Computer Lab 3: Large Excitatory and Inhibitory Networks

- Propagation of activity through an excitatory network
- Network-generated reverberatory/persistent activity as a mechanism for working memory in excitatory networks
- Clustering in inhibitory networks

Readings:

- Amit, Brain Behav Sci 1995 – intro to attractor networks as a mechanism for working memory
- Durstewitz et al Nat Neurosci 2000 – review of models for working memory
- Wang J Neurosci 1999 – spiking neuron network model for working memory

Izhikevich 2D LIF (ILIF) Model

- 2 variables:
  - V = membrane voltage
  - u = membrane recovery variable, which provides negative feedback to v like K^+ currents
  - No explicit modeling of AP biophysics
  - No units but V takes on realistic voltage values and time may be assumed to be ms

$$\frac{dV}{dt} = 0.04\,V^2 + 5V + 140\ - u + I$$

$$\frac{du}{dt} = a(bV - u)$$

Reset condition: If V ≥ 30, then set V = c and u = u + d

Vector format for equations

$$\frac{d}{dt}\begin{bmatrix} V_1 \\ \vdots \\ V_n \end{bmatrix} = 0.04 \begin{bmatrix} {V_1}^2 \\ \vdots \\ {V_n}^2 \end{bmatrix} + 5 \begin{bmatrix} V_1 \\ \vdots \\ V_n \end{bmatrix} + 140 - \begin{bmatrix} u_1 \\ \vdots \\ u_n \end{bmatrix} + \begin{bmatrix} I_1 \\ \vdots \\ I_n \end{bmatrix} + g_{syn}\, W \begin{bmatrix} s_1 \\ \vdots \\ s_n \end{bmatrix}$$

- Connectivity or adjacency matrix W (n x n) sets coupling between cells

Synaptic currents in n cell network

- Use instantaneous rise and exponential decay profile
- For each cell, compute sum of synaptic currents generated for each spike it fires

$$s_j(t) = \sum_{t_j} e^{-(t-t_j)/\tau}$$

where t_j are the times of all the spikes fired by Cell j up to time t

Matlab codes

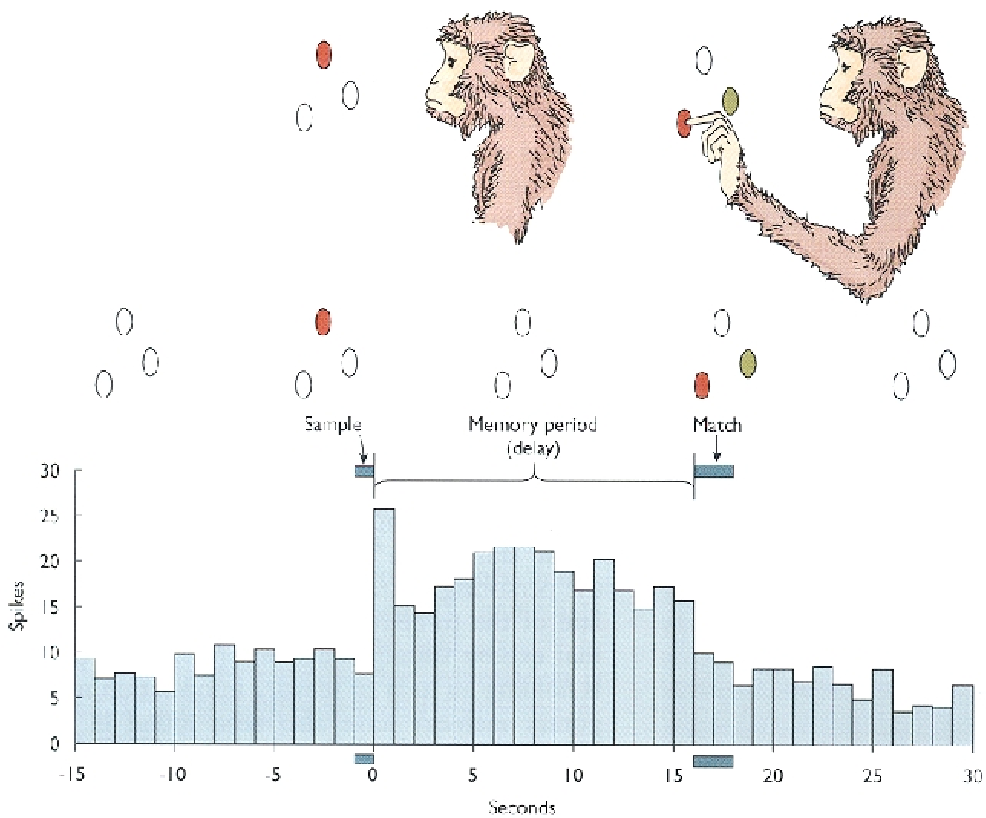
- ConnectivityMatrix.m
  - Key parameters:
    - n = number of cells in network
    - crad = connectivity radius (each cell as 2crad number of outgoing synapses
- ILIF_ExcNetwork.m
  - Key parameters:
    - Iapp = applied current vector, constant or pulse
    - gsyn = synaptic strength
    - taus = synaptic decay time constant

Excitatory Network Behaviors

- Synchrony
- Propagation of activity
- Reverberatory/persistent activity

Working memory

Delayed-match-to-sample task



Fuster J Neurophysiol 1973: Delayed response experiments in monkeys with recordings in prefrontal cortex

- Monkey is shown a food reward hidden under 1 of 2 objects
- Screen is lowered and door is locked to hide objects
- Screen is lifted and door is unlocked so monkey can retrieve reward

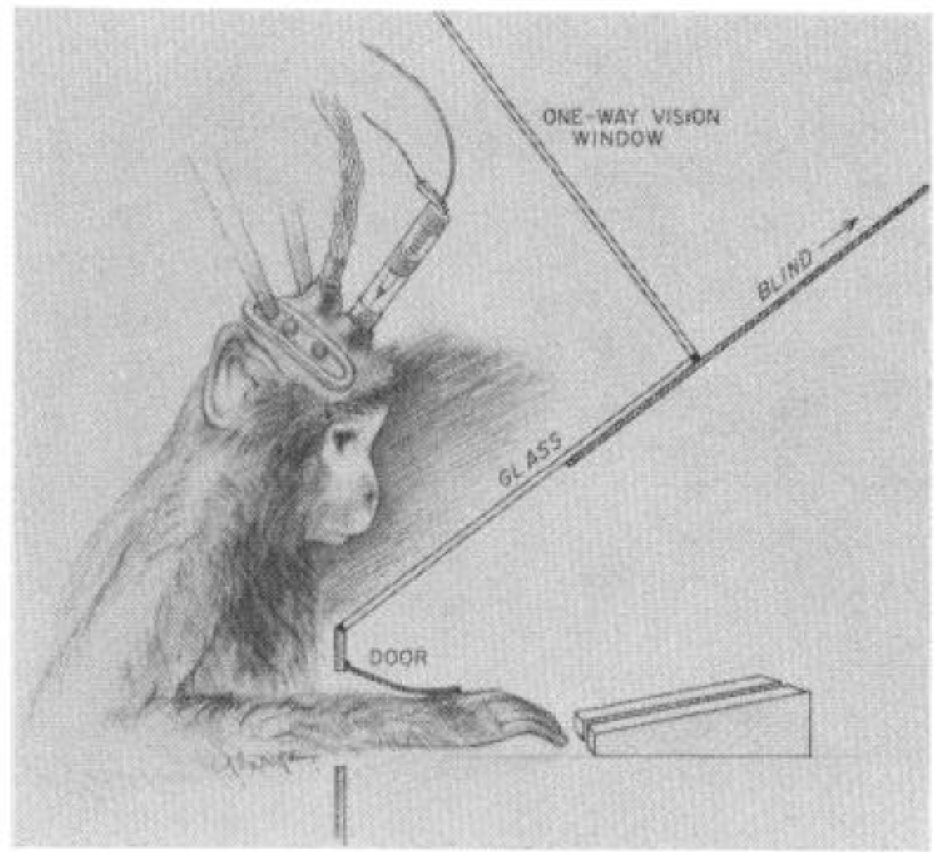


FIG. 1. Diagram of an experimental animal in the testing apparatus.

