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Firing patterns in model networks of hippocampal persistent firing neurons

Motivation

- Persistent firing has long been thought to be the neural mechanism underlying short-term memory encoding and storage [1]
- Intrinsic neural mechanisms [2] can sustain persistent firing in hippocampal CA1 neurons [3] in the absence of external stimulation
- We analyse the dynamics of networks of persistent firing hippocampal neurons
- We hypothesise that these circuits could contribute to the **emergence of theta oscillations in the hippocampus**

Neuron Model

- Neuron Model [4]:

$$C_m \cdot \frac{dV_m}{dt} = -I_{Leak} - I_K - I_{Na} - I_M - I_{Ca} - I_{CAN} - I_{Syn} + I_{Stim}$$

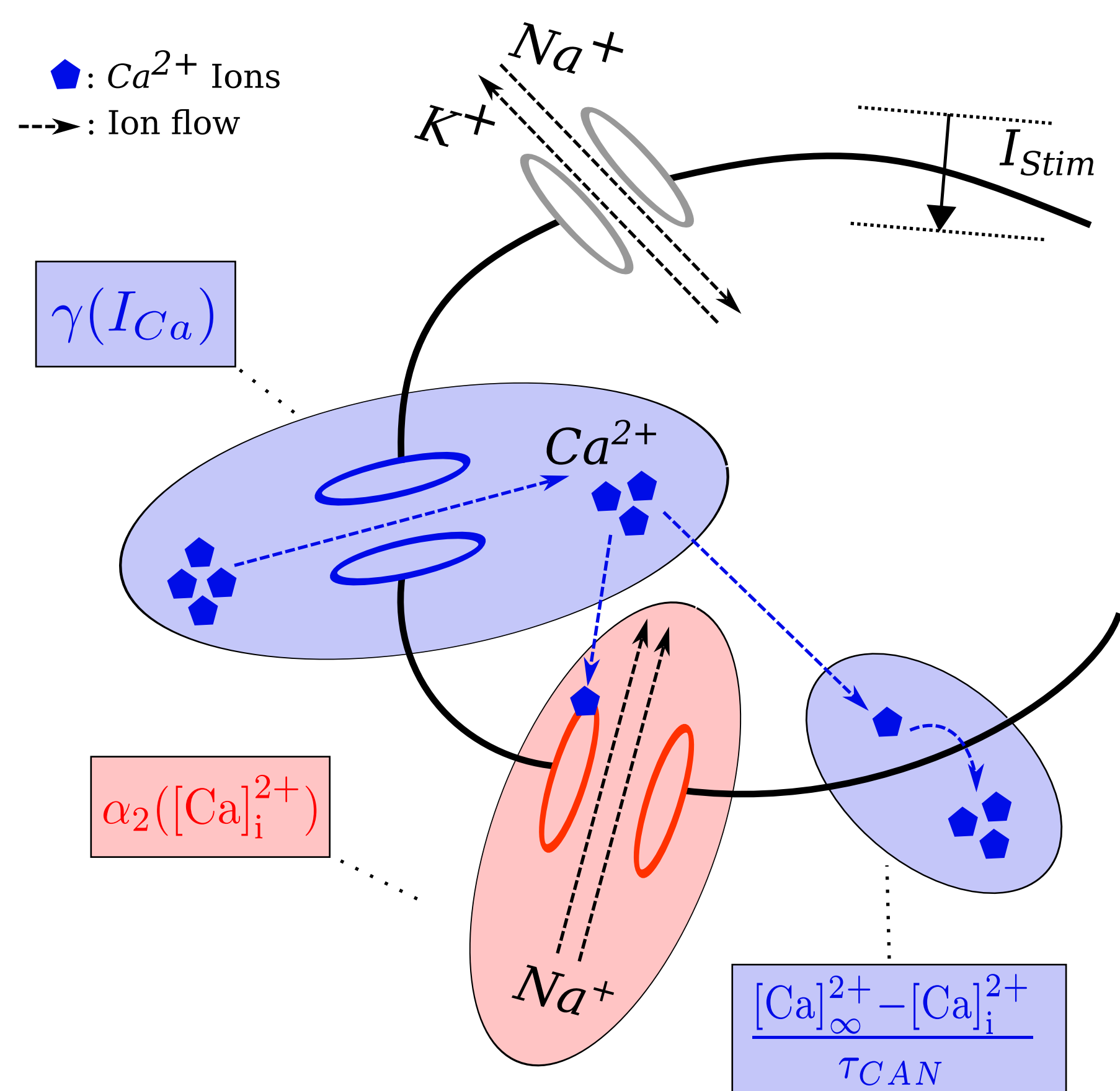
- Hodgkin-Huxley and M Currents:

$$I_{Leak} = f(V_m) \quad I_K = f(V_m, n^4) \quad I_{Na} = f(V_m, m^3, h) \quad I_M = f(V_m, m)$$

