Computational Model of CA3 Hippocampal Network

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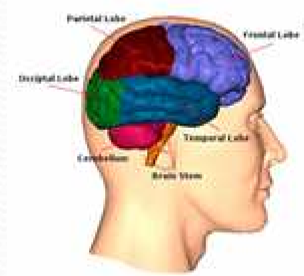
Facts About Human Brain



Holds only 2% of our body's weight but consume 20% of the energy. This energy is enough to light a 25 watt bulb.

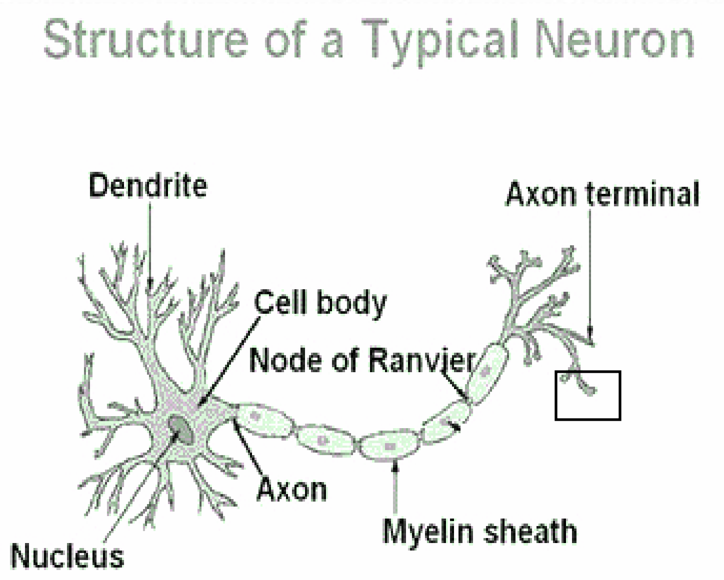
There are about 100 billion neurons in the human brain.

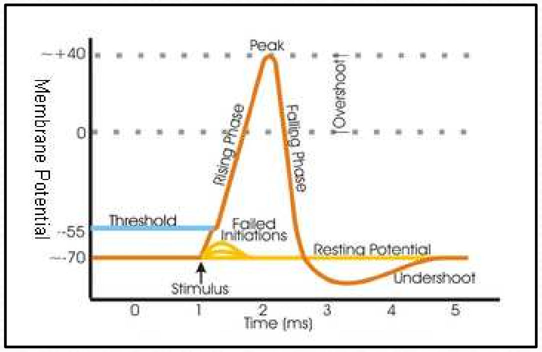
More electrical impulses are generated in one day by a single human brain than by all the telephones in the world.

An average human brain produces about 70,000 thoughts per day.

About 1000 ml of blood flow through the brain every minute. In that minute the brain will consume 46 cm^3 of oxygen from that blood.

Neuron-Building Block of Nervous System



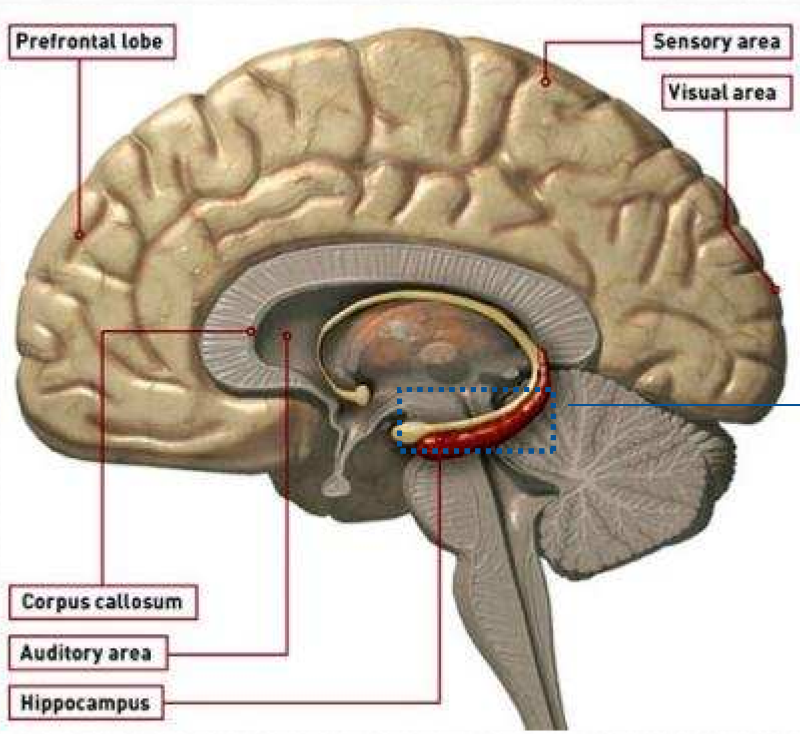


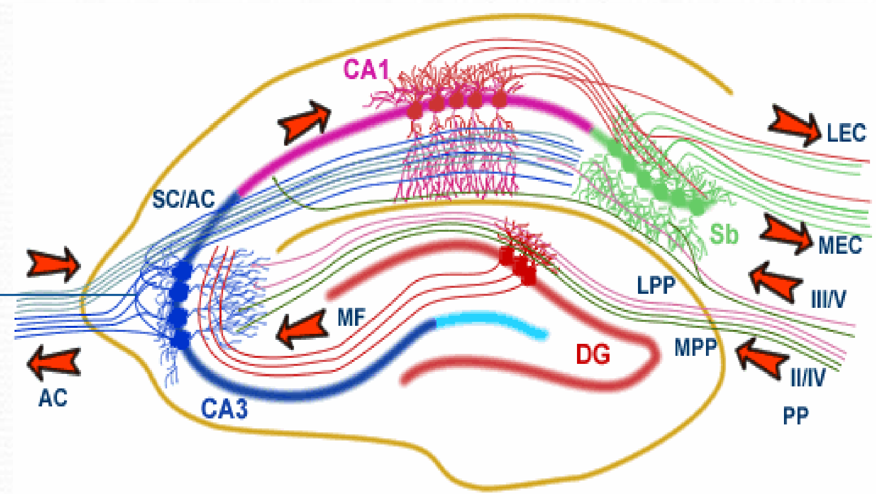
Input:
Synaptic Input to Dendrite from Other Neurons