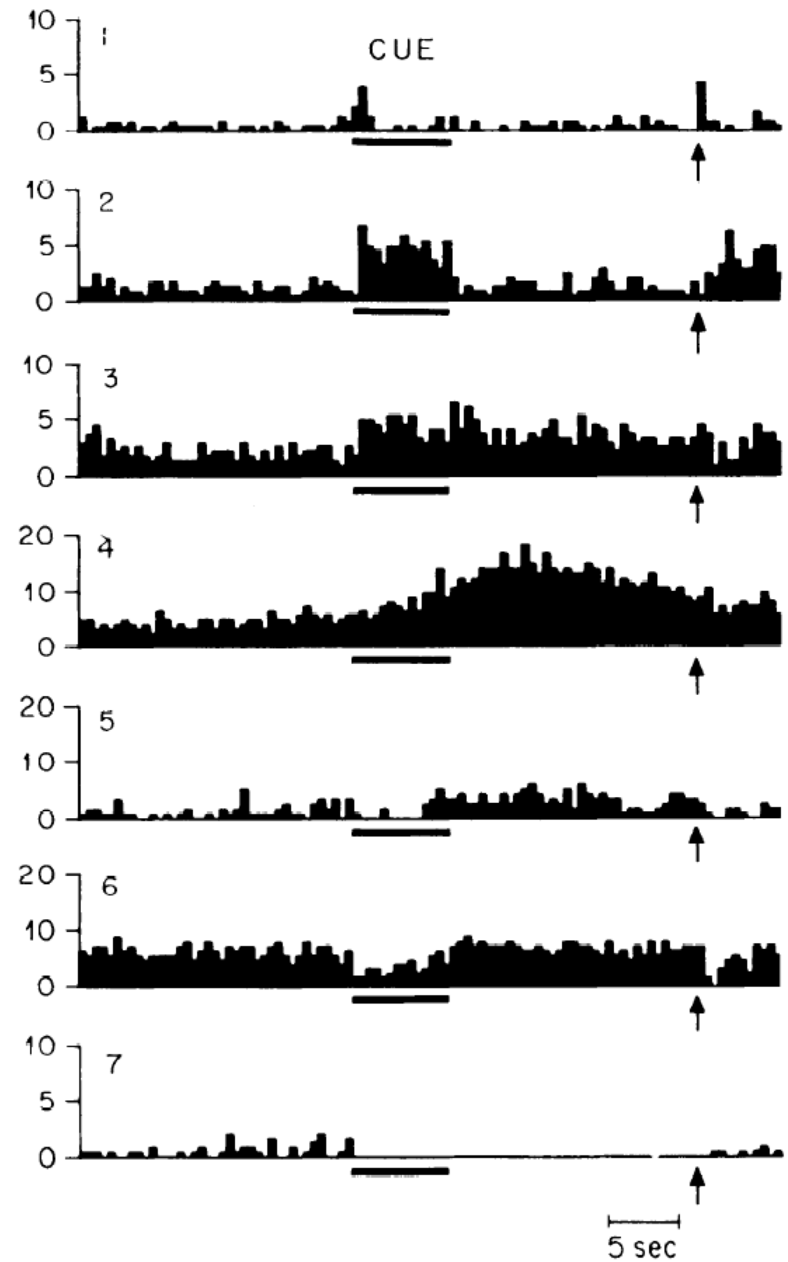


FIG. 2. Spike-frequency histograms from seven units in the prefrontal cortex during delayed-response trials with 18-sec delays. Each histogram (0.5-sec bins) represents the average discharge of a unit in the course of five trials. The temporal display begins at left with 20 sec of spontaneous pretrial discharge. The horizontal bar marks the cue period and the arrow, the end of the delay.

Fuster 1973

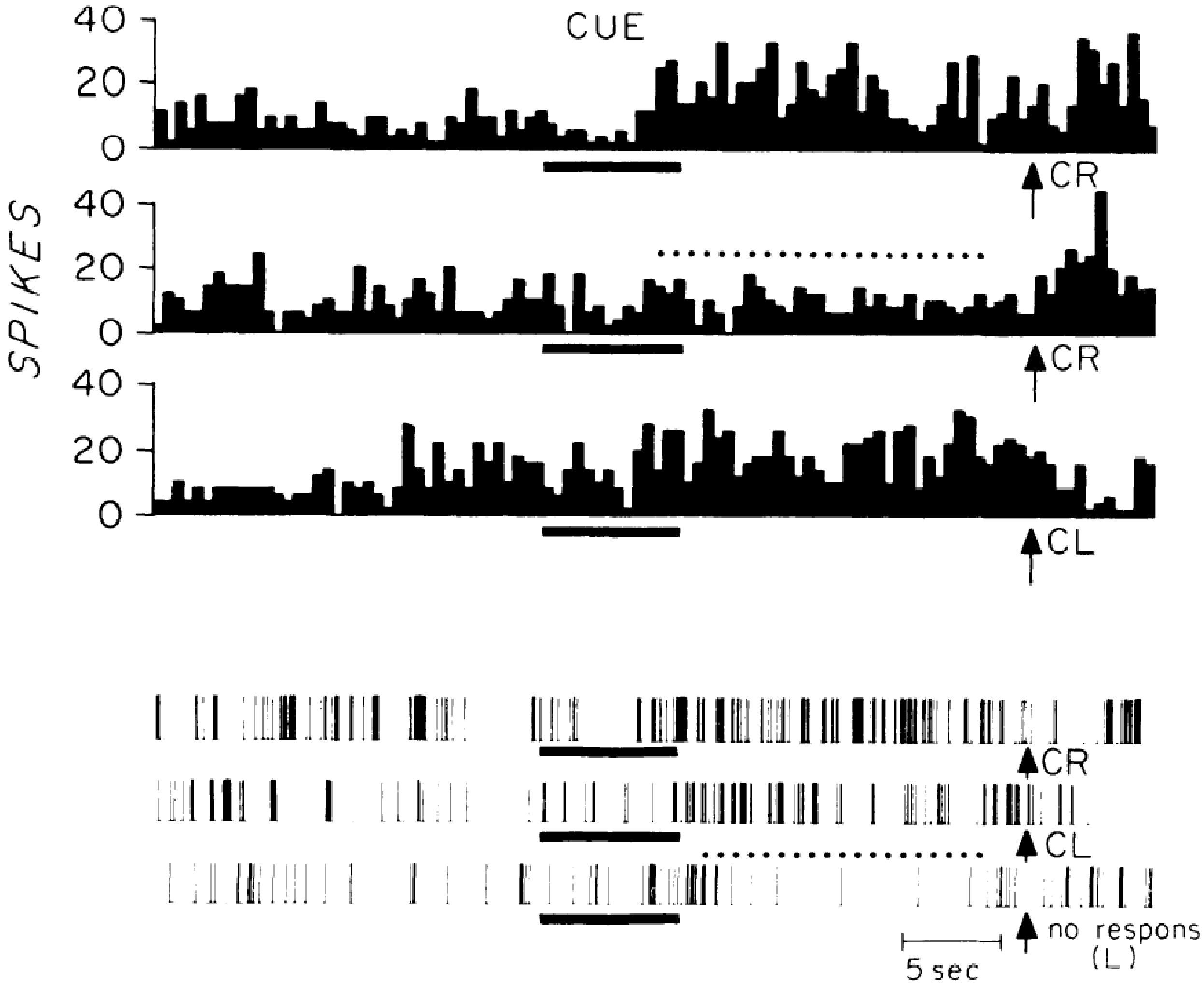


FIG. 10. Frequency histograms of the sum of spikes recorded by a microelectrode simultaneously from several prefrontal units—at least three could be identified by spike-amplitude differences. On the second of three delayed-response trials, monkey cries were used as distracting stimuli during the period marked by dots. Excerpts at the bottom represent three additional trials with the microelectrode in the same position and selecting by Schmitt-trigger only the unit from which the largest spikes were recorded. Distracting stimuli were presented during the delay of the third trial, which ended by failure of the animal to respond; (L) indicates position of the reward on that trial.

Fuster 1973

Short-term working memory

- Seems to rely on the maintenance of elevated firing rates in specific subpopulations of neurons rather than on synaptic plasticity, which might underlie long-term memory.

Durstewitz et al 2000

Funashi et al J Neurophysiol 1989: Oculomotor delayed response experiments in monkeys with recordings in prefrontal cortex

