# Bringing math into the loop

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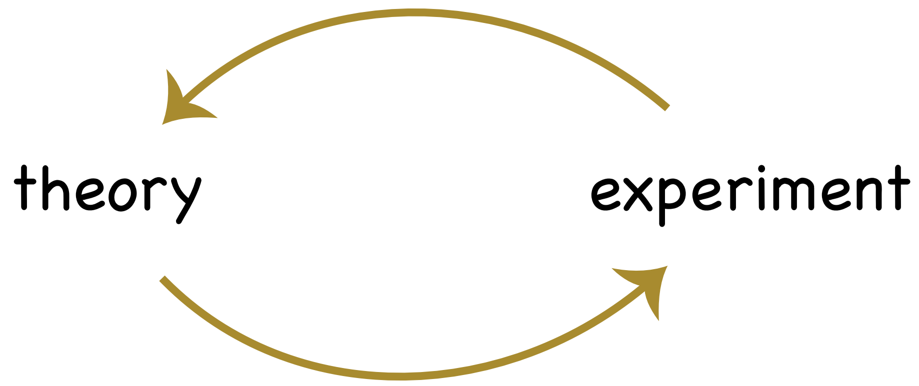
MSRI Theory of Neural Computation Workshop
October 7, 2015

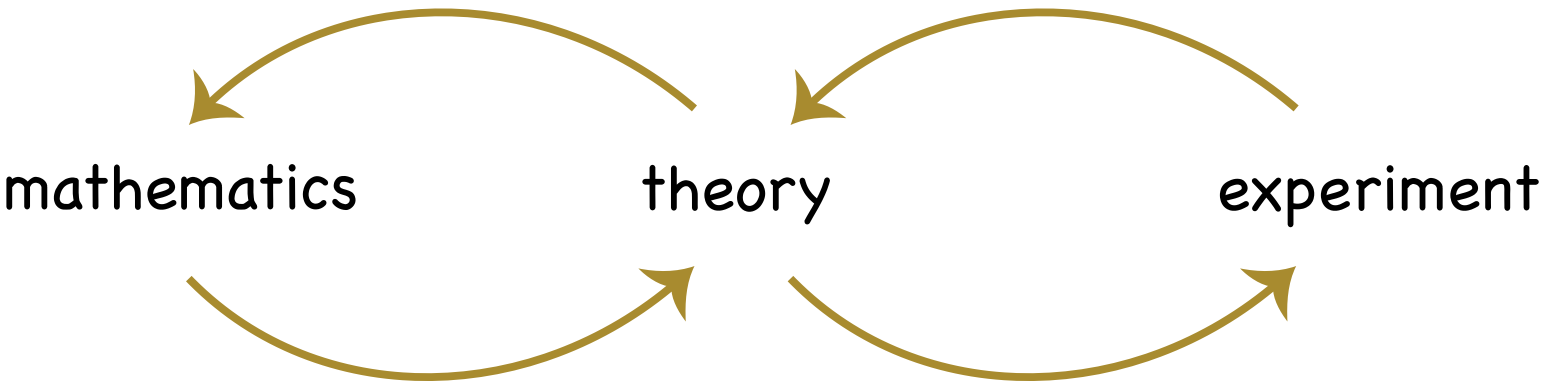
# Neuroscience



# Neuroscience

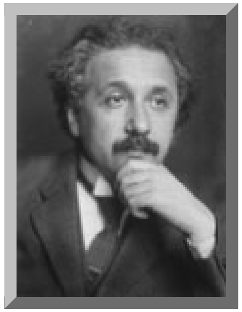
mathematics → theory ⇄ experiment

# Physics

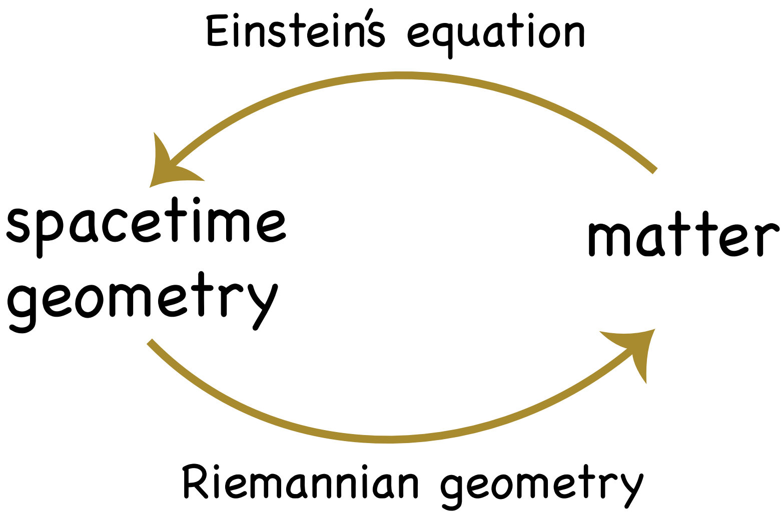



Sometimes the mathematical technology was just sitting there, and sometimes it had to be developed in tandem with theory.

# 100th anniversary of General Relativity

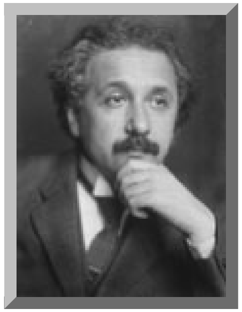



