Exploring a Simple Discrete Model of Neuronal Networks

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Joint work with
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Each excitatory (E-) cell satisfies

$$\begin{aligned}
\frac{dv_i}{dt} &= f(v_i, w_i) - g_{EI} \sum s_j^I (v_i - v_{syn}^I) \\
\frac{dw_i}{dt} &= \epsilon g(v_i, w_i) \\
\frac{ds_i}{dt} &= \alpha(1 - s_i) H(v_i - \theta_E) - \beta s_i.
\end{aligned}$$

Each inhibitory (I-) cell satisfies

$$\begin{aligned}
\frac{dv_i^I}{dt} &= f(v_i^I, w_i^I) - g_{IE} \sum s_j (v_i^I - v_{syn}^E) - g_{II} \sum s_j^I (v_i^I - v_{syn}^I) \\
\frac{dw_i^I}{dt} &= \epsilon g(v_i^I, w_i^I) \\
\frac{dx_i^I}{dt} &= \epsilon \alpha_x (1 - x_i^I) H(v_i^I - \theta_I) - \epsilon \beta_x x_i^I \\
\frac{ds_i^I}{dt} &= \alpha_I (1 - s_i^I) H(x_i^I - \theta_x) - \beta_I s_i^I.
\end{aligned}$$

Mathematical Neuroscience is Difficult!

- Individual neurons are usually modeled by the the Hodgkin-Huxley Equations.
  - Nonlinear ODEs involving multiple time scales.
  - Hard to analyze both mathematically and computationally.
- Neuronal networks involve a large number of individual neurons.
  - Details of the connectivity not usually known.
  - Hard to analyze how connectivity influences ODE dynamics.

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Fortune cookie: Doing the impossible is kind of fun.

Some Simple Facts

The following is true in at least some neuronal networks.

- Neurons fire or are at rest.
- After a neuron has fired, it has to go through a certain *refractory period* when it cannot fire.
- A neuron will fire when it has reached the end of its refractory period and when it receives firing input from a specified minimal number of other neurons.

Can we build a simple and useful model of neuronal networks based on these observations?

A Discrete Dynamical System Model

A directed graph $D = [V_D, A_D]$ and integers n (size of the network), p_i (refractory period), th_i (firing threshold).

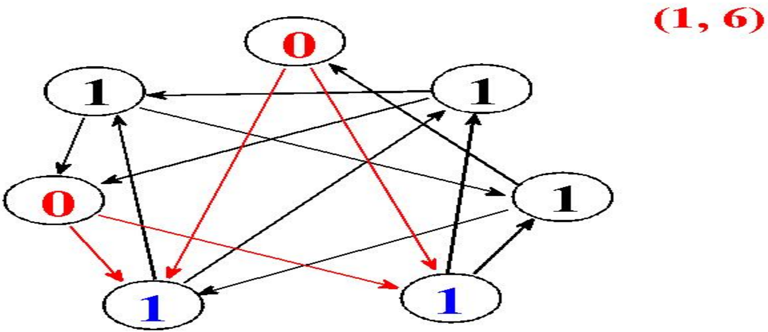
A state $\vec{s}(t)$ at the discrete time t is a vector:
$\vec{s}(t) = [s_1(t), \ldots, s_n(t)]$ where $s_i(t) \in \{0, 1, \ldots, p_i\}$ for each i.
The state $s_i(t) = 0$ means neuron i fires at time t.

Dynamics on the discrete network:

- If $s_i(t) < p_i$, then $s_i(t+1) = s_i(t) + 1$.
- If $s_i(t) = p_i$, and there exists at least th_i neurons j with $s_j(k) = 0$ and $< j, i > \ \in A_D$, then $s_i(t+1) = 0$.
- If $s_i(t) = p_i$ and there do not exist th_i neurons j with $s_j(t) = 0$ and $< j, i > \ \in A_D$, then $s_i(t+1) = p_i$.

