$ (open)
- charge (Na^+) flows in \rightarrow depolarize I-cell (push to 0 mV)

Note: $[\text{Na}^+]_{\text{out}} \gg [\text{Na}^+]_{\text{in}}$



PING

Include synapses



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

P-cell voltage

Synaptic gate dynamics

Synaptic current

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

maximal
conductance

inh. synapse gate

equilibrium voltage
for inh. synapse (-80 mV)

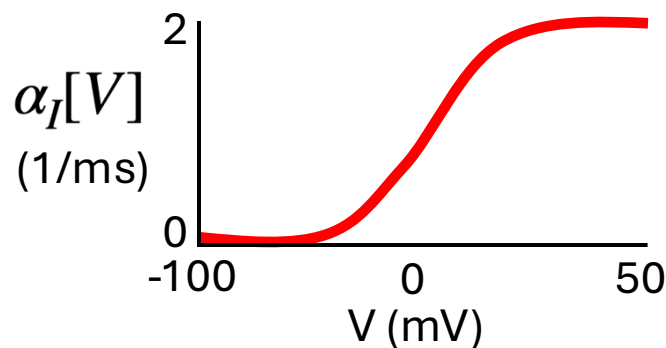
P-cell voltage

post-synaptic cell

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

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

backward rate fxn



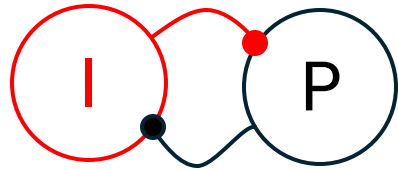
$$\beta_I[V] = \beta_I = \frac{1}{\tau_d}$$

constant

decay time ≈ 10 ms

PING

Put it all together



10 variables

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

$$\left. \begin{aligned} \frac{dm_P}{dt} &= \\ \frac{dh_P}{dt} &= \\ \frac{dn_P}{dt} &= \end{aligned} \right\} HH$$

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

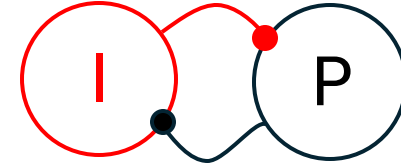
$$\frac{dV_I}{dt} = I_{Na} + I_K + I_L + I_{inj,I} + \underbrace{g_P S_P (E_P - V_I)}_{\text{ex. synaptic input}}$$

$$\left. \begin{aligned} \frac{dm_I}{dt} &= \\ \frac{dh_I}{dt} &= \\ \frac{dn_I}{dt} &= \end{aligned} \right\} HH$$

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

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 \rightarrow excitation to I-cell \rightarrow I-cell spikes

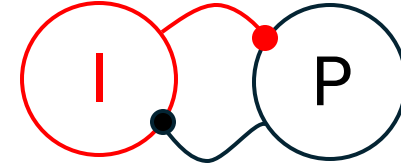
$t \approx 0$ I-cell spikes \rightarrow inhibition to P-cell

$t=25$ P-cell recovers \rightarrow P-cell spikes

Repeat ...

PING

Q. Consistent with experimental observations?



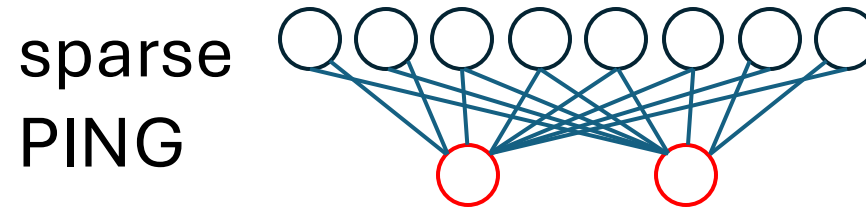
Experimental observations

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

Python Homework

Sparse PING

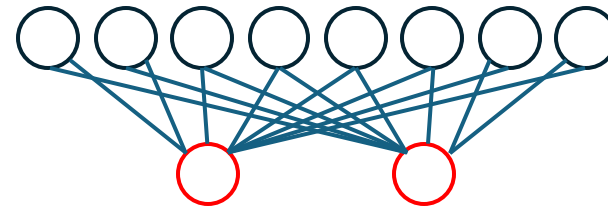
Sparse **P**yramidal **I**nterneuron **N**etwork **G**amma