An international conference to celebrate 100 years of general relativity will be held at the Universit Park campus from Sunday, June 7 through Friday, June 12, 2015 under the auspices of th International Society on General Relativity and Gravitation (ISGRG) and the Topical Group o Gravitation (GGR) of the American Physical Society.




"Spacetime (geometry) tells matter how to move; matter tells spacetime how to curve." - John Archibald Wheeler

# 100th anniversary of General Relativity

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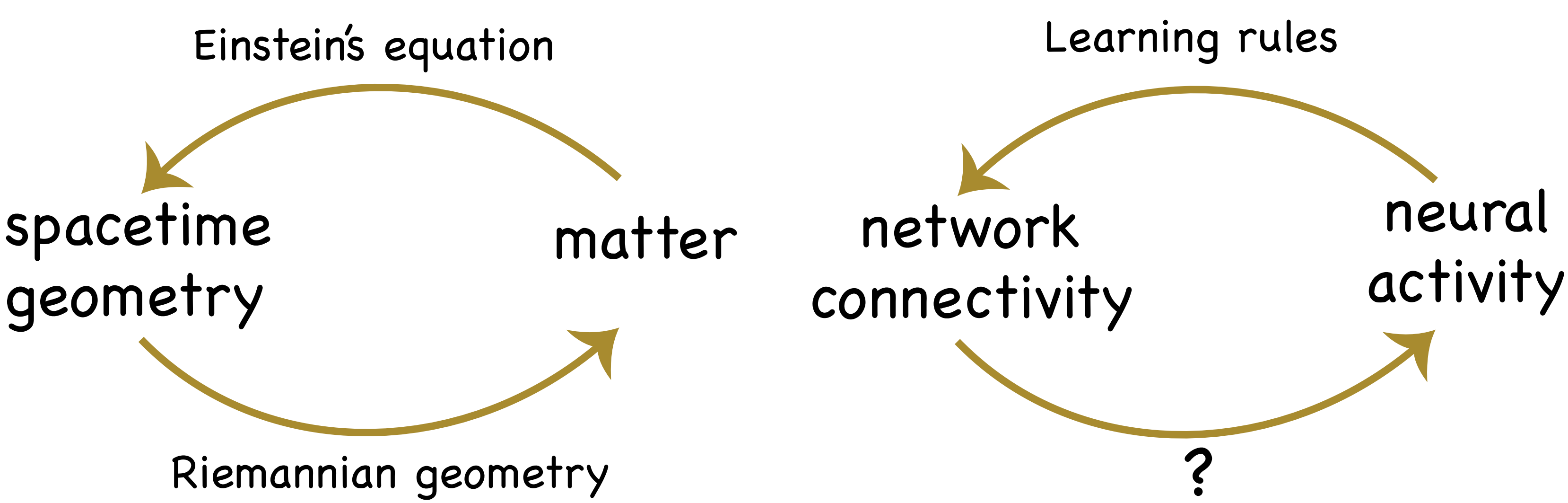