An Example

Assume that refractory period$= 1$ and threshold$= 1$.



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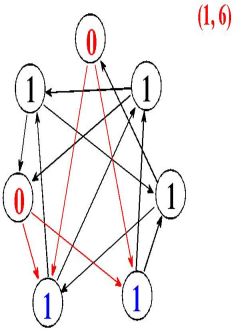

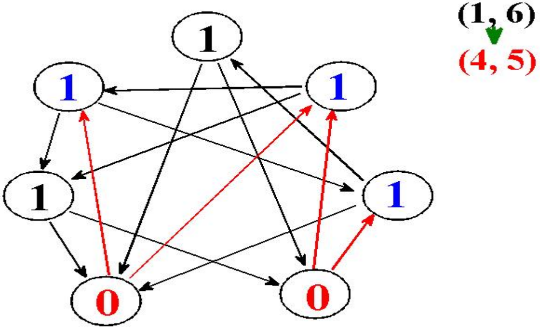

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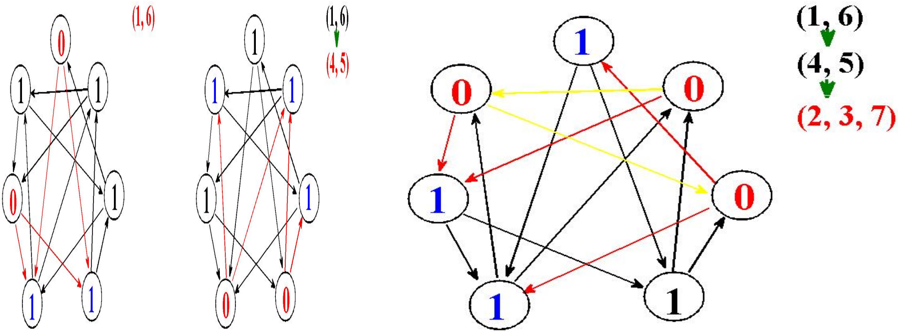

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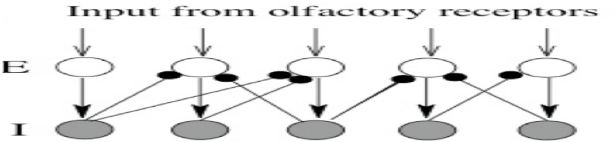
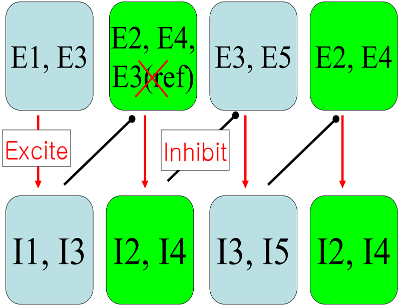
Is Modeling with Discrete Time Steps Realistic?

Experimentalists observed that there are parts of real brains (e.g. antennal lobe of insects, olfactory bulb of mammals) where the firing activity shows distinctive intervals during which some neurons fire together while the other neurons are at rest.

Are there ODE models of neuronal networks that predict this type of dynamics?

An Architecture





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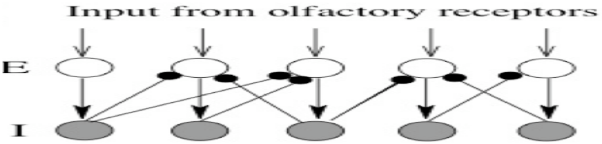
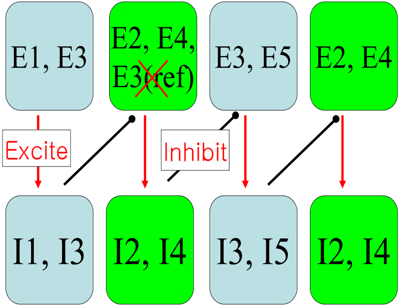