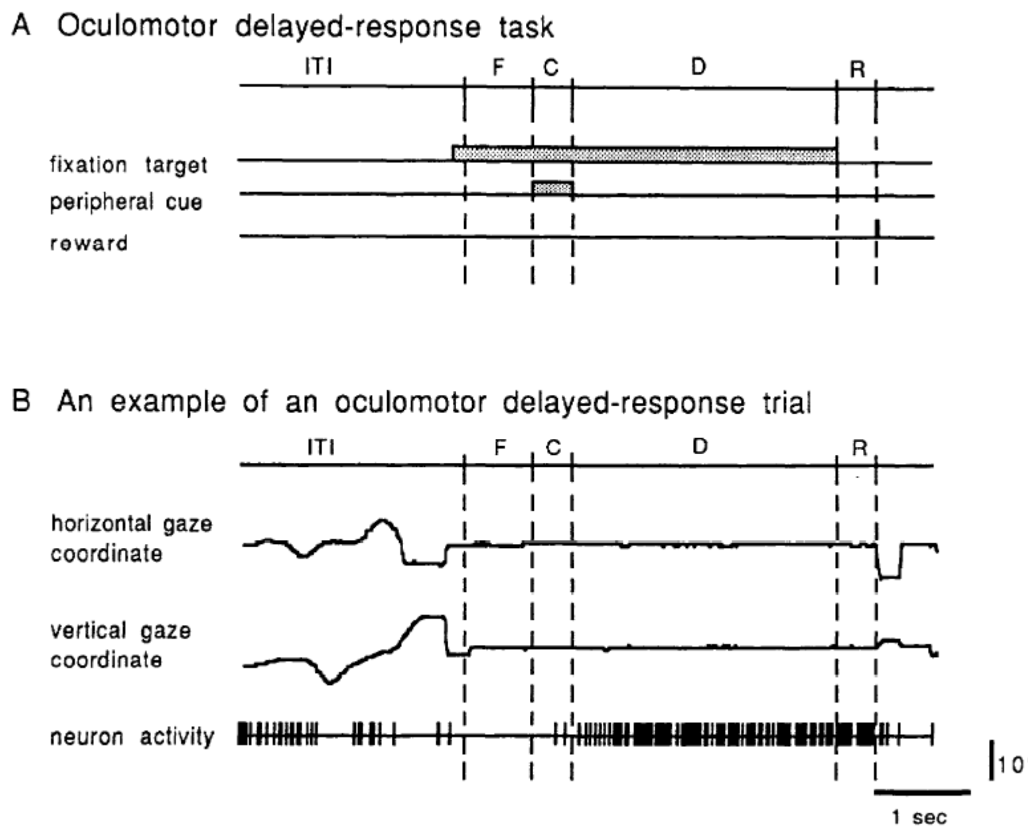
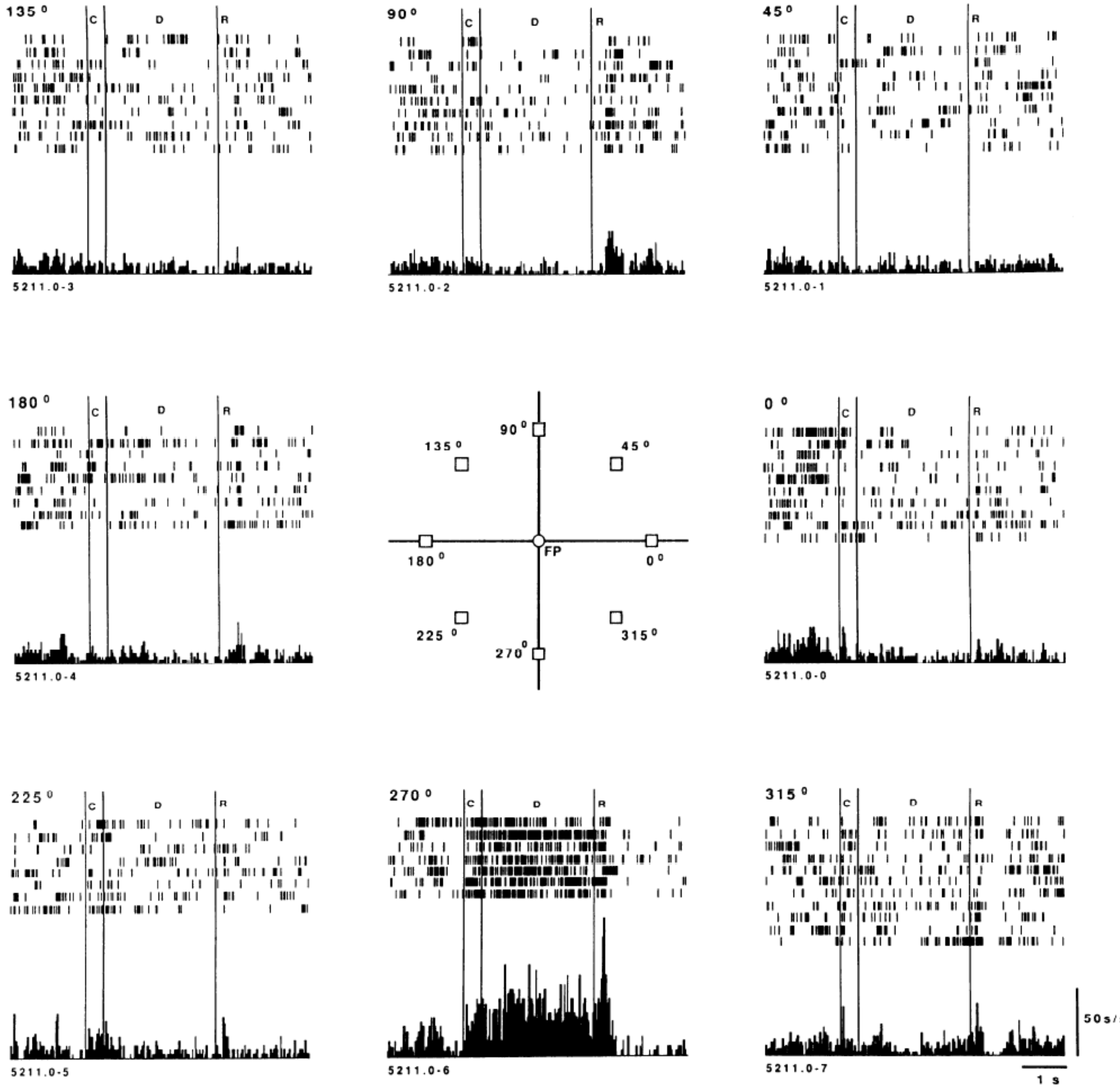
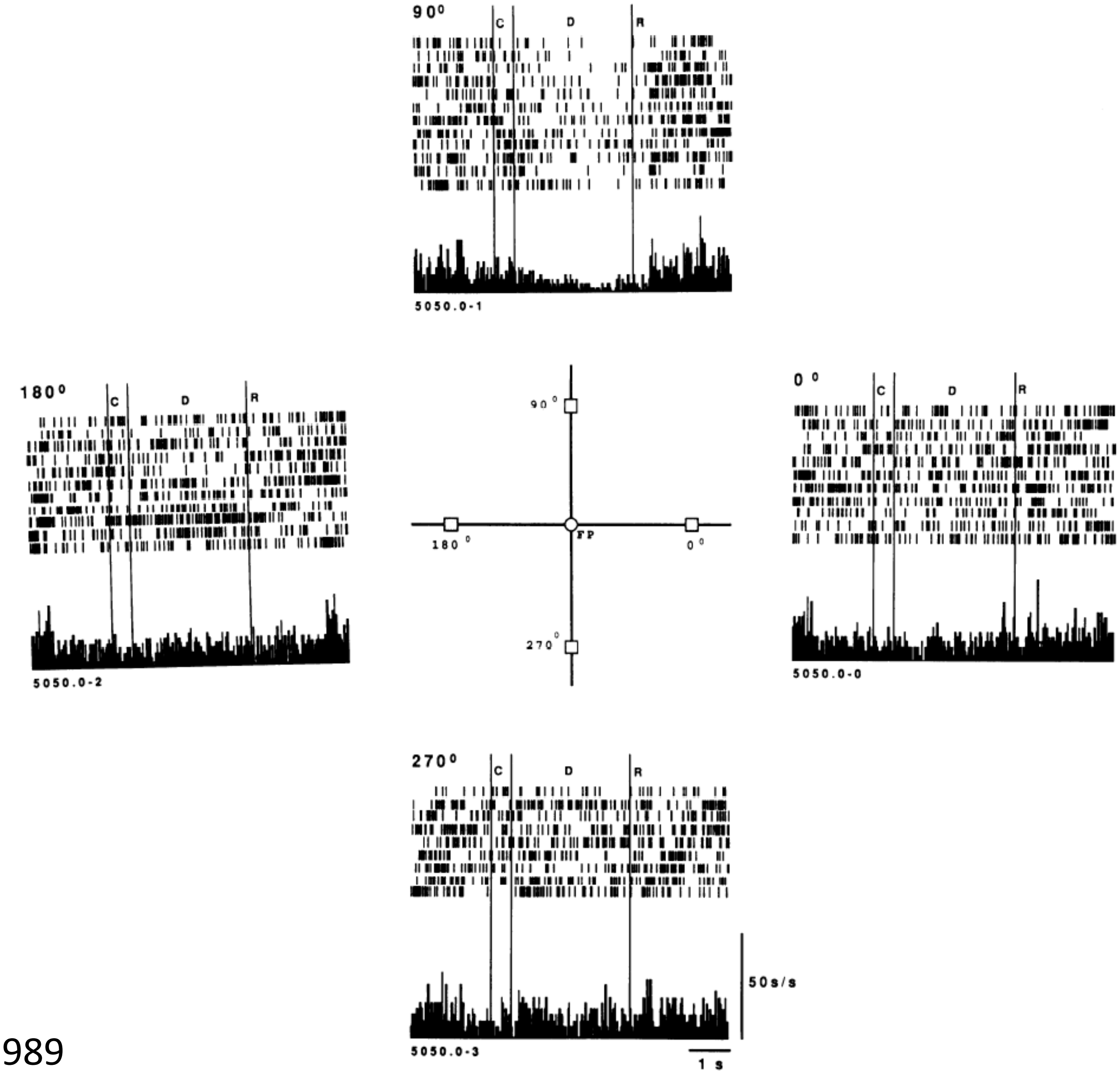


FIG. 1. *A*: temporal sequence of events in the oculomotor delayed-response task. *B*: eye movements and single neuron activity during an oculomotor delayed-response trial. ITI, intertrial interval; F, fixation period (0.75 s); C, cue period (0.5 s); D, delay period (3 s); R, response period (0.5 s).