Output:
Action Potential to Axon Terminal

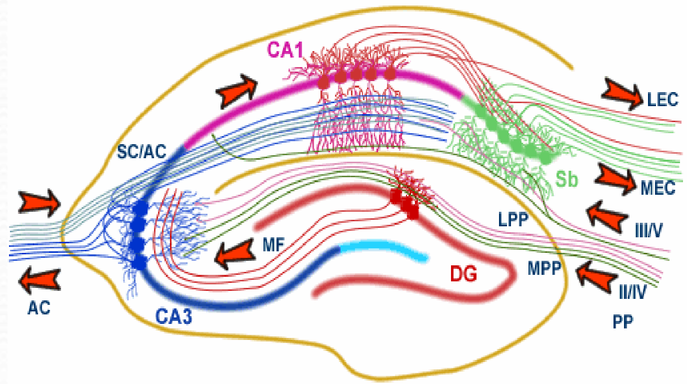
HIPPOCAMPUS

Key player behind the formation <u>long term memories</u> and <u>spatial navigation</u>





CA3 Region



CA3 region holds a strategic position in the hippocampus because it receives sensorial information from the external and internal environment via two main pathways: the mossy fibres and the perforant path.

It is essential for spatial memory processes and specifically in memory consolidation of spatial information.

CA3 pyramidal neurons (excitatory) communicate mainly through bursts of spikes rather than trains of regular firing action potentials.

Key Features

No spontaneous firing in the absence of current.

Characteristics of Spikes

$$\text{Half width } = 1.0 \pm 0.1ms$$

$$dV/dt = 101.6 \pm 5.4mV/ms$$

$$\text{Amplitude} = 97.6 \pm 1.9mV$$

$$fAHP = 10.2 \pm 0.5mV$$

Weak input current (Rheobase) -------------- 50-400 pA for 400 ms pulse

Strong input current (above rheobase) ------ 100-1500 pA for 400 ms pulse

Early and late Spike: -------------------------- 50-400 pA for 400 ms pulse

Hemmond et al: Hippocampus (2008)

Behaviour of the CA3 Neurons

3 Different Firing patterns were observed.*

Regular firing with strong Spike frequency adaptation
(approx 8-10 spikes)--37%

Weak or no Spike frequency adaptation
(approx 8-10 spikes) --- 46%

Rapid burst
(5-6 spike train of > 50Hz in initial 100 ms of 400 ms pulse) -------- 17%

Hemmond et al: Hippocampus (2008)

CA3 Neuron Model

$$C\dot{V} = k(V - V_r)(V - V_t) - u + I \qquad if \quad V \geq V_{peak}$$

$$\dot{u} = a[b(V - V_r) - u] \qquad V \leftarrow c, \; u \leftarrow u + d$$

Parameter Descriptions and their Values

Parameter	Description	Value
C	Capacitance	352.5 pF
V_r	Resting Membrane Potential	-65 mV
V_t	Threshold Membrane Potential	-45 mV
V_{peak}	Peak Potential	35 mV

Izhikevich, MIT Press, (2007)

Hippocampal Parameters

$$C\dot{V} = k(V - V_r)(V - V_t) - u + I \qquad \text{if} \quad V \geq V_{peak}$$

$$\dot{u} = a[b(V - V_r) - u] \qquad V \leftarrow c, \; u \leftarrow u + d$$

a- ***time scale of the recovery variable. Smaller values means slow recovery (ms^{-1}).***

b- ***Sensitivity of the recovery variable u to the sub-threshold fluctuation of the membrane potential V. (nS).***

c- ***After spike rest value of membrane potential (mV)***

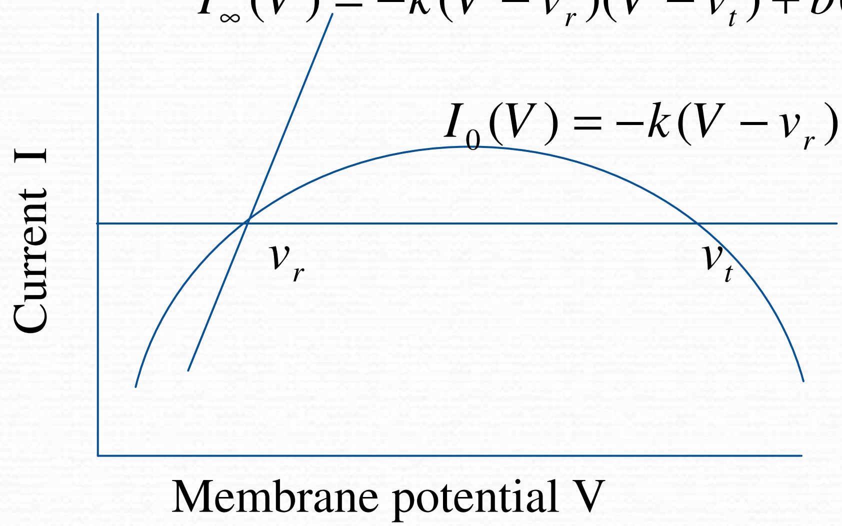
d- ***After spike reset of the recovery variable (pA)***

k- ***Scaling factor for the membrane potential V ($pA/(mV)^2$)***

General Method of Finding the Parameter Values

$$I_\infty(V) = -k(V - v_r)(V - v_t) + b(V - v_r)$$

$$I_0(V) = -k(V - v_r)(V - v_t)$$



$\boldsymbol{I_\infty}$ - sub-threshold part of the steady state IV relation

$\boldsymbol{I_0}$- sub-threshold part of the instantaneous IV relation

b and k: Maximum of $\boldsymbol{I_\infty}$ approx. rheobase current for $b<0$ and its derivative *wrt V* at v_r corresponds to input conductance. Knowing both the rheobase and input conductance, we can solve them to find *b* and *k.*

a- is the time scale of the recovery variable, which is equivalent to inactivation of $\boldsymbol{K^+}$ current, $\boldsymbol{I_K}$. Therefore a≈*1/inactivation time constant of* $\boldsymbol{I_K}$.

d - describes the total amount of outward minus inward currents activated during the spikes and affecting the after spike behavior. Therefore, for each model we use different values of d to obtain a reasonable behavior