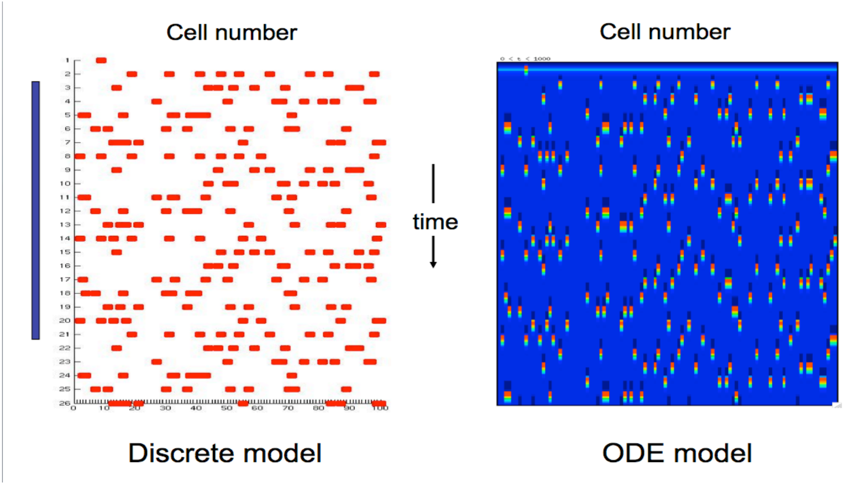


$$
\begin{array}{lcl}
E1 & \rightarrow & E2, E3 \\
E2 & \rightarrow & E3 \\
E3 & \rightarrow & E2, E4 \\
E4 & \rightarrow & E5 \\
E5 & \rightarrow & E4
\end{array}
$$

Assume: E-cells can excite one another v
interneurons.

The ODE Model Predicts Discrete Episodes

Consider 100 E-cells and 100 I-cells. Each E-cell excites one I-cell and each I-cell inhibits nine E-cells.



Two Research Problems

- When can we reduce the differential equations model to the discrete model?
- What can we prove about the discrete model?

Reducing Neuronal Networks to Discrete Dynamics,

by Terman D, Ahn S, Wang X, Just W, Physica D. 2008

Theorem

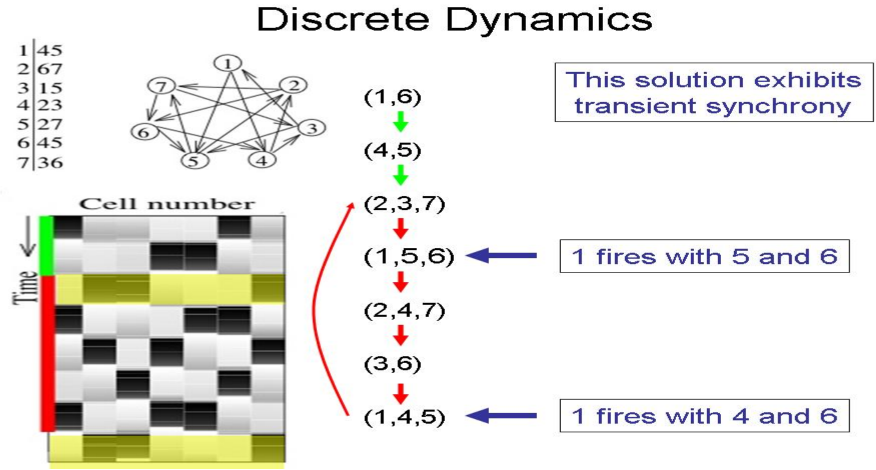
For the network architecture described above, if the intrinsic and synaptic properties of the cells are chosen appropriately, then there is an exact correspondence between solutions of the continuous and discrete systems for any connectivity between the excitatory and inhibitory cells.

What Properties are we Interested in?