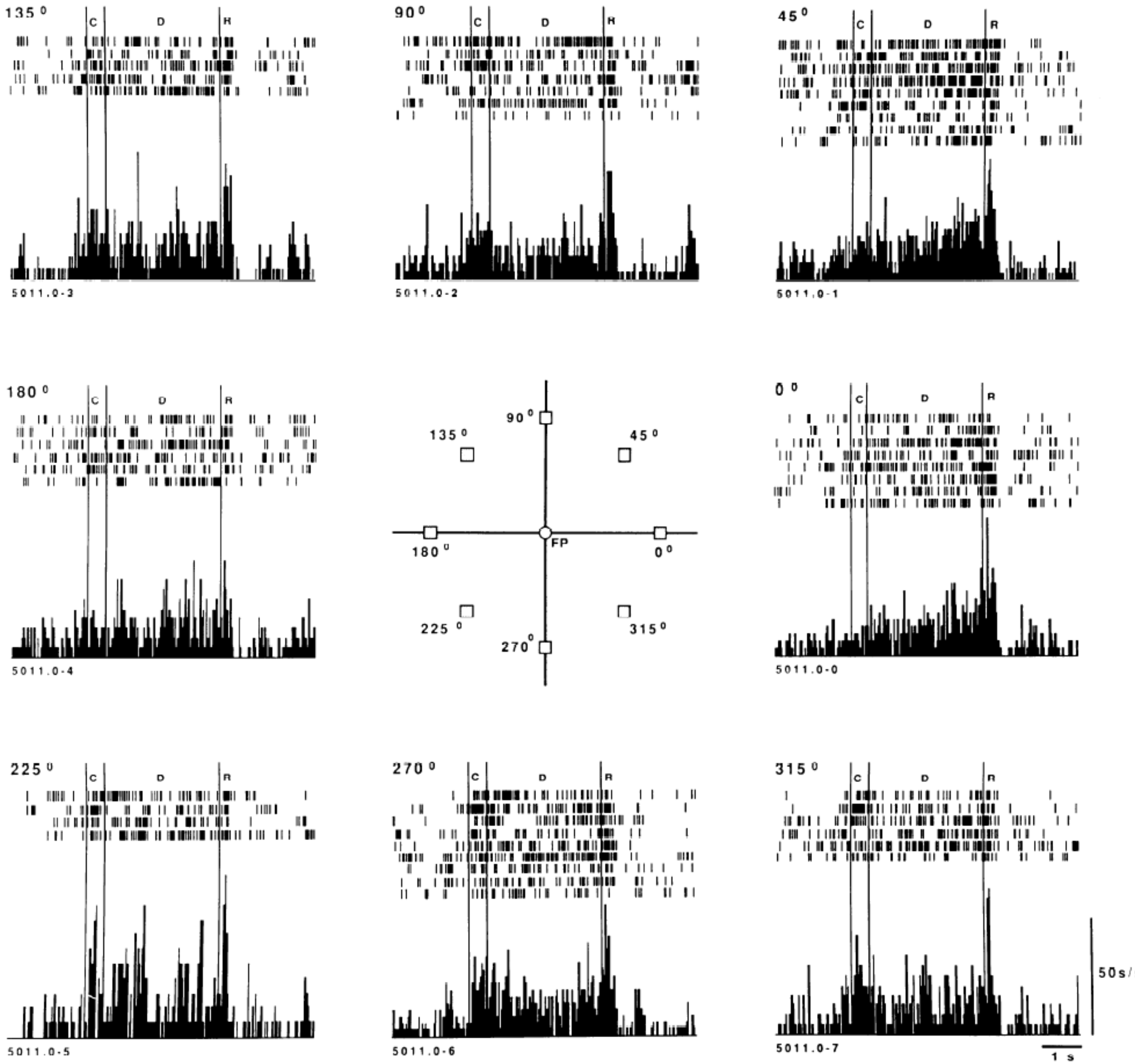
Funahashi et al 1989

Inhibited firing during delay period



Funahashi et al 1989

Omnidirectional response during delay period

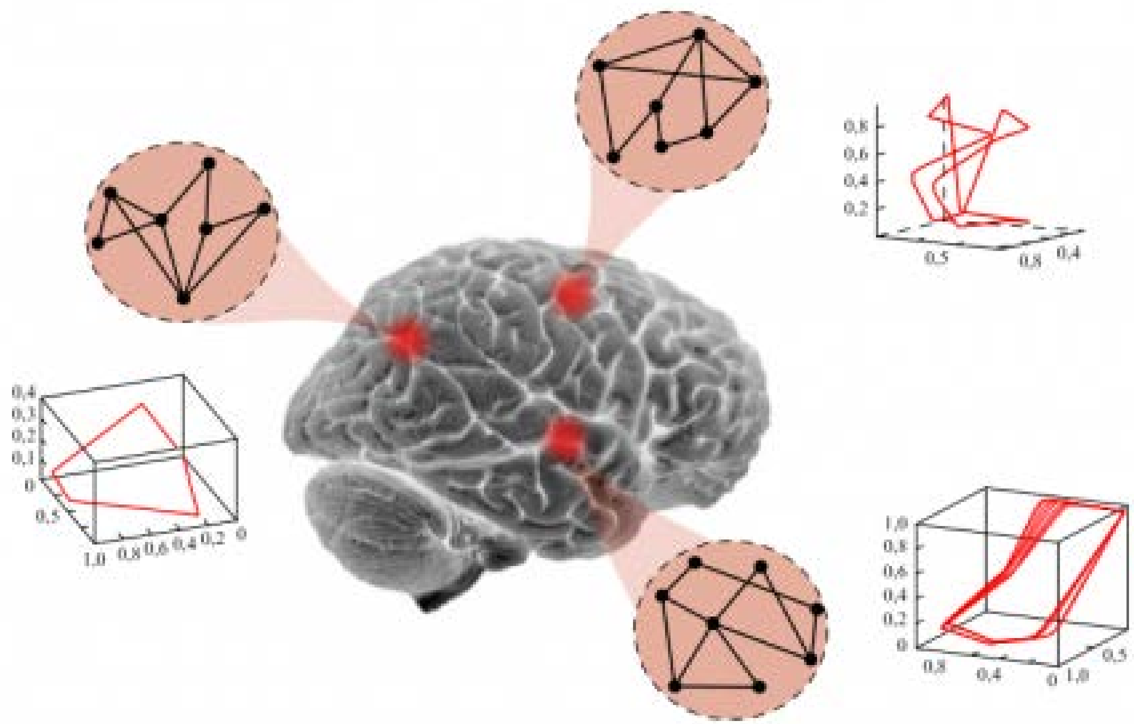


Funahashi et al 1989

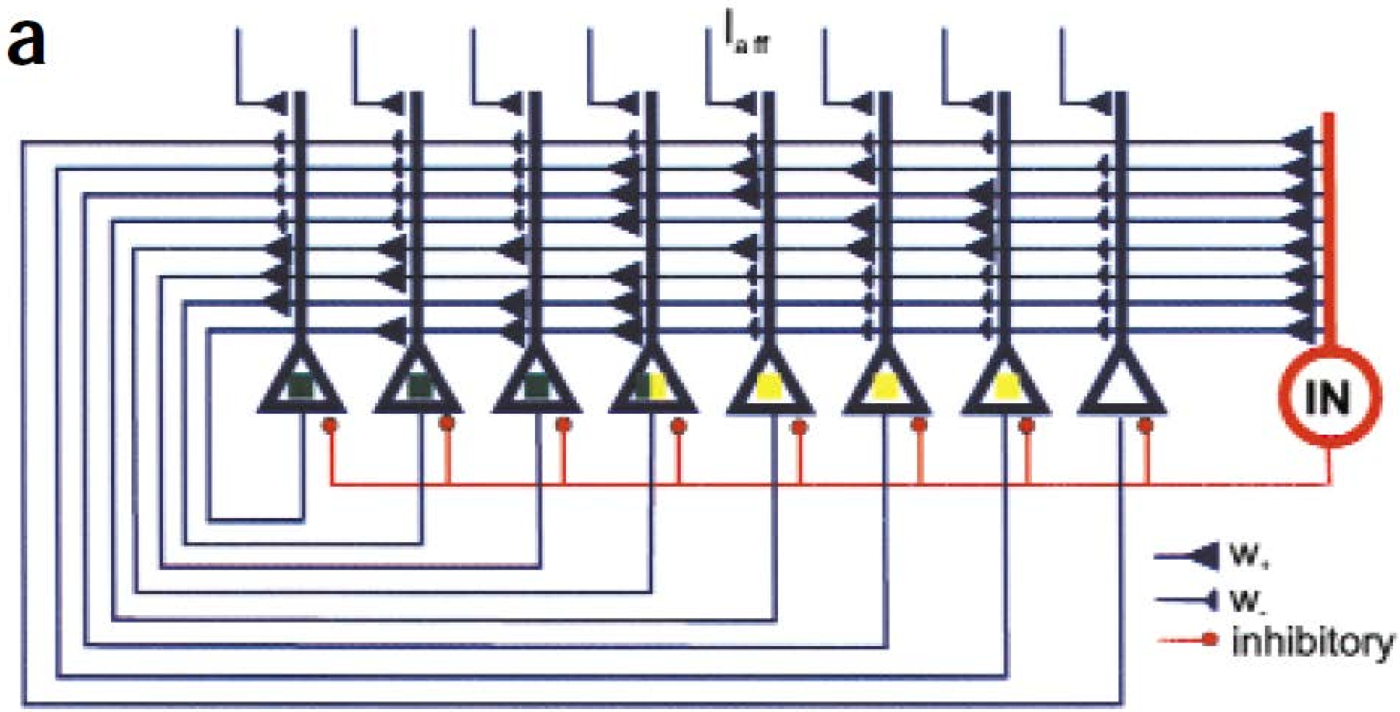
Attractors in brain networks

- During stimulus learning, synapses among an assembly of cells are strengthened to store the stimulus memory
- Re-exposure of the stimulus, reactivates the cell assembly
- Strong recurrent excitatory connections within assembly promote its sustained activity when stimulus is removed