Summary of our Models

$$352.5\dot{V} = k(V+65)(V+45) - u + I \qquad \text{if} \quad V \geq 35$$

$$\dot{u} = a[b(V+65) - u \qquad\qquad V \leftarrow c \quad u \leftarrow u + d$$

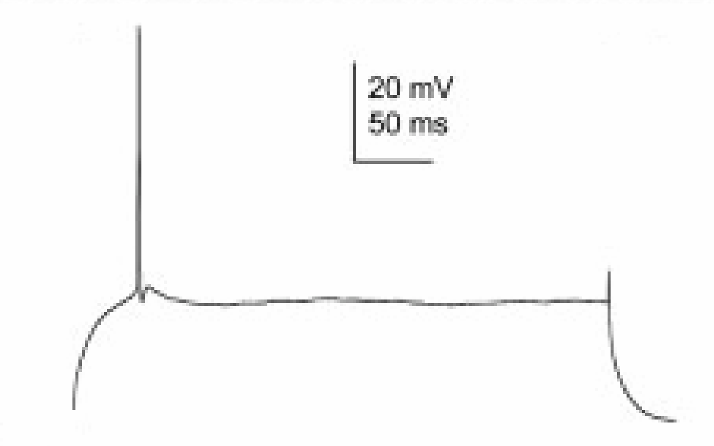
MODEL	PARAMETER VALUES	Figures Matched from Hemond Paper	Comments
1	***a=0.005*** ***b=-2*** ***c=-55*** ***d=350*** ***k=2.5***	Early Spike, Strong Adapting More Spikes	**I=400 pA for early spike,** **I=1100 pA for the strong adaptation** **More spikes for higher values of I.**
2	***a=0.025*** ***b=-2*** ***c=-55*** ***d=200*** ***k=2.5***	Late spikes Weakly Adapting More spiking for higher current	**I=240 pAfor late spike,** **I=500 pA for the weak adapting** **More spikes for higher values of I**
3	***a=0.005*** ***b=6.5*** ***c=-55*** ***d=4*** ***k=8***	Early Spike Burst Longer duration burst	**I=390 pA Early Spike (this is rheobase current value),** **Burst at I=550 pA ,** **Longer duration burst at I=470 pA**

Simulation Results

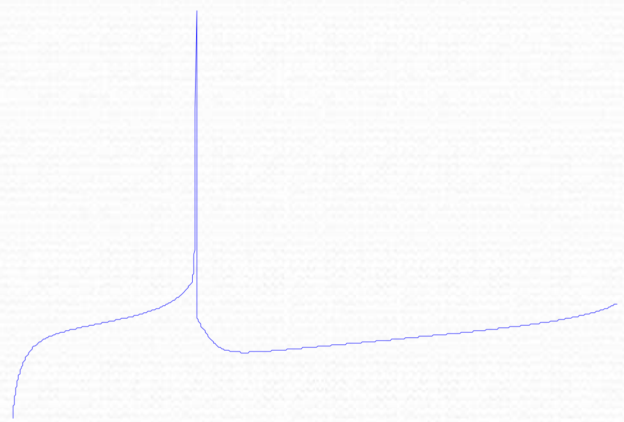
MODEL-1

Early Spike

Experimental



Our Model

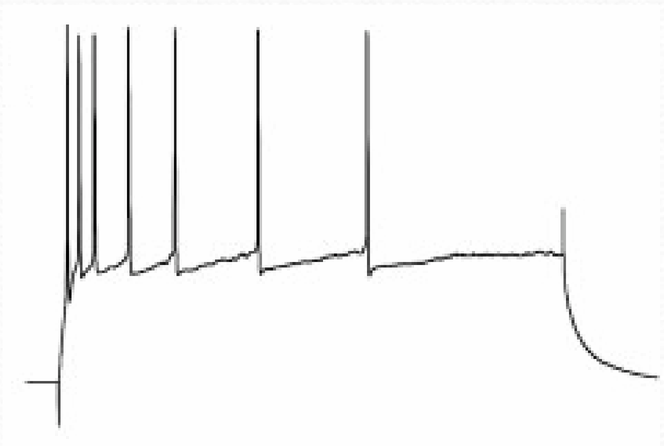


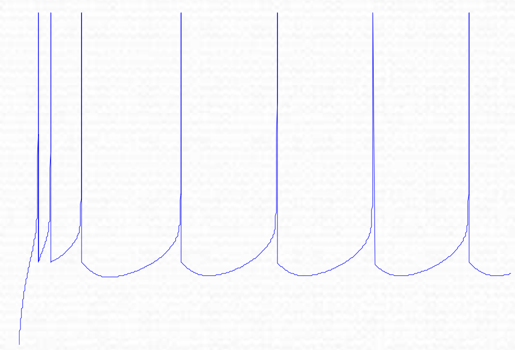
I=400 pA (Rheobase)

Strong Adapting

Experimental

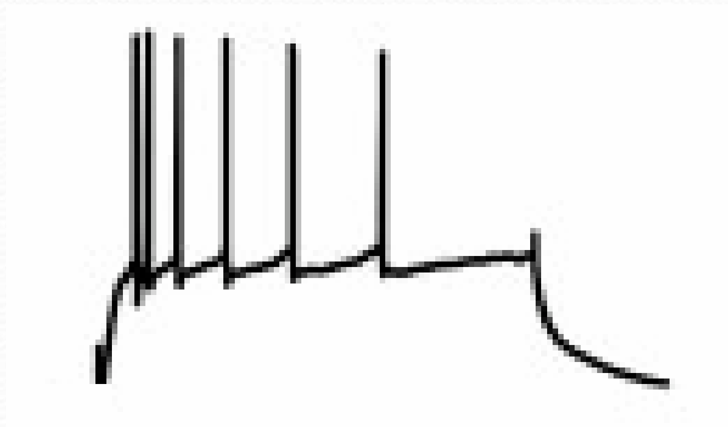
Our Model

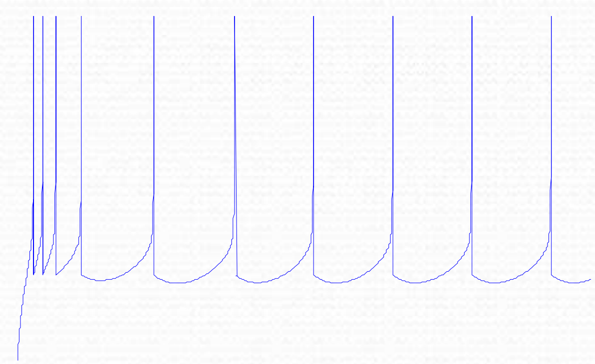




I=1100 pA

More spikes for higher values of I.