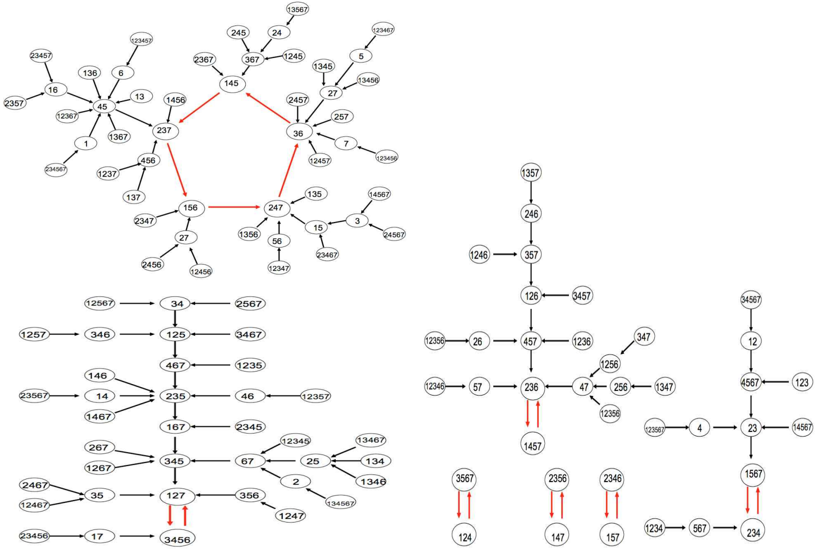
For a given discrete model (that is, specified connectivity digraph, refractory periods, firing thresholds) we may ask about the (possible, maximal, average)

- Lengths of the attractors.
- Number of different attractors.
- Lengths of transients.

Assume that refractory period= 1 and threshold= 1.



Different Transients and Attractors



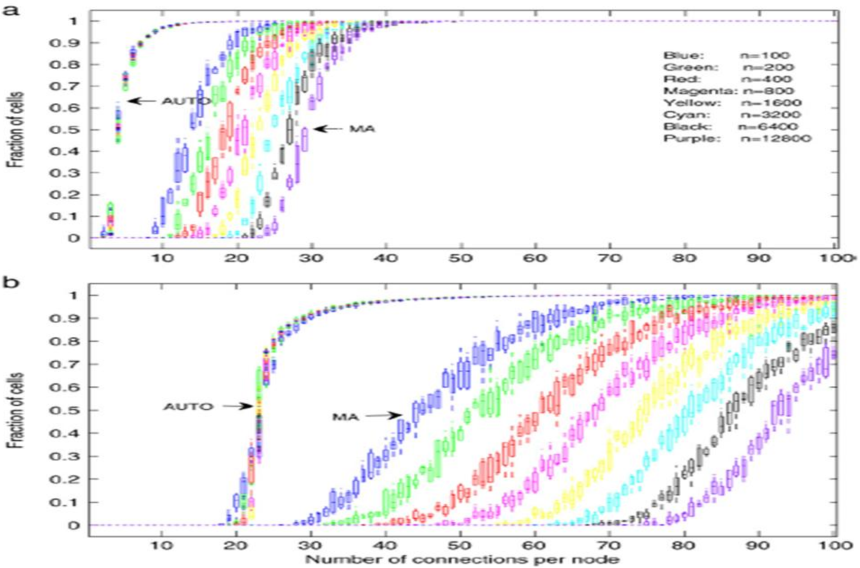
Some Special Objects

- $\vec{s}_{\vec{p}} = [p_1, \dots, p_n]$ is the only steady state attractor.
- A *minimal attractor* is one in which each neuron either never fires or fires as soon as it reaches the end of its refractory period.
- A *fully active* attractor is one in which every neuron fires at some time.
- An *autonomous set* consists of neurons that fire as soon as they reach the end of their refractory periods, regardless of the dynamics of neurons outside of this set.

Random Connectivities

- For given n, we randomly generate a digraph with n nodes by including each possible arc $< i, j >$ with probability $\rho(n)$; independently for all arcs (Erdős-Rényi random digraph).
- We randomly generate many initial conditions.
- We collect statistics on the proportion of initial states that are in minimal attractors, fully active minimal attractors, as well as the size of the largest autonomous set.
- How do these properties depend on $\rho(n)$?