- Excitatory Postsynaptic Current:

$$I_{Syn} = -g_E \cdot (V_m - E_E) \quad \frac{dg_E}{dt} = -\frac{g_E}{\tau_E} \quad g_E \leftarrow g_E + w_{cc} \quad E_E = 0 \text{ mV} \quad \tau_E = 5 \text{ ms}$$

Calcium Dynamics



Schematic of the Calcium dynamics (influx and efflux) and the activated CAN current. Ca^{2+} ions (blue) enter the cell membrane, and bind on CAN receptors (red) causing them to open and permeate K^+ and Na^+ ions.

- The Calcium Dynamics:

$$I_{Ca} = f(V_m, m^2, h) \quad \frac{d[Ca]_i^{2+}}{dt} = \gamma(I_{Ca}) + \frac{[Ca]_{\infty}^{2+} - [Ca]_i^{2+}}{\tau_{Ca}} \quad \gamma(I_{Ca}) = \frac{-10^4 \cdot I_{Ca}}{area \cdot 2 \cdot F \cdot depth}$$

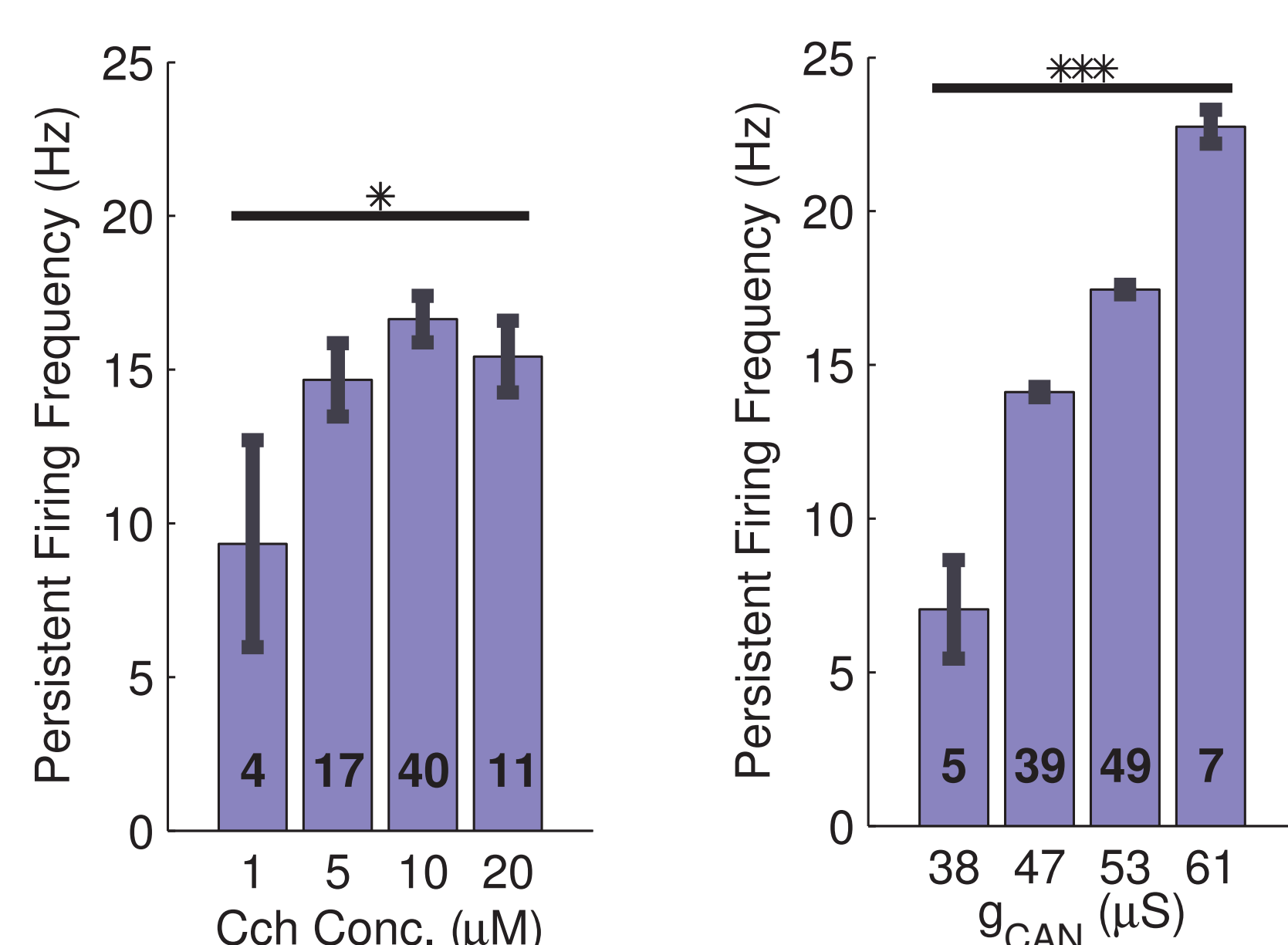
$[Ca]_{\infty}^{2+} = 24 \mu M$ $\tau_{Ca} = 200 \text{ ms}$