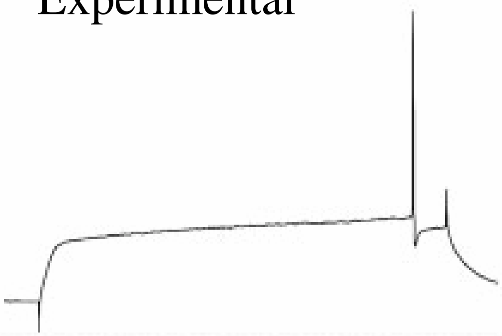


I=1500 pA

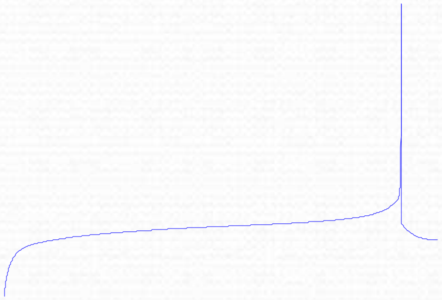
MODEL-2

Late Spike

Experimental

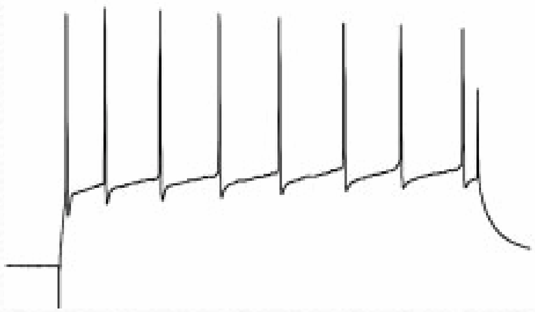


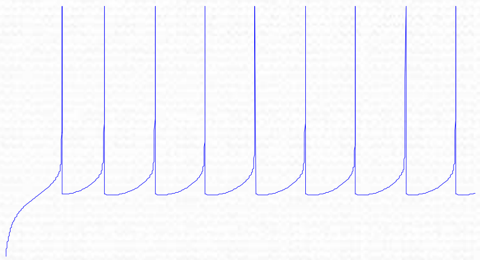
Our Model



I=240 pA

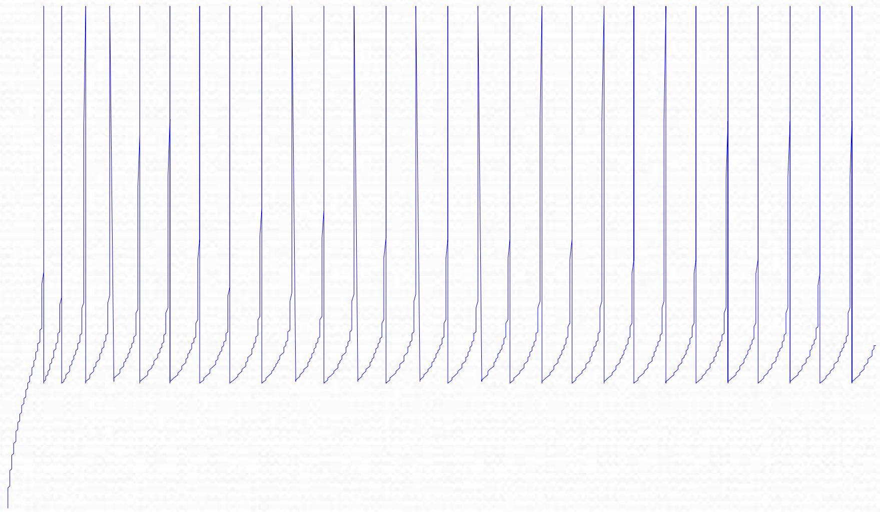
Weak Adaptation





I=500 pA

More spiking for higher current

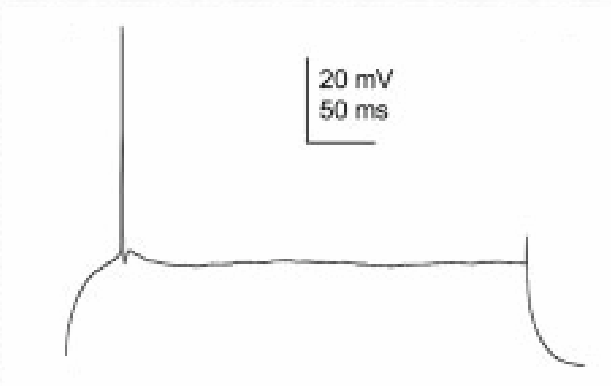


I=1000 pA

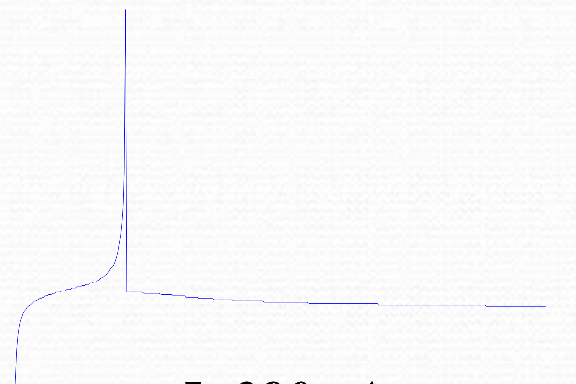
MODEL-3

Early Spike

Experimental



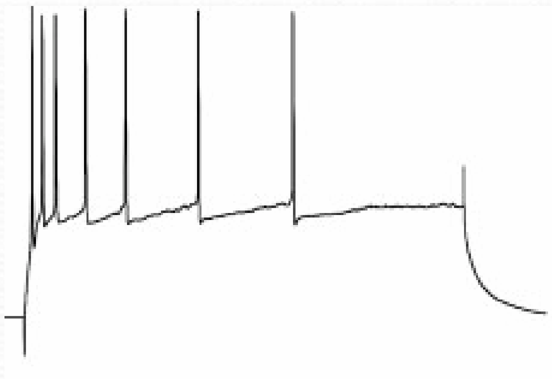
Our Model