"Spacetime (geometry) tells matter how to move; matter tells spacetime how to curve." - John Archibald Wheeler

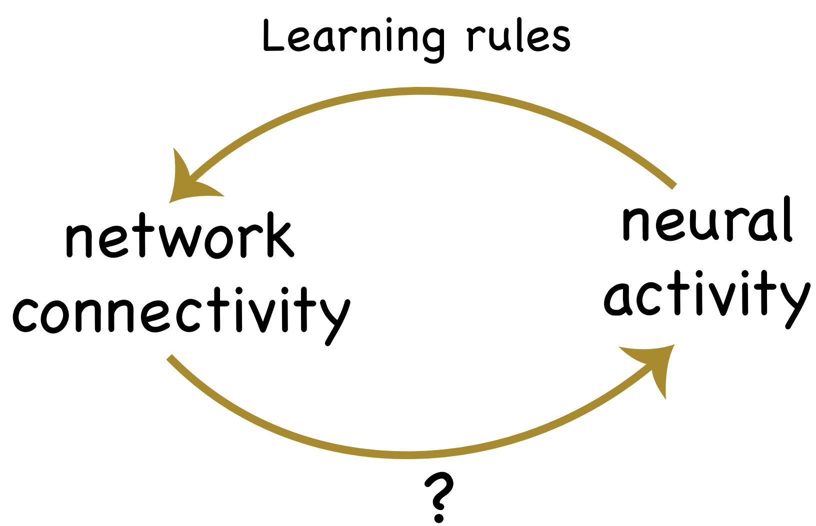
# Plan of the talk

I will present 2 examples where I think we can benefit from bringing mathematics into the loop.