- The CAN Current:

$$I_{CAN} = f(V_m, m^2) \quad \frac{dm}{dt} = \alpha_m \cdot (1 - m) - (\beta_m \cdot m) \quad \alpha_m = \alpha_2([Ca]_i^{2+}) \cdot T \quad \beta_m = \beta_{CAN} \cdot T$$

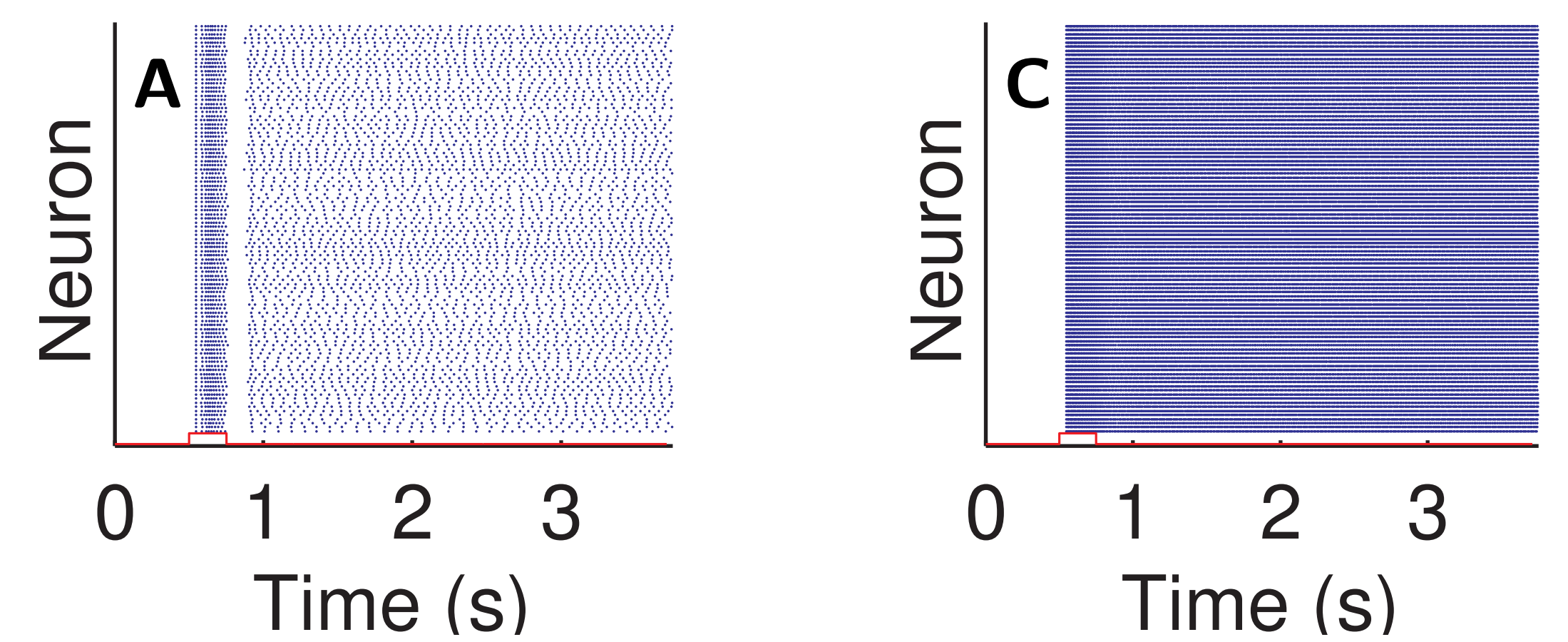