Amit 1995



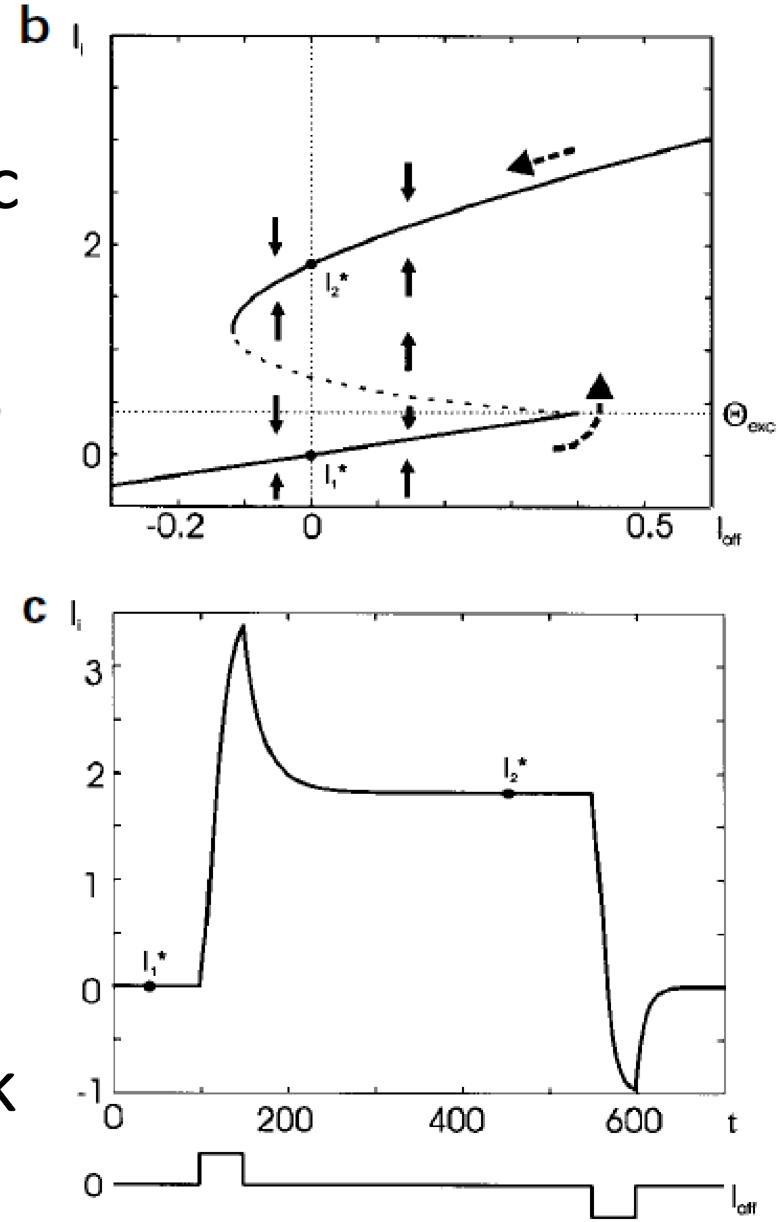
Simple attractor neural network



- Two cell assemblies coding for different objects (green and yellow boxes)
- Strong excitatory synapses within each assembly, weak synapses to other neurons
- Global feedback inhibition allows only 1 pattern to stay active at a time.

Durstewitz et al 2000

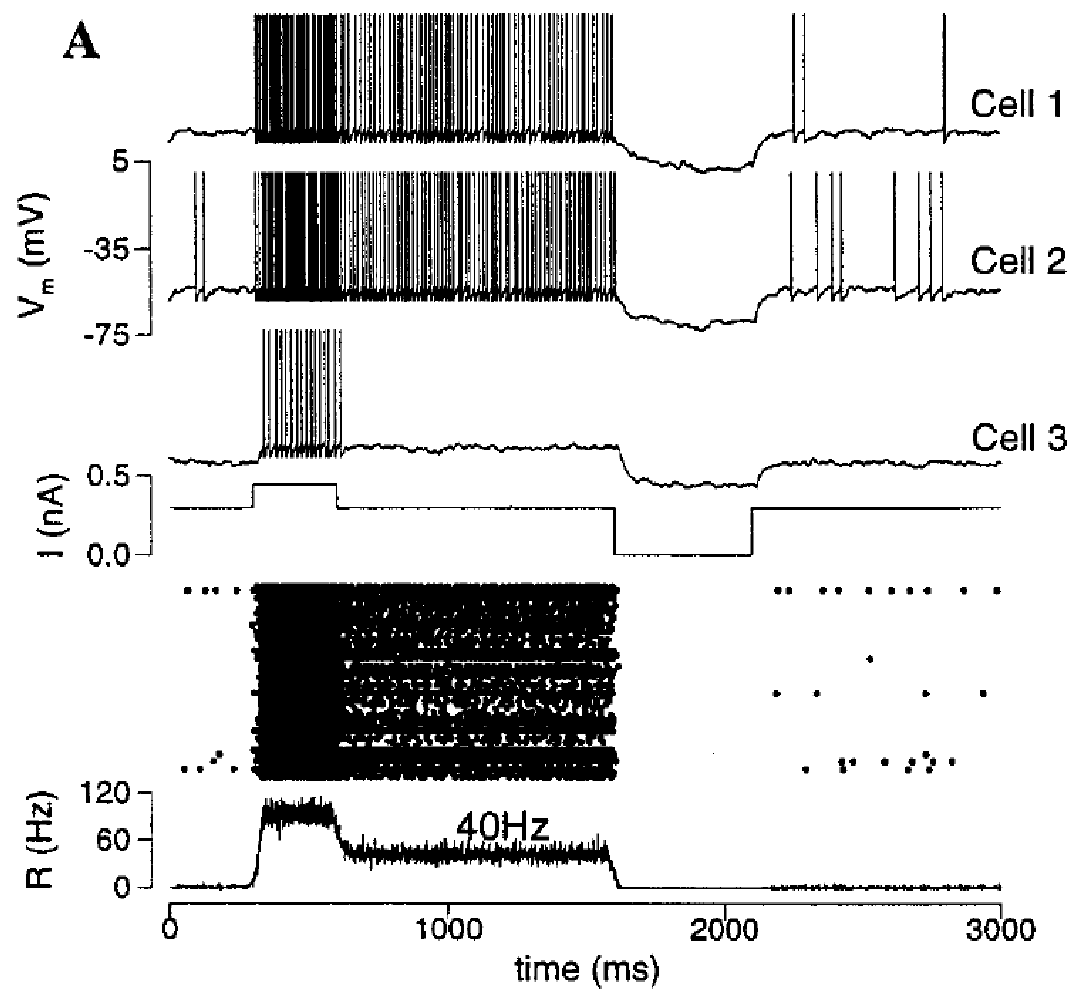
- In response to external input exciting an assembly, synaptic activity within the assembly can jump to a higher state
- When stimulus is removed, synaptic activity in the assembly remains elevated, i.e. network is in one of its attractor states
- Another external input is needed to kick assembly back down to its resting state