Part I: network dynamics

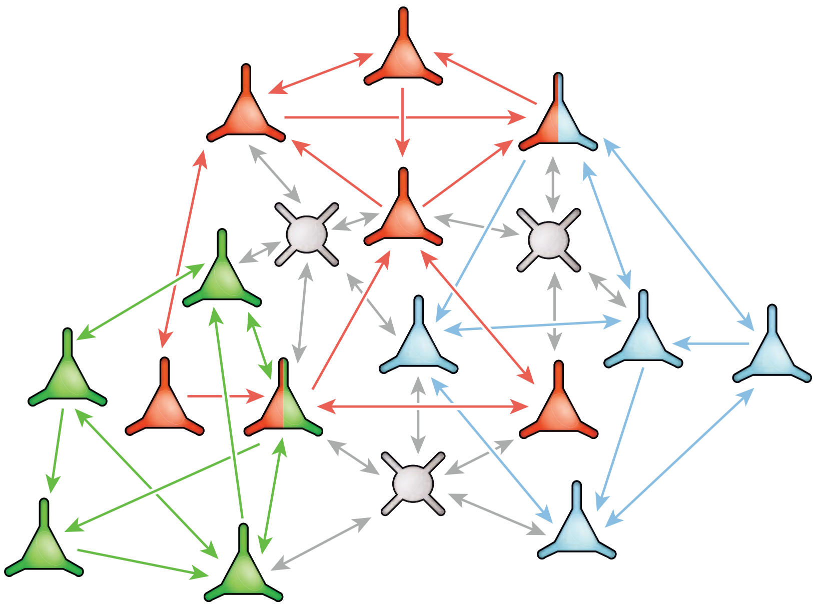
Part II: data analysis

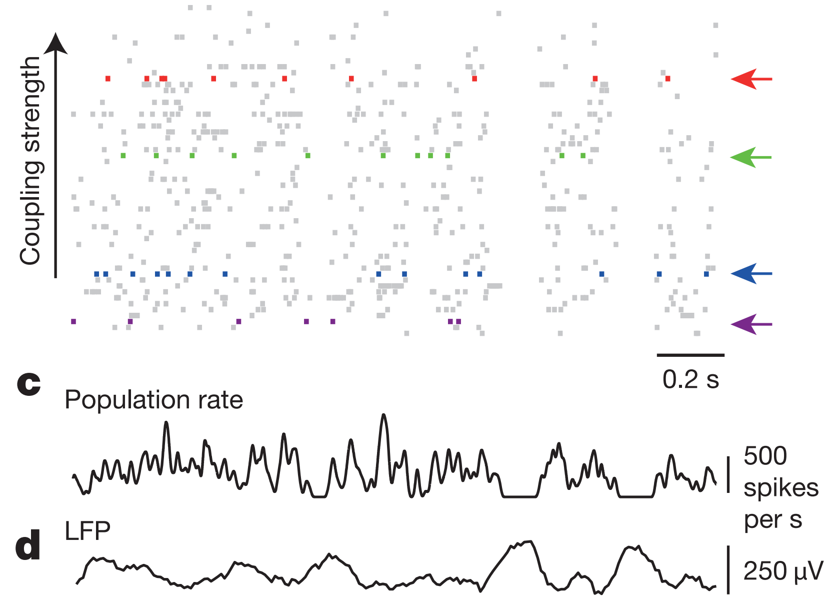
# Part I: network dynamics




Motivating Question: How does recurrent connectivity shape population activity?

# Recurrent network dynamics (cortex)

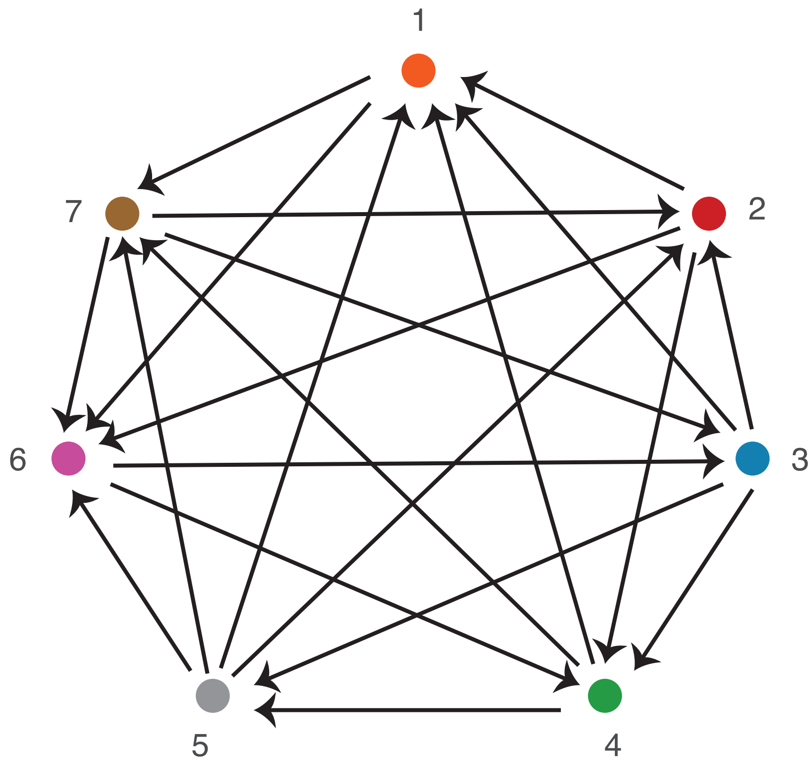





Cortical connectivity and sensory coding
K.D. Harris & T.D. Mrsic-Flogel, Nature 2013 (Review)

Diverse coupling of neurons to populations in sensory cortex. Okun et. al., Nature 2015