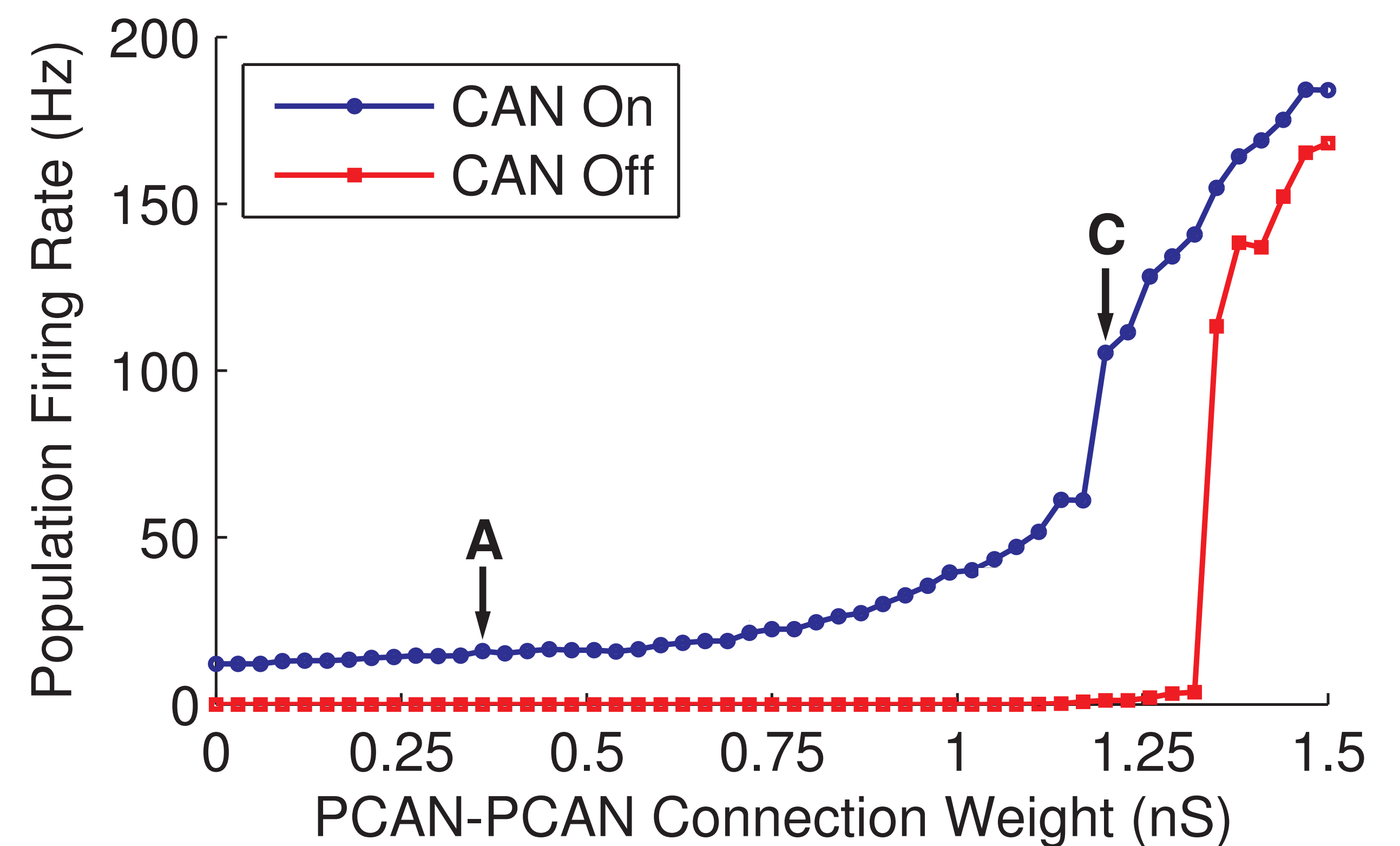
$$\alpha_2([Ca]_i^{2+}) = \beta_{CAN} \cdot \left(\frac{[Ca]_i^{2+}}{[Ca]_c^{2+}} \right)^2 \quad \beta_{CAN} = 0.2 \text{ s}^{-1} \quad [Ca]_c^{2+} = 50 \mu M$$