Durstewitz et al 2000

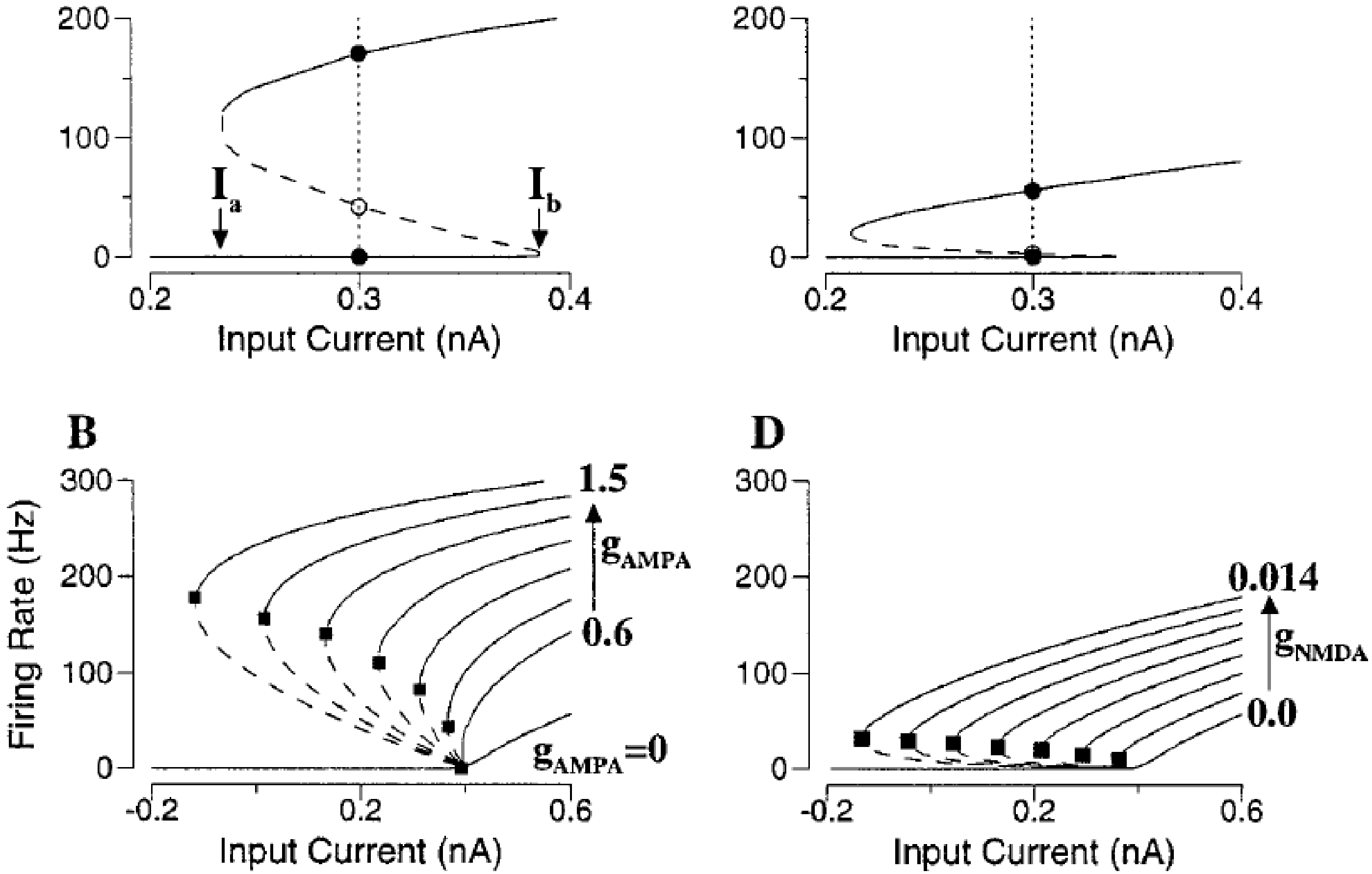
Attractor state/persistent activity in a large network of modified LIF neurons with excitatory synapses

- 1000 cells, all-to-all connectivity
- Heterogeneous cell properties
- Both AMPA and NMDA excitatory synaptic currents
- R = averaged firing rate across network



Wang 1999

Stability of attractor state depends on synaptic strength

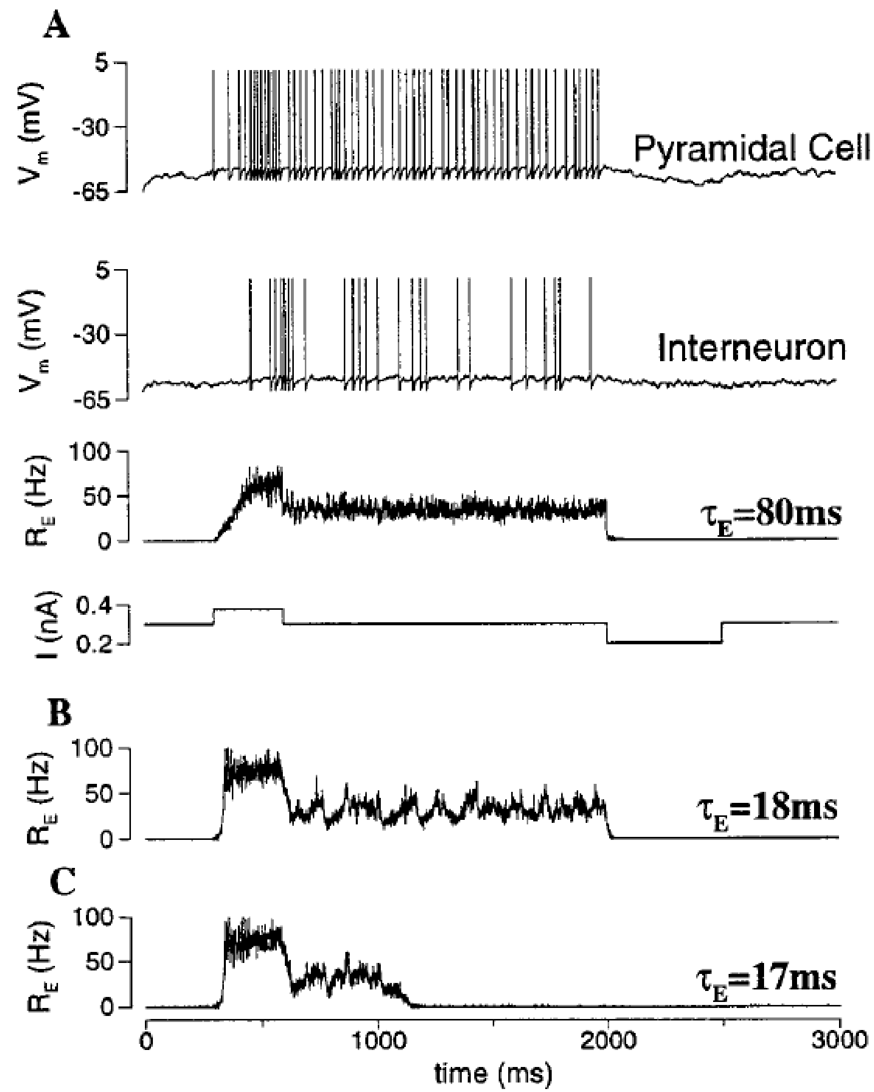


- Higher synaptic weight increases the external current interval at which persistent activity occurs
- Higher AMPA weight increases frequency of persistent activity

Wang 1999

Stability of persistent activity depends on synaptic decay rate

- Excitatory and inhibitory neurons with all-to-all coupling
- Excitatory synapse must have slow decay for stable persistent activity
- R_E = averaged firing rate of excitatory neurons
- τ_E = decay time constant of excitatory synapses



Wang 1999

Wang-Buzsaki neuron model

- Similar to Hodgkin-Huxley model
  - Fast (instantaneously activating Na+ current
  - K+ delayed rectifier current
  - Leak current
- Channel gating equations slightly modified so spikes are narrower

$$C\frac{dV}{dt} = g_{\mathrm{Na}} m_\infty(V)^3 h(V_{\mathrm{Na}} - V) + g_{\mathrm{K}} n^4 (V_{\mathrm{K}} - V) + g_L(V_L - V) + I$$

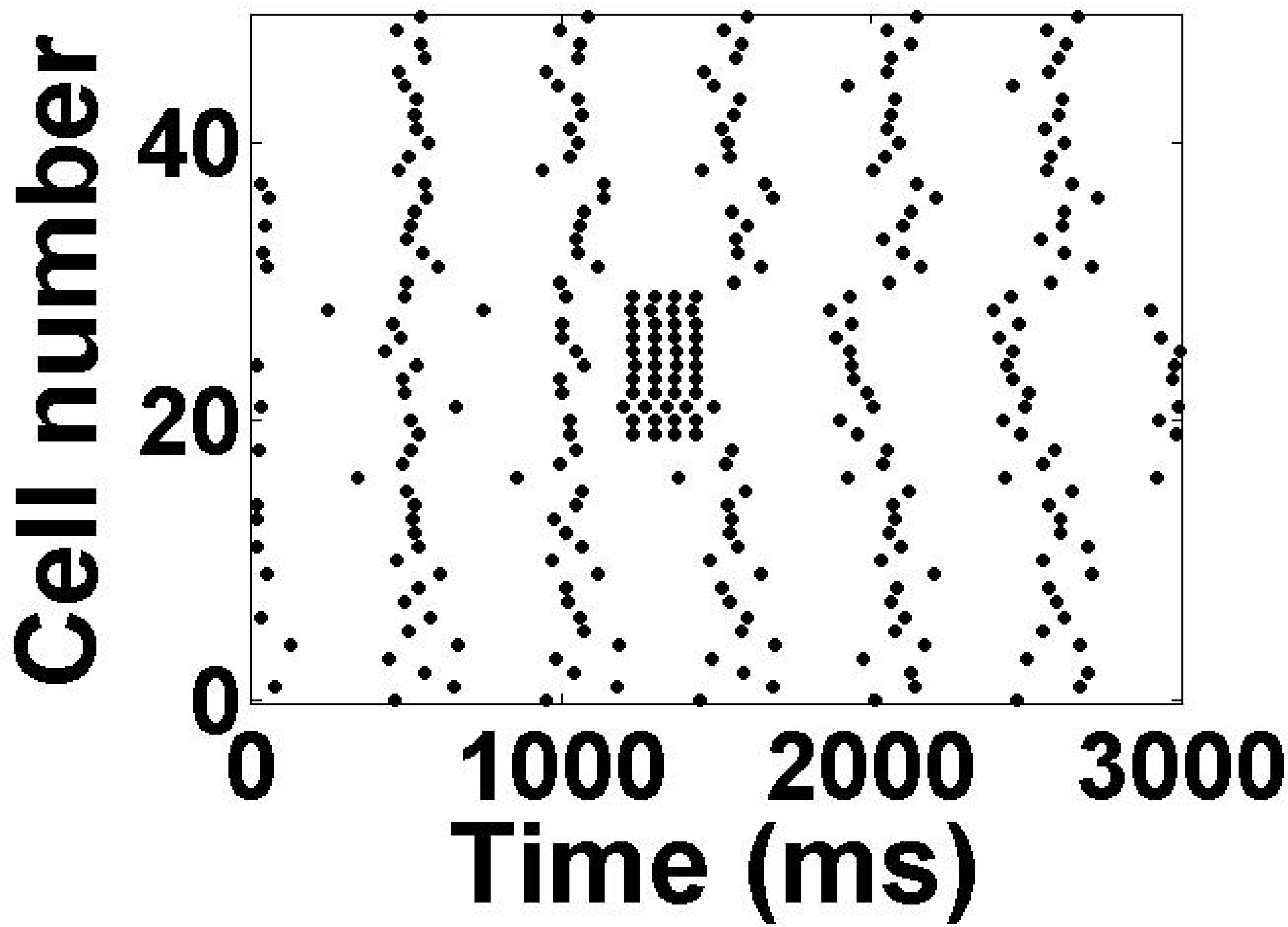
$$\frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)}$$