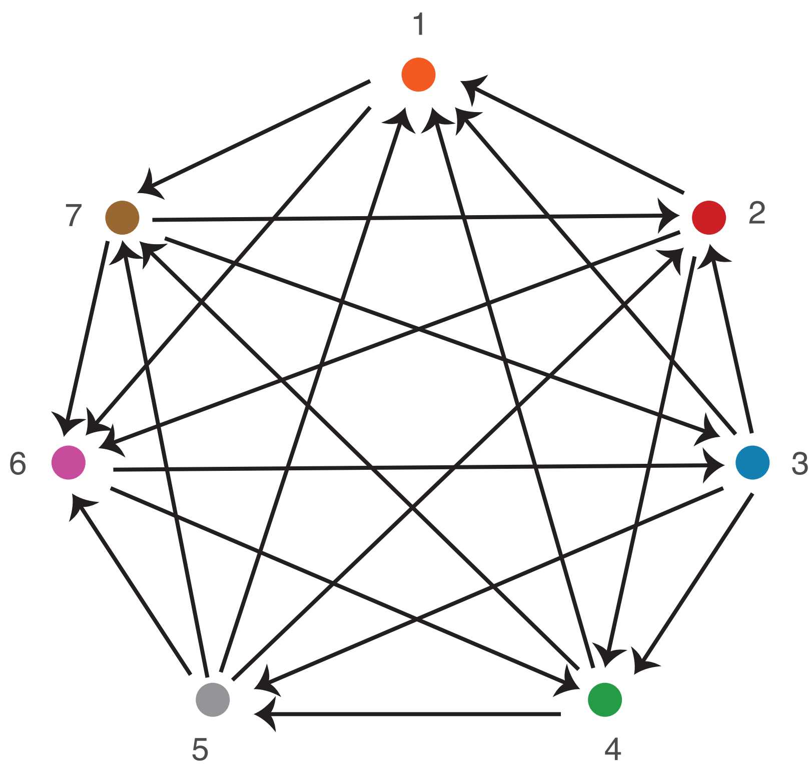
# What does connectivity tell us about dynamics?




Suppose we had the connectome for a network.

Q: What can we say about the dynamics?

# What does connectivity tell us about dynamics?




Suppose we had the connectome
for a network.

Q: What can we say about the dynamics?

A: It's complicated.

complex synapses
intrinsic neuron dynamics
cell types
neuromodulators
dendrites
stochasticity of spikes
noise
etc.

# A mathematician's approach

"If you can't solve a problem, then there is an easier problem you can solve: find it."

– George Polya, How to Solve It (1945)

# Often, technology is developed on simple model systems

A good model system has:

Tractability
Transparency
Complex behavior

C elegans

# Often, technology is developed on simple model systems

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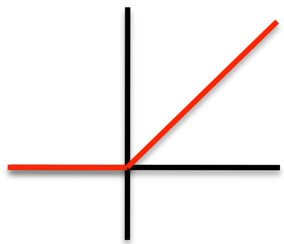
We also need to study simple model systems in order to develop mathematical technology.

# A toy model of a recurrent network

A threshold-linear network:

$$\frac{dx_i}{dt} = -x_i + \left[ \sum_{j=1}^{n} W_{ij} x_j + \theta \right]_+$$



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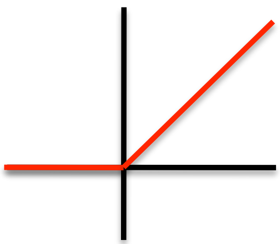
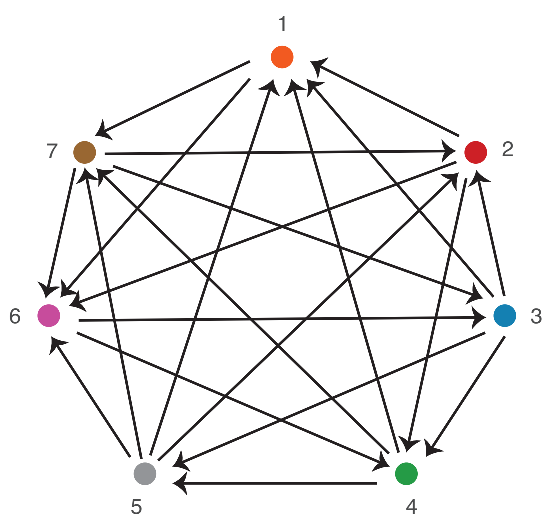


determined from a directed graph G.