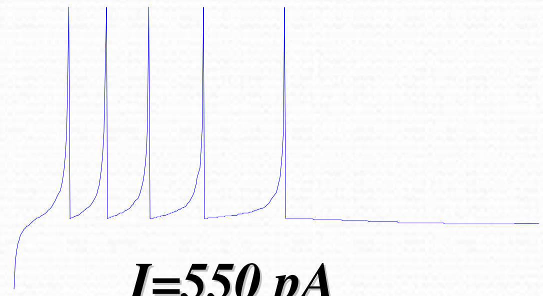
I=390 pA

A Burst

Experimental

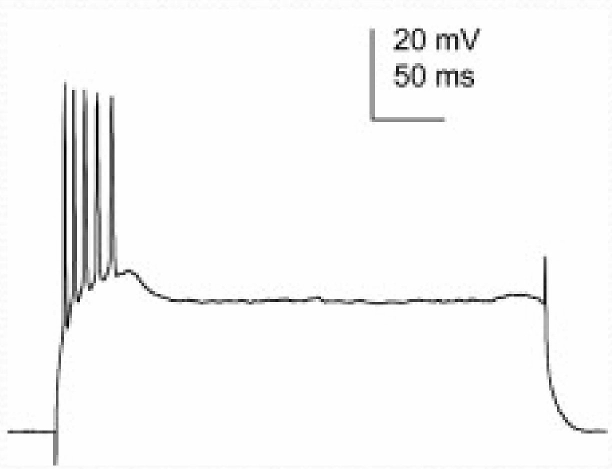


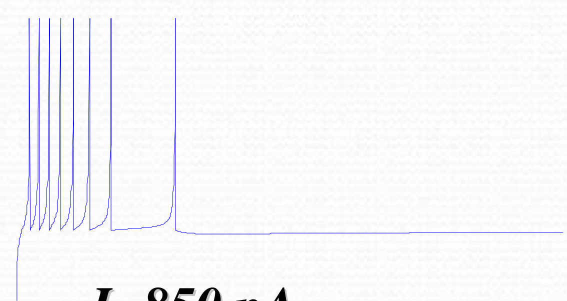
Our Model



I=550 pA

Longer Duration Burst

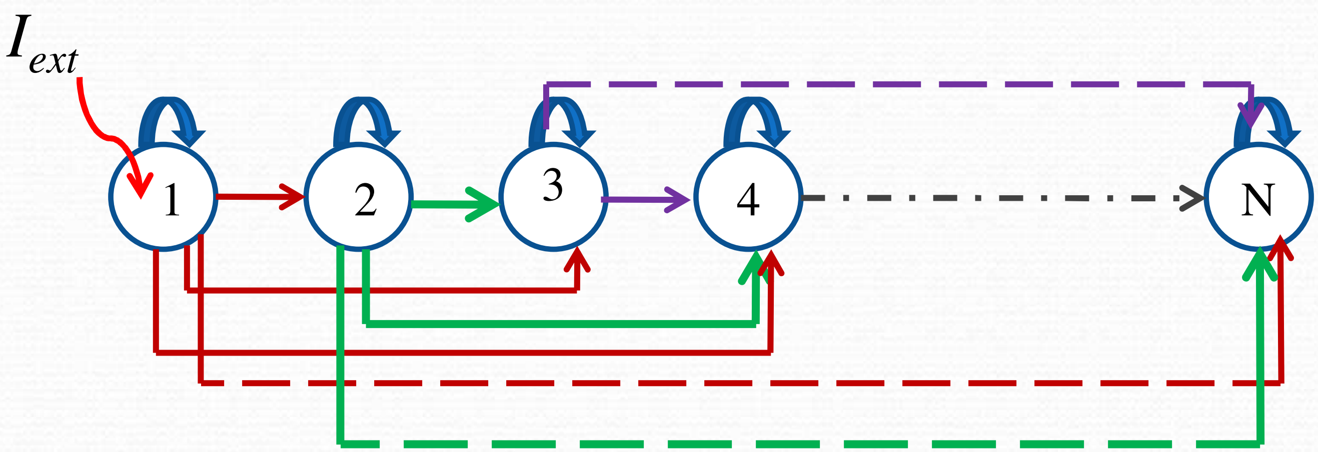




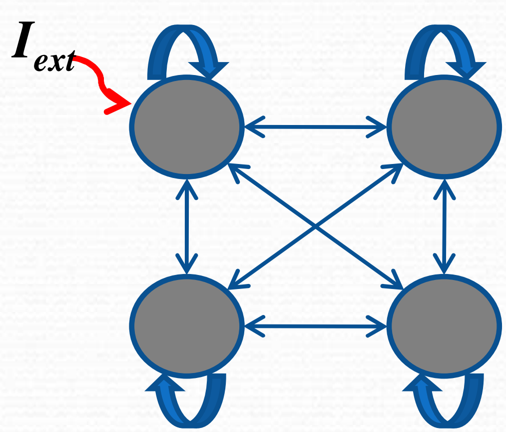
I=850 pA

Neuronal Network

Feed-Forward Network



All-to-All Coupled



Network Model

$$C\frac{dV_j}{dt} = k\left(V_j - v_r\right)\left(V_j - v_t\right) - u_j + I_{ext} + \left(E - V_j\right) * \bar{g}\sum_{i=1}^{N} s_{j,i}(t, V_i)$$