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

Reverberatory activity in excitatory networks

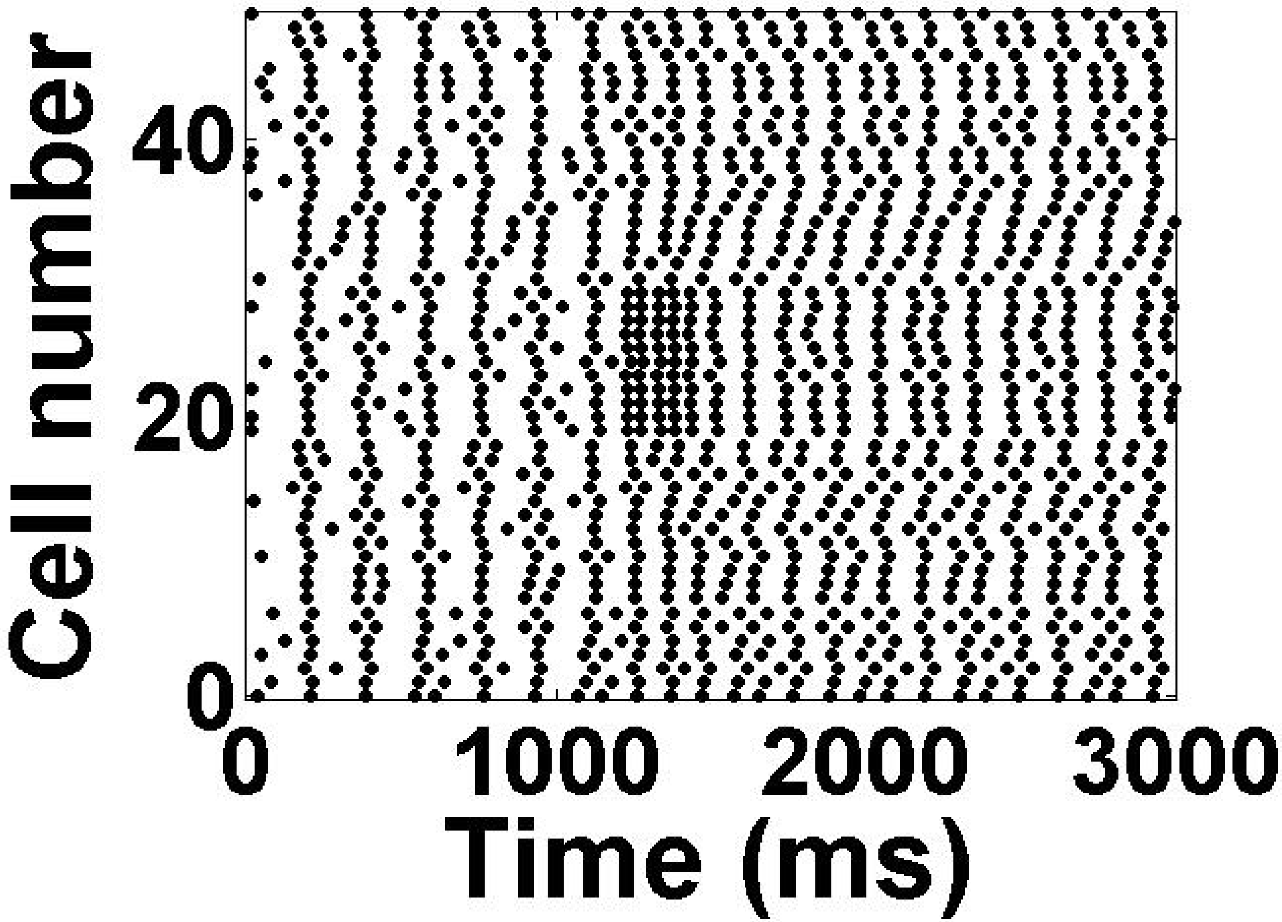
- 50 cell network of Wang-Buzsaki model neurons with all-to-all coupling
- Excitatory synapses
- Heterogeneous firing frequencies
  - I_{app} to each cell chosen uniformly from interval of values containing current threshold
- Cells 20-30 receive brief external input