Fitting Model to In-Vitro Data



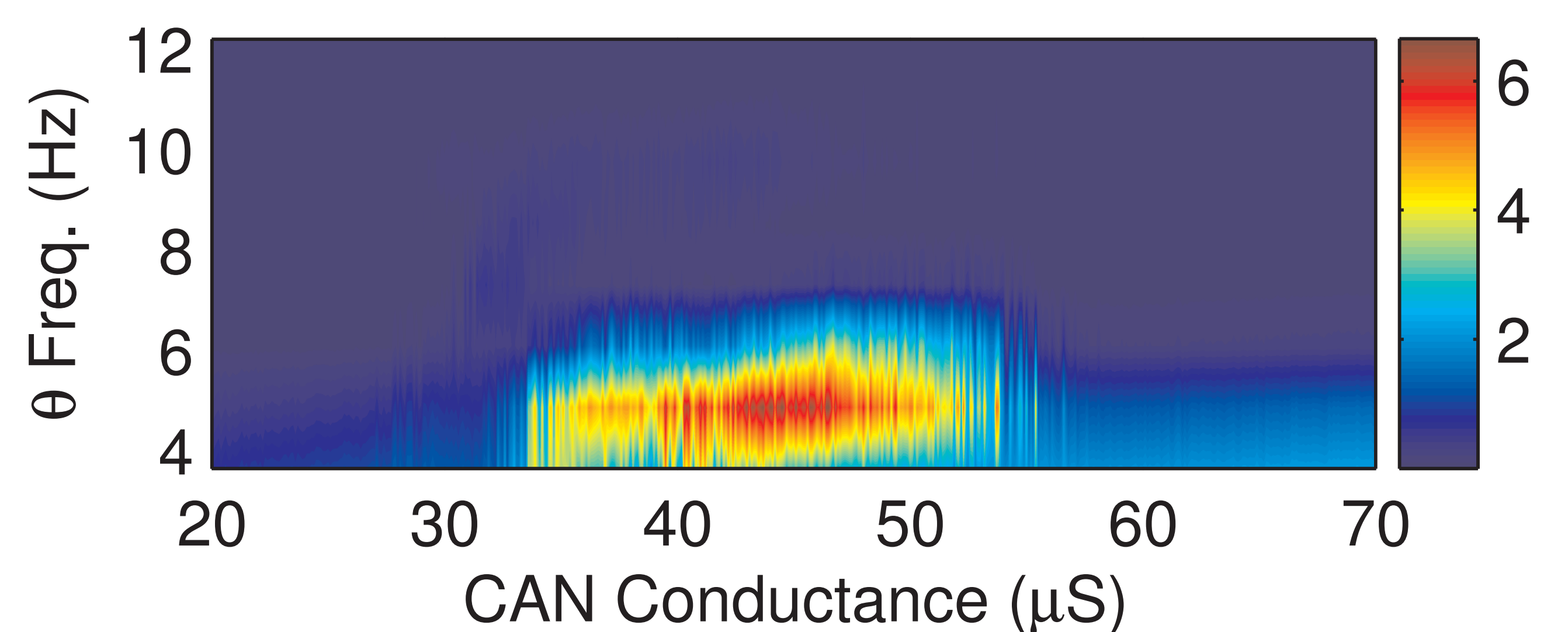
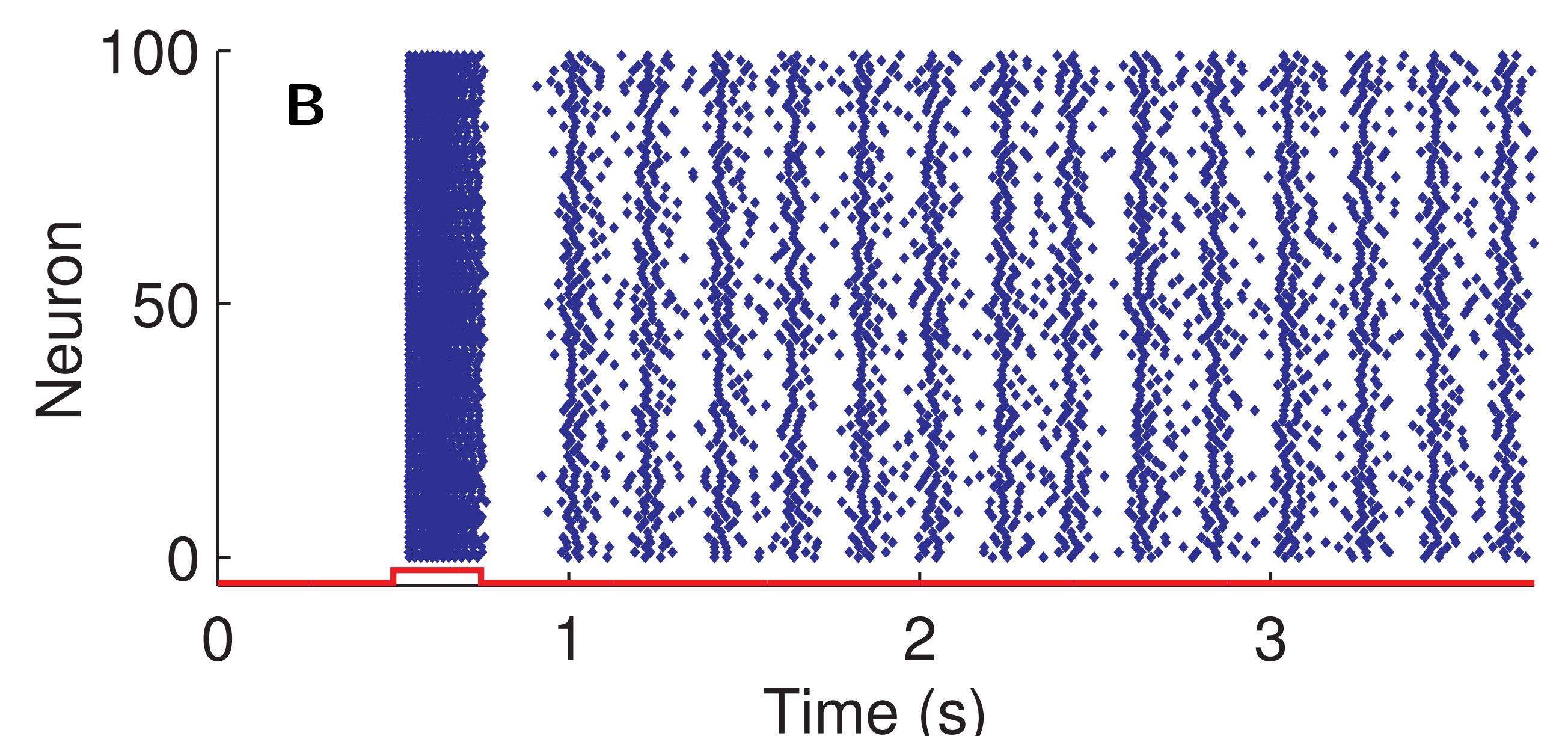
The persistent firing frequency is modulated by the activation of CAN receptors in the model (right) in accordance with *in vitro* recordings [3] (left).

Results – Network Firing Regimes



The CAN current activation allows a 100-cell network to display persistent firing in biologically plausible frequency bands. Conversely, a pyramidal network without CAN current (bottom line) does not display such a rich firing regime.

Results – CAN-Mediated Theta Oscillations



The interaction between CAN-mediated persistent firing and synaptic activity allow for the emergence of self-sustained synchronous theta oscillations in the CAN pyramidal network.

Conclusion

- Networks of CAN-equipped neurons display a rich array of firing regimes
- Self-sustained theta oscillations emerge from the interaction between CAN-mediated persistent firing and synaptic activity

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