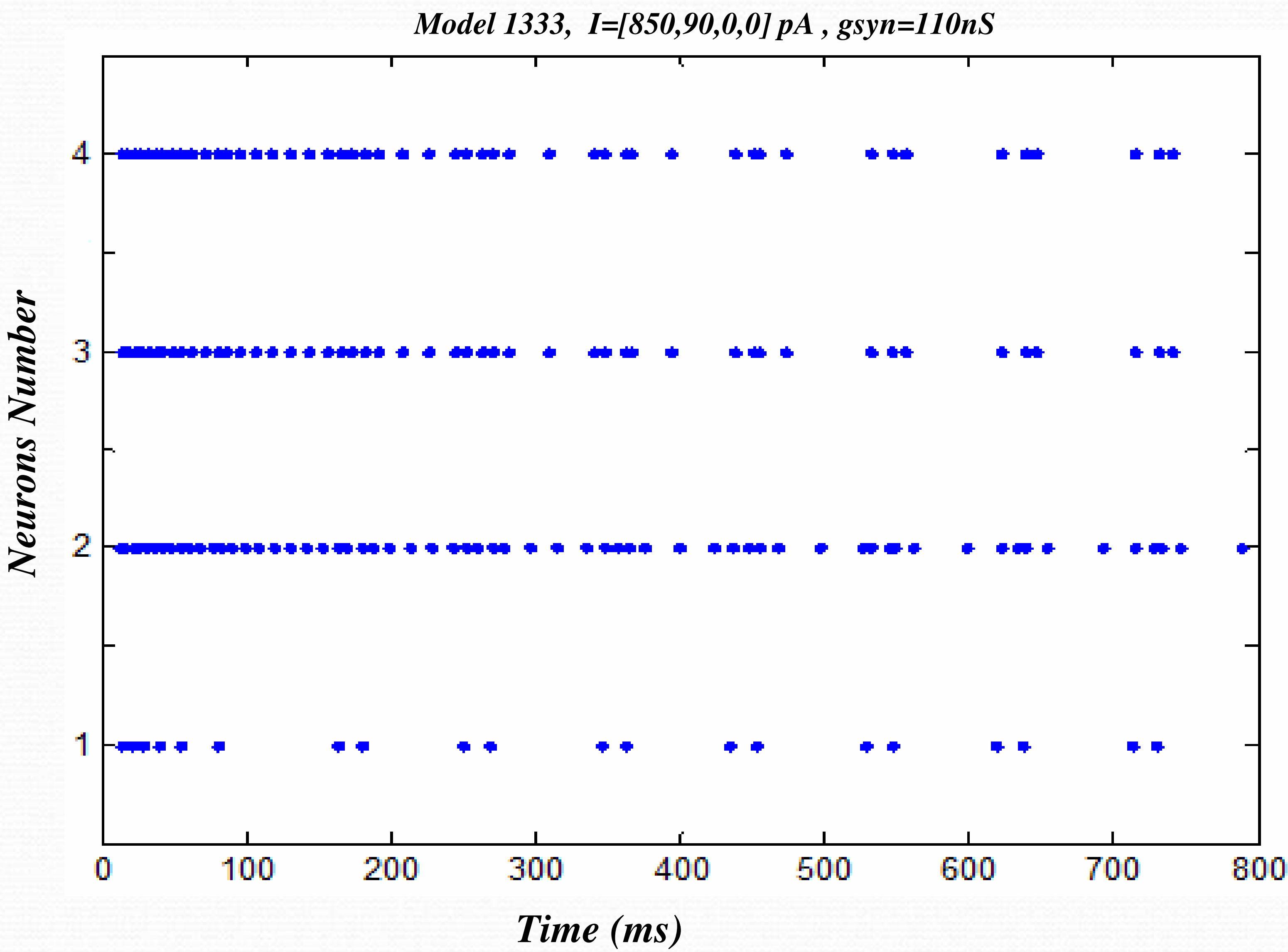
$$\frac{du_j}{dt} = a\left\{b\left(V_j - v_r\right) - u_j\right\}$$

$$V_j \leftarrow c \ , \ u_j \leftarrow u_j + d \ \ whenever V_j \geq V_{peak} \ , \ \ j = 1,2,\cdots,N$$

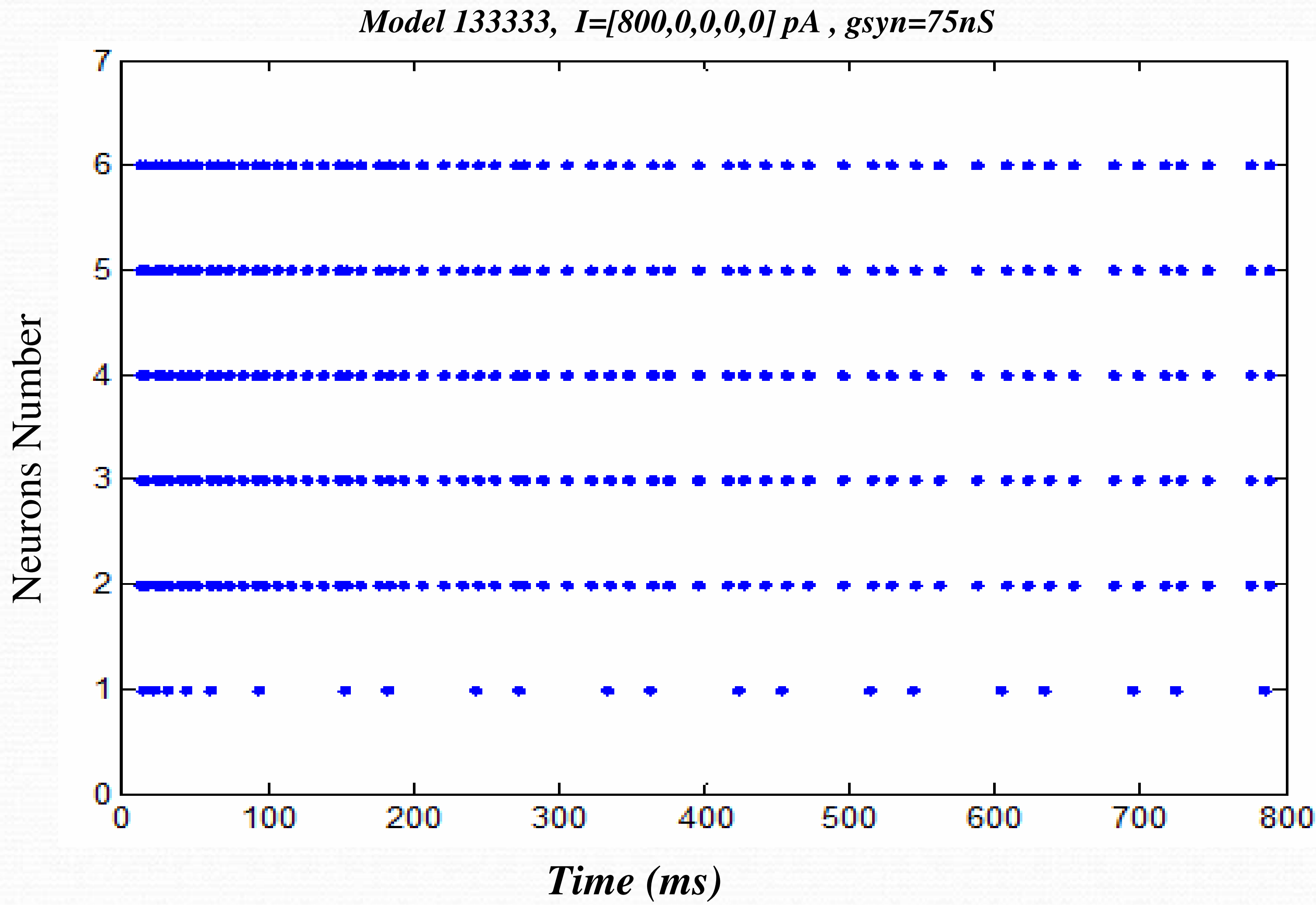
$$\tau_{syn}\frac{ds_{j,i}}{dt} = -s_{j,i}$$

$$s_{j,i} \leftarrow s_{j,i} + S_{\max} \ \ whenever\ V_i > 0 \quad from \quad below, \quad for\ i = 1,2,\ldots,N$$