Low frequency firing in network when cells are uncoupled



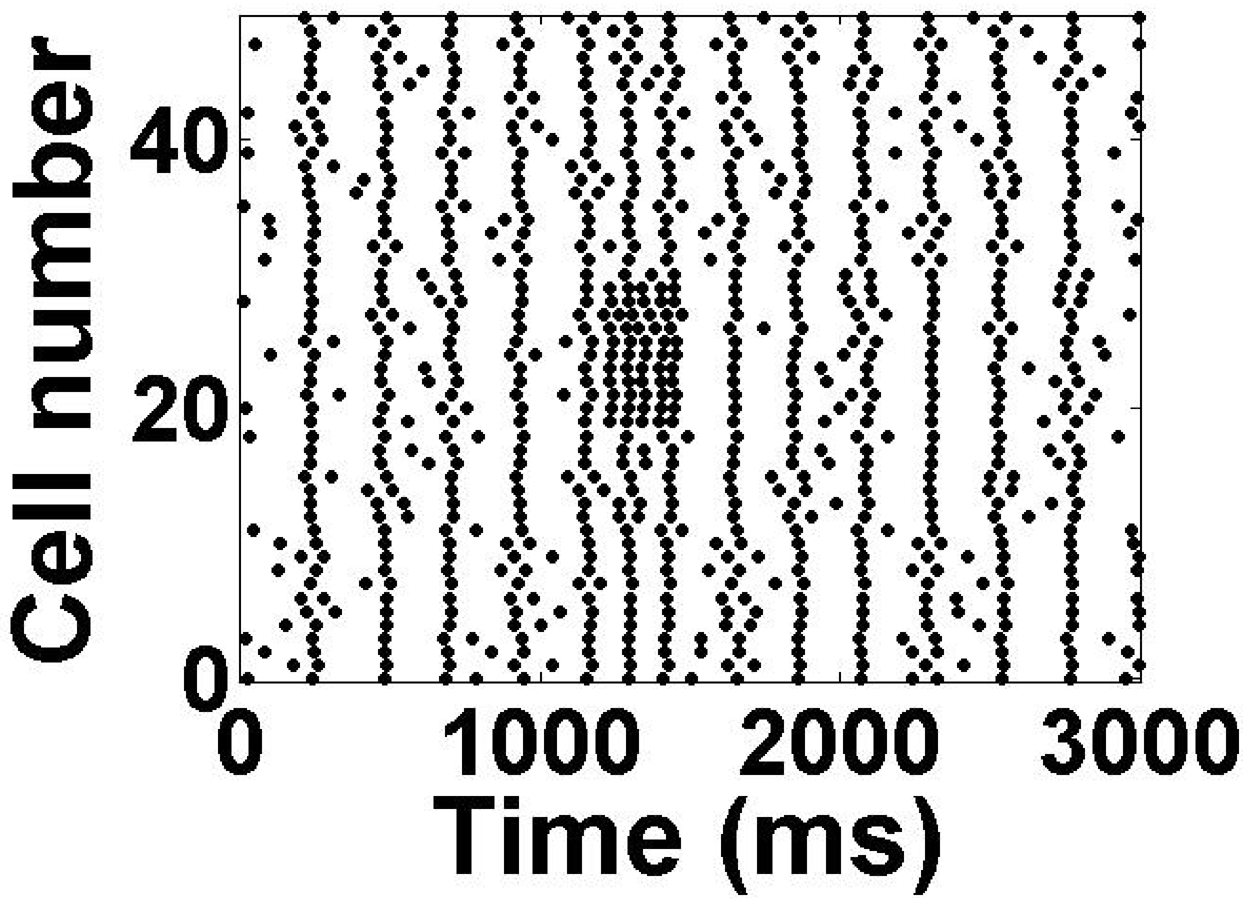
$g_{syn} = 0\ mS/cm^2$

Persistent activity



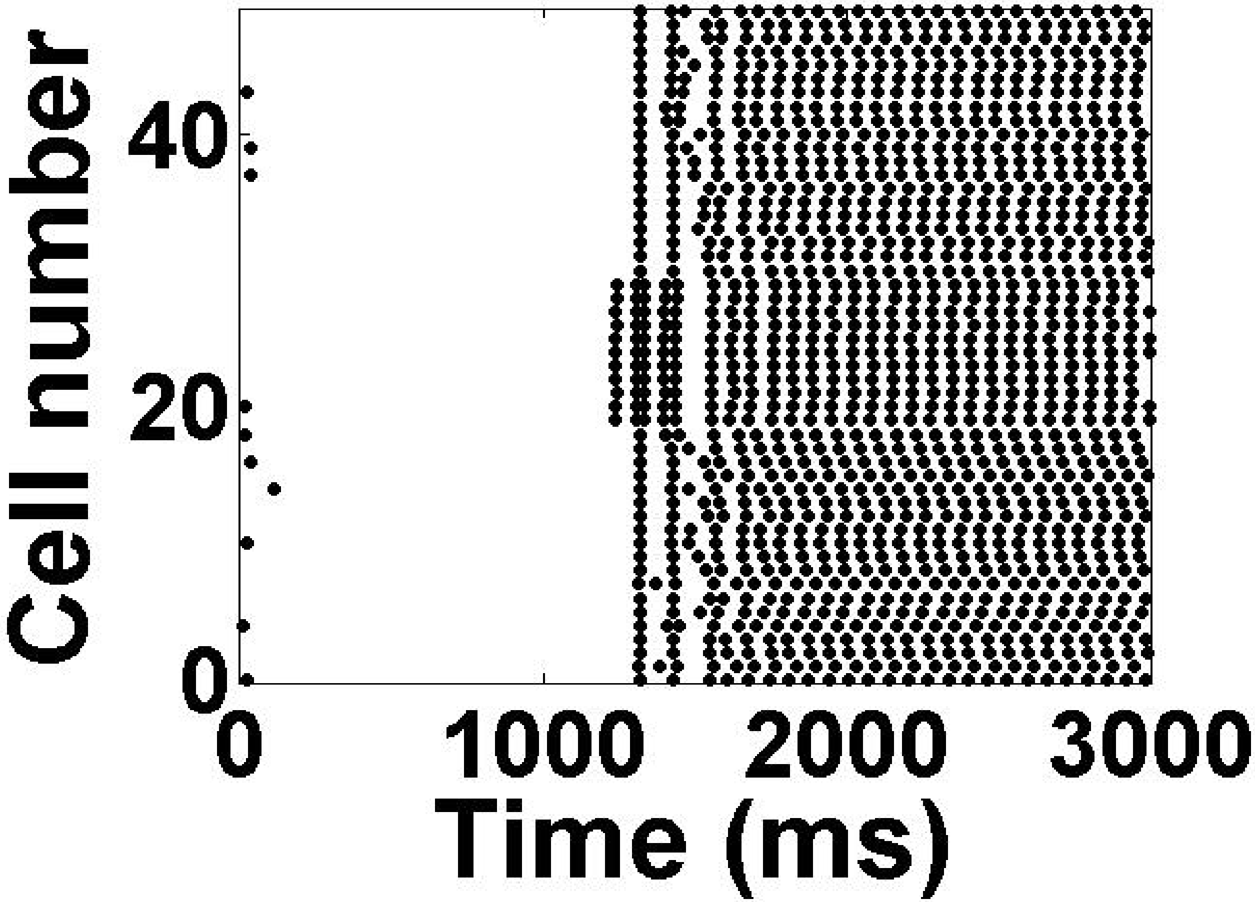
g_{syn} = 0.001 mS/cm^2, taus = 2ms

Weaker synaptic strength does not support persistent activity



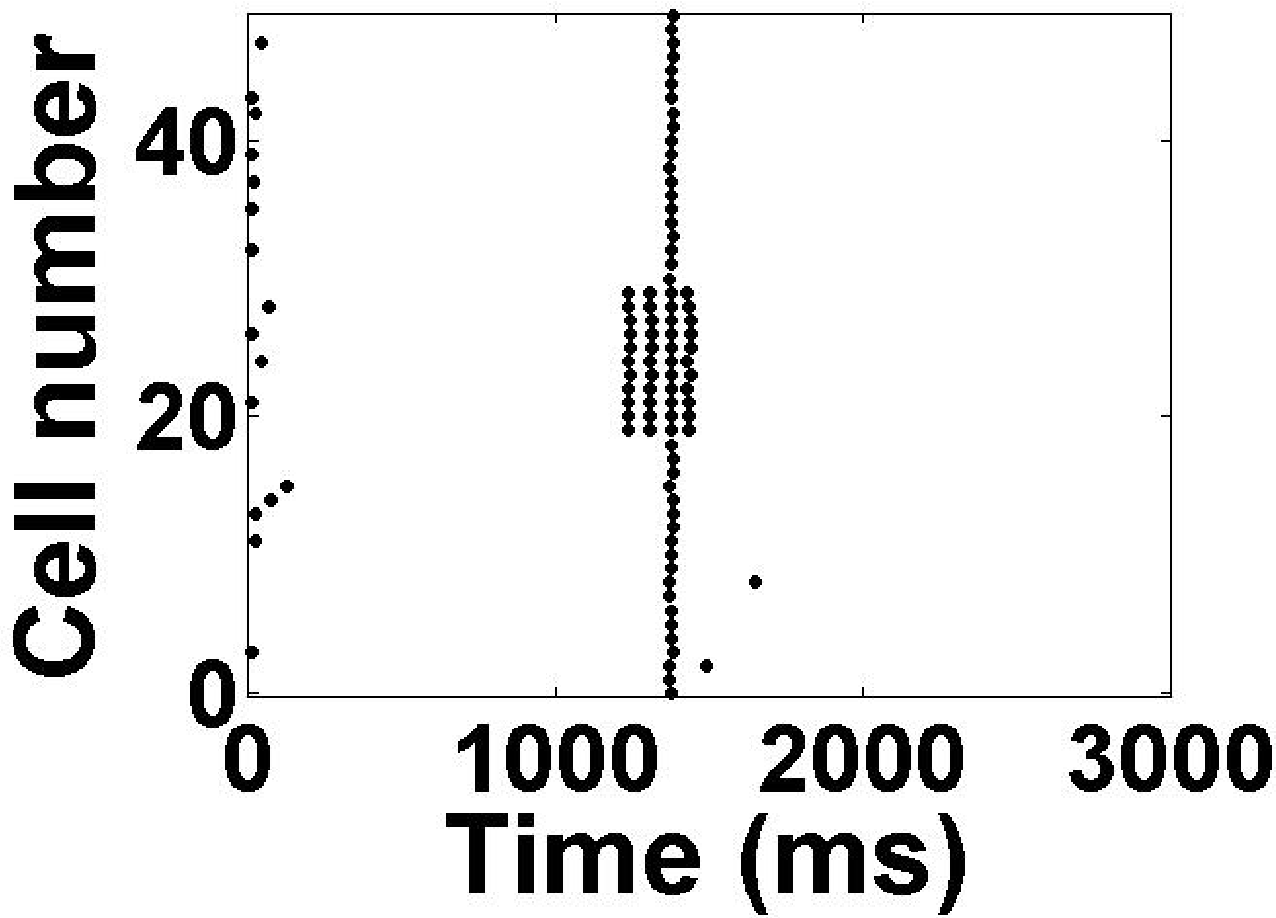
- g_{syn} = 0.0009 mS/cm^2, taus = 2ms

Silent cells can be induced into persistent firing with longer lasting synaptic current



- I_{app} lower, g_{syn} = 0.001 mS/cm^2, taus = 3ms

When synaptic current decays quickly, persistent activity does not occur



- I_{app} low, g_{syn} = 0.001 mS/cm^2, taus = 2ms

Small excitatory network generating reverberatory activity

- 1-dimensional network of 10 cells with all-to-all coupling (synaptic weight `gsyn`)
- Wang-Buzsaki model neurons
- Synaptic current modeled with instantaneous activation and exponential decay, governed by `taus`
- Matlab codes
  - ConnectivityMatrix.m
  - WBnetwork.m, WBeqns.m
  - Output:
    - spiketimes = (time of spike, cell number)
    - Average cell frequencies before and after current pulse

Inhibitory network model

- 1-dimensional ring network of 50 cells
- Cells modeled by ILIF model in Regular Spiking and Fast Spiking parameter regimes
- All-to-all coupling
- Synaptic current modeled with instantaneous activation and exponential decay

Matlab codes:

- ConnectivityMatrix.m
- ILIFNetwork_clusters.m

ILIFNetwork_clusters.m

Output:

- spiketimes = (time of spike, cell number)
- freqs = average frequency of each cell
- nisis = interspike interval between each spike fired in the network

Printed on screen:

- Average of cell frequencies (from freqs)
- Average network frequency (mean nisis)

Inhibitory network behaviors depend on cell firing frequency and time scale of synaptic currents

- If cells fire at low frequency and synaptic inhibition is fast, then get clusters of synchronous firing
  - Number of clusters depends on relationship between intrinsic firing frequency and decay time constant of synaptic current
- If cells fire at high frequency and synaptic inhibition is slower, then get full network synchronization
  - Frequency of population rhythm depends on synaptic current magnitude and decay time constant