Results of the Simulations Just W, Ahn S, Terman D, Physica D. 2008



Minimal Attractors in Digraph System Models of Neuronal Networks, by Just W, Ahn S, Terman D, Physica D. 2008

Theorem

1. *The first phase transition at $\rho(n) \sim \frac{\ln n}{n}$:*
   - *Above this threshold: a generic initial state belongs to a fully active minimal attractor.*
   - *Below this threshold: a generic initial state will not belong to a minimal attractor.*
2. *The second phase transition at $\rho(n) \sim \frac{c}{n}$:*
   - *Above this threshold: the fraction of nodes that belong to the largest autonomous set will rapidly approach one as ρ increases.*
   - *Below this threshold: this fraction will rapidly dwindle to zero.*

Directions for Further Research

- Another phase transition was detected for $\rho(n) \sim \frac{1}{n}$. Systematically explore what is going on in this region.
- Explore these phenomena for random digraphs other than Erdős-Rényi random digraphs (e.g., scale-free degree distributions).

Some Special Digraphs

- Cyclic digraphs.
- Cyclic digraphs with one shortcut.
- Hamiltonian digraphs: There is a Hamiltonian cycle (a directed cycle that visits every node exactly once).
- Strongly connected digraphs: There is a directed path from every node to every other node.

What kind of dynamical properties are implied by these special connectivities?

Theorem

Let $\vec{p} = [p_1, \ldots, p_n], \vec{th} = [1, \ldots, 1] >$, *and* $p^* = \max \vec{p}$. *Then*

- *The length of any transient is at most* $\max\{n + p^* - 1, 3n - 2\}$.
- *The length of any attractor is a divisor of* n.
- *The number of different attractors is equal to the number of different necklaces consisting of* n *black or red beads where all the red beads occur in blocks of length that is a multiple of* $p^* + 1$. *It is equal to*

$$\sum_{k=1}^{\lfloor \frac{n}{p^*+1} \rfloor} \left[\frac{1}{n - kp^*} \sum_{a \in \{\textit{divisors of } \gcd(k, n-kp^*)\}} \phi(a) \binom{\frac{n-kp^*}{a}}{\frac{k}{a}} \right] + 1,$$

where ϕ *is the Euler's phi function.*

Empirical Results on Strongly Connected Digraphs

Sungwoo Ahn, Ph. D. Thesis 2010

Let $D \in \mathcal{D}_\rho^n$ be a strongly connected digraph and $\vec{p} = \vec{th} = [1, \ldots, 1]$. For a given integer n, we run the computer simulation (Matlab) and record the lengths of the transients/attractors by changing $\rho \in \{\frac{1}{n}, \frac{1.4}{n}, \frac{1.8}{n}, \frac{2.2}{n}, \ldots\}$. The values below are the longest lengths obtained from 50 simulation for each fixed ρ.

n	4	5	6	7	8	9	10	11	12	13	$\cdots$
Transient	6	9	11	14	21	24	35	39	53	58	$\cdots$
Attractor	4	5	6	7	8	9	10	11	12	13	$\cdots$

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The lengths of attractors are bounded by n.

Some Conjectures Sungwoo Ahn, Ph. D. Thesis 2010

Let n be the number of nodes; assume that all refractory periods and all firing thresholds are 1.

1. **Conjecture 1.** In strongly connected digraphs any attractor has length at most n.
2. **Conjecture 2.** In Hamiltonian digraphs any attractor has length at most n.
3. **Conjecture 3.** In cyclic digraphs with one shortcut any attractor has length at most n.

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Conjecture 3 was proved to be true in the thesis; in fact, it was proved that the length of any attractor must be a divisor of either n or n_1, the length of the shortcut.

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Conjectures 1 and 2 are still completely open.