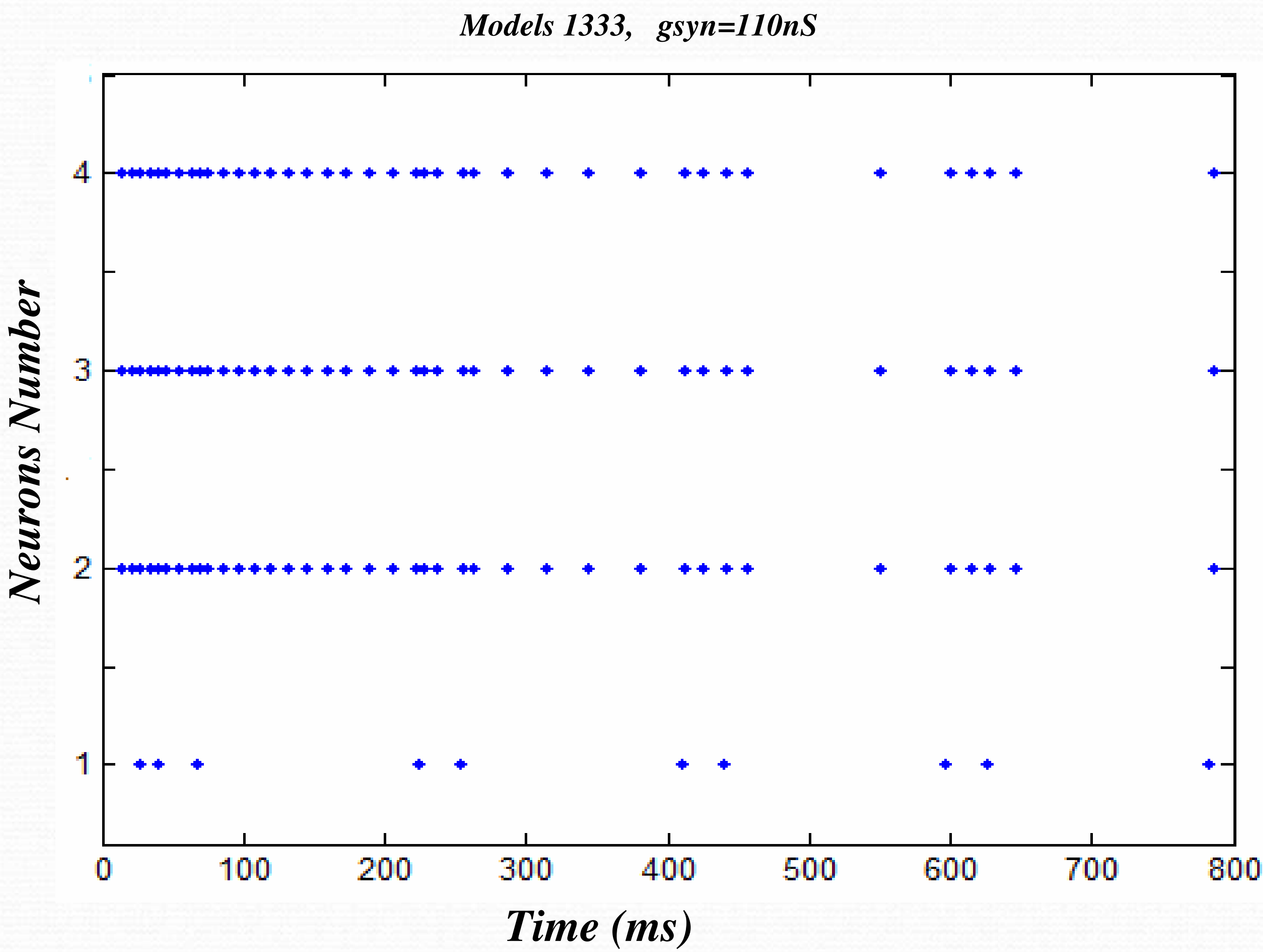
Bursting in 4-cell network



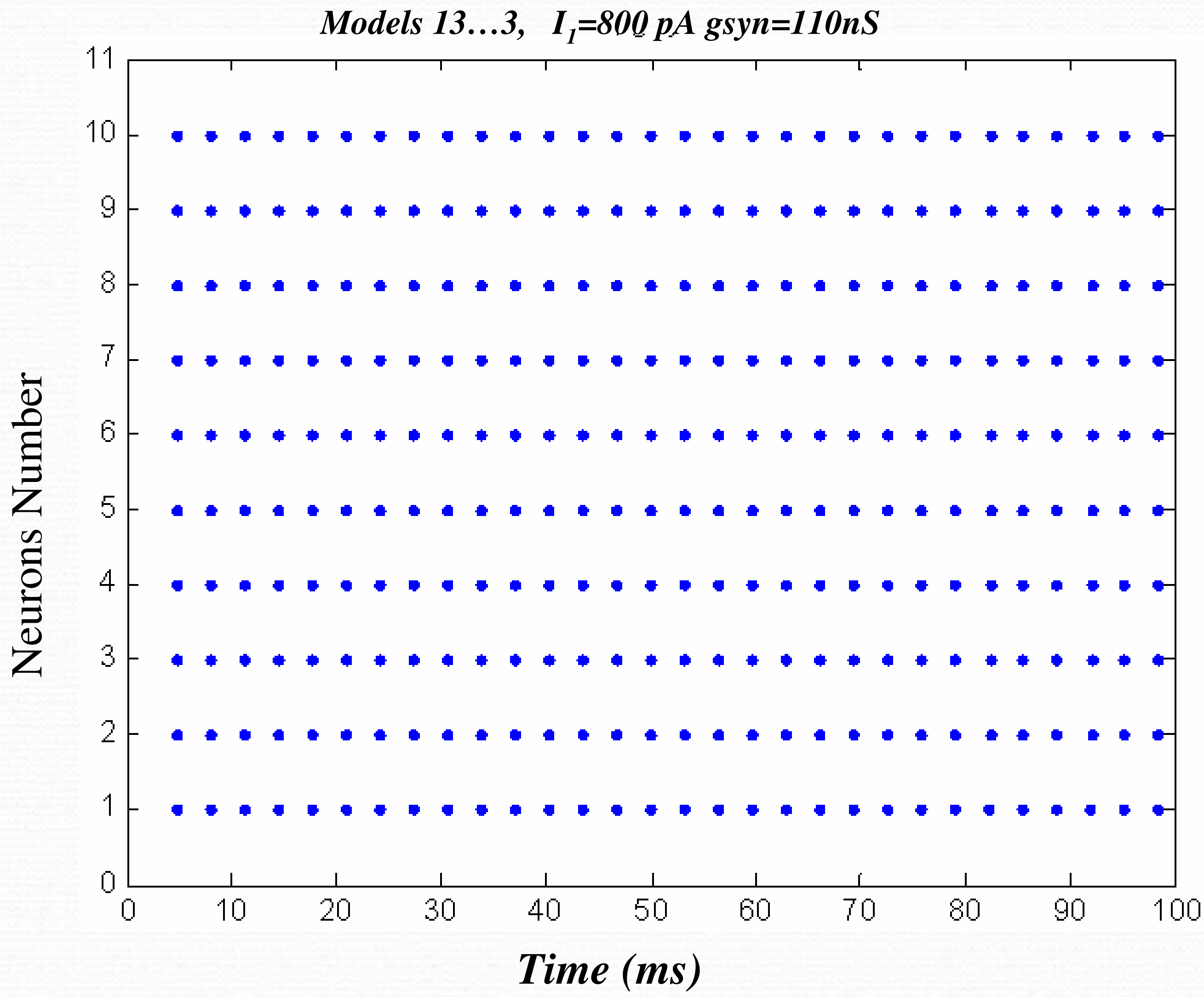
6-Cell Bursting



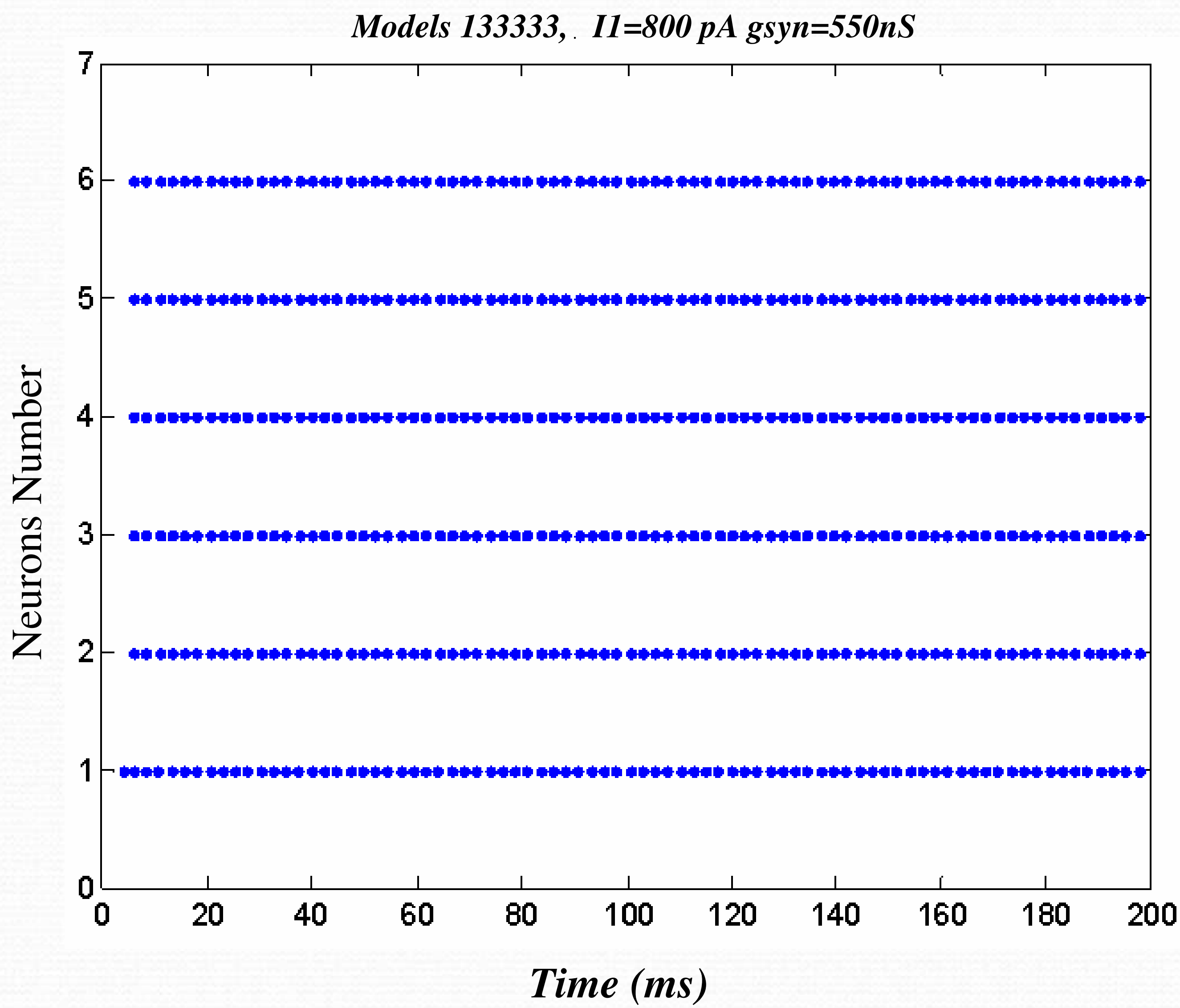
4-Cell Bursting without External Injected Current



Synchronized Firing in All to All Coupled Cells



Bursting in All to All Coupled Cells



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