$$W_{ij} = \begin{cases} 0 & \text{if } i = j \\ -1 + \varepsilon & \text{if } i \leftarrow j \text{ in } G \\ -1 - \delta & \text{if } i \not\leftarrow j \text{ in } G \end{cases}$$

parameter constraints

$$\theta > 0 \qquad \delta > 0 \qquad 0 < \varepsilon < \frac{\delta}{\delta + 1}$$

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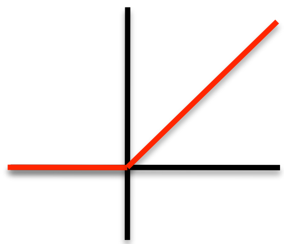

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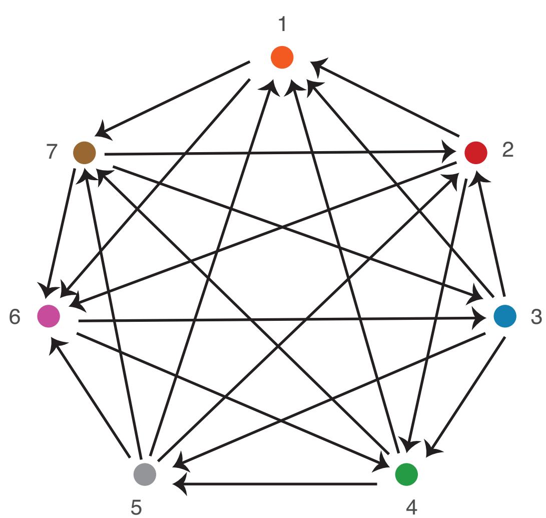



Is this model...

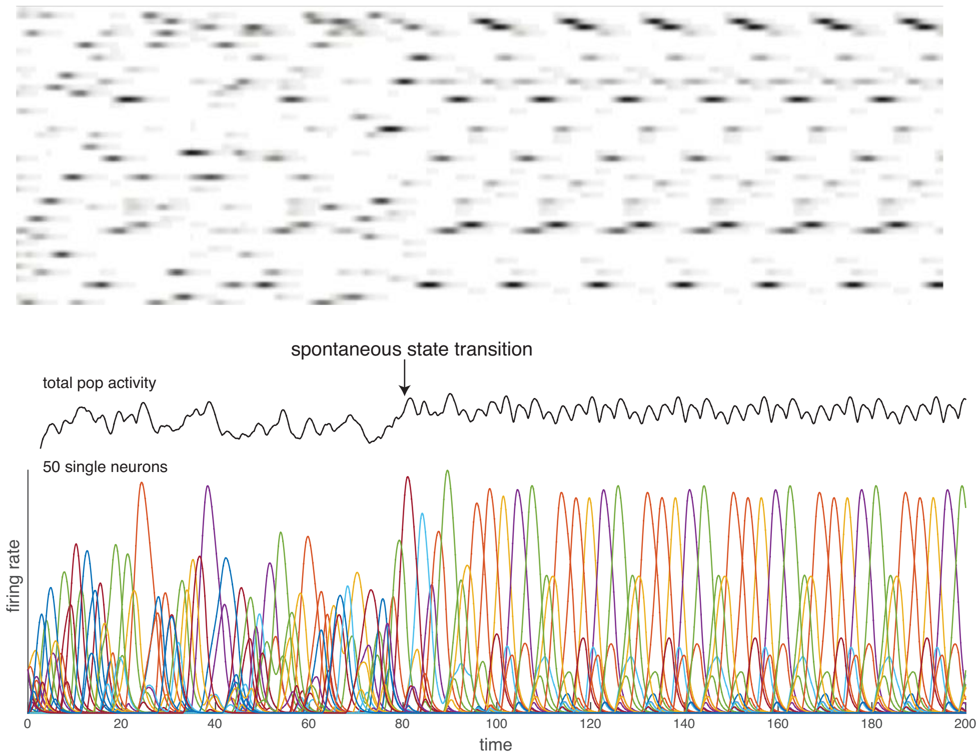
Tractable?

Transparent?

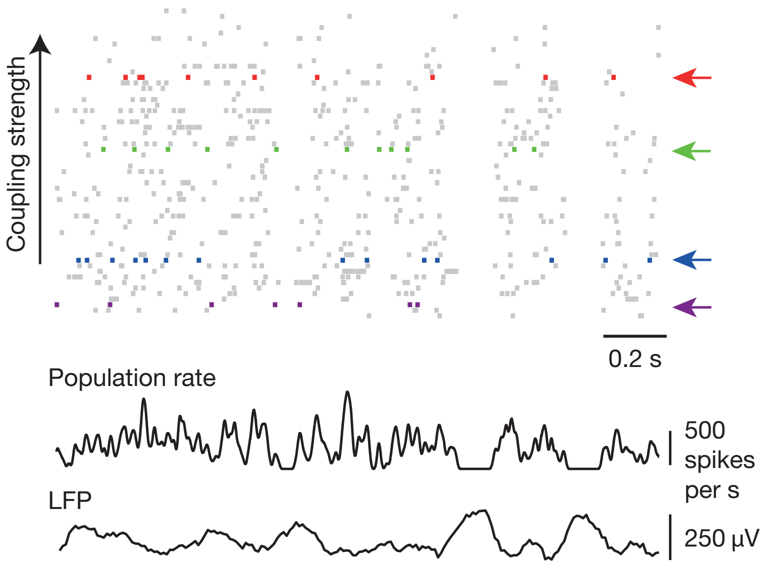
Capable of complex behavior?

# The model (generically) exhibits complex behavior...

## Model (50 neurons)

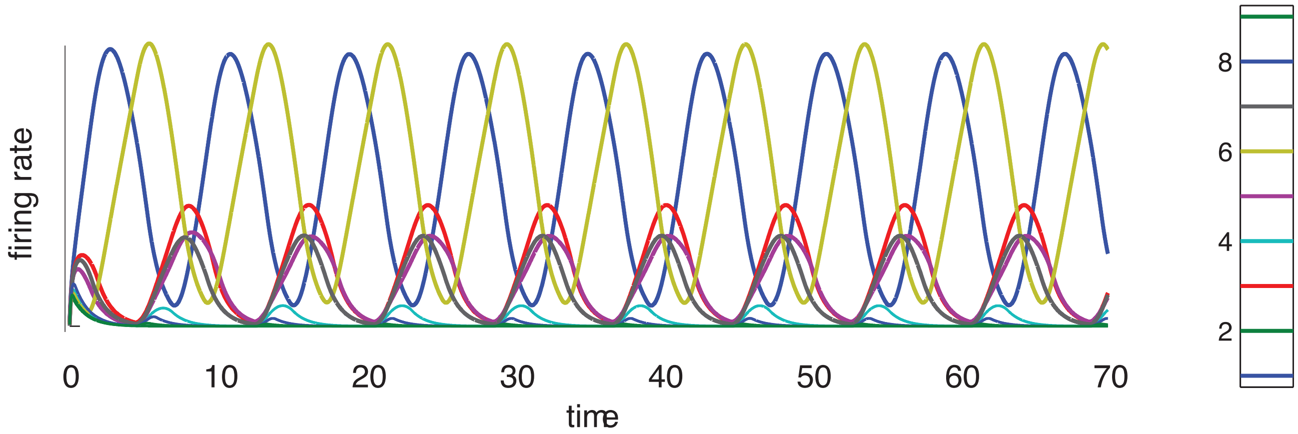



## Data (66 neurons)




Okun et. al., Nature 2015

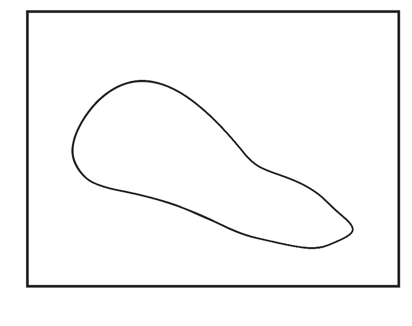
# The model (generically) exhibits complex behavior…




Graph adjacency matrix