Sparse PING

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

Ex. 80 P cells & 20 I cells



Each a HH model

P1

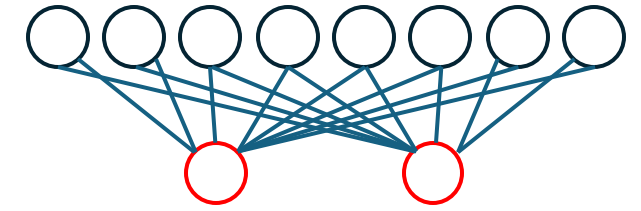
P2

P3

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

400 differential
equations

Sparse PING



Connect with synapses

Each P \rightarrow all I (with ex. synapses)

Each I \rightarrow all P (with inh. synapses)

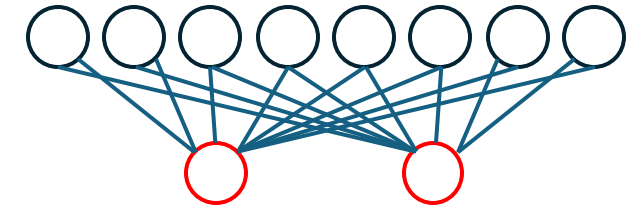
Then (for P1)

$$C \frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_K n^4 (V - V_K) - \bar{g}_{\text{Na}} m^3 h (V - V_{\text{Na}}) - \bar{g}_L (V - V_L) + I_{\text{syn } I1 \rightarrow P1} + I_{\text{syn } I2 \rightarrow P1} + \dots$$

many terms

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

Sparse PING

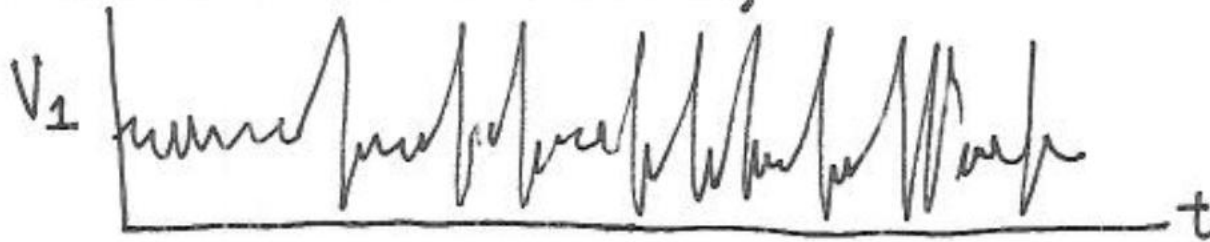


Q. How will the model work?

Idea:

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

Then, for some P-cell. in isolation,

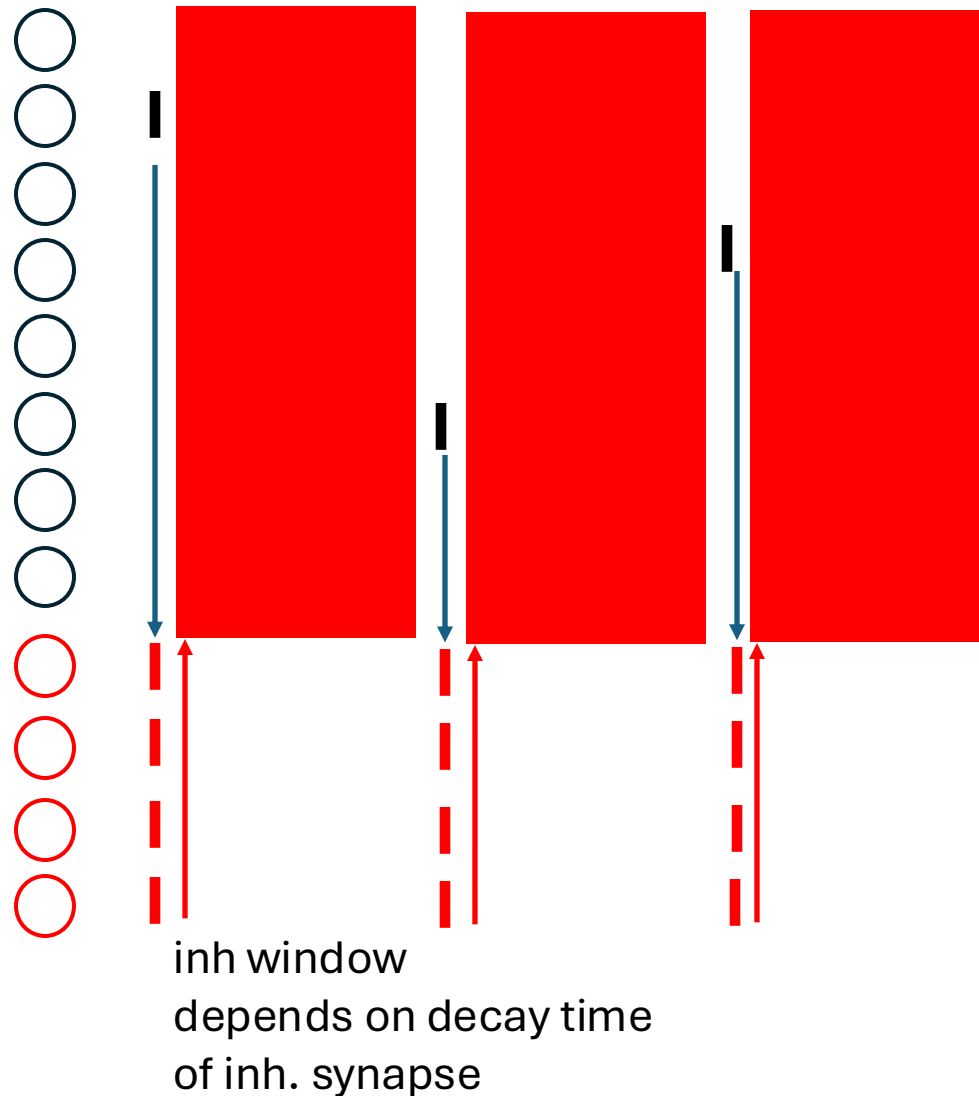


P-cell spikes.

Time between spikes
varies due to noise.

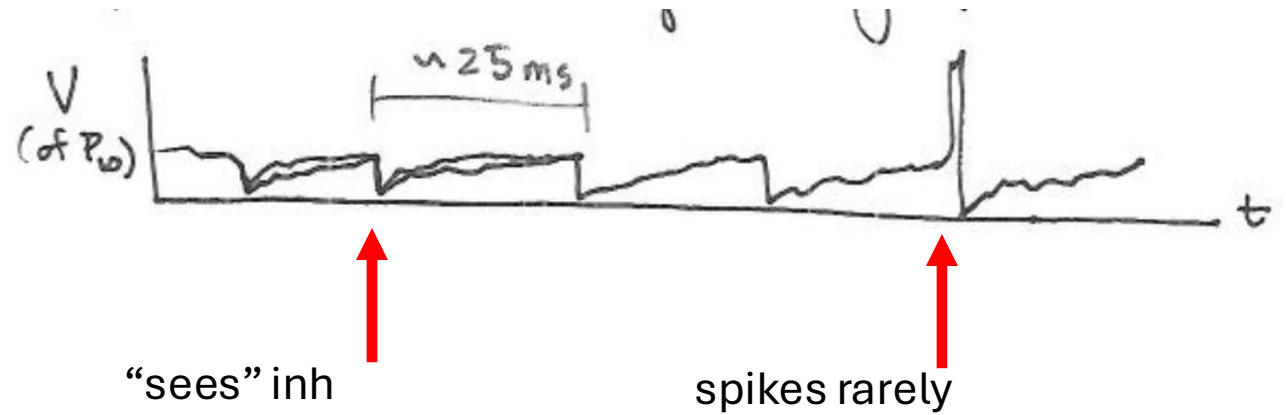
- Make synapses strong

Sparse PING



Note: 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

Cost: more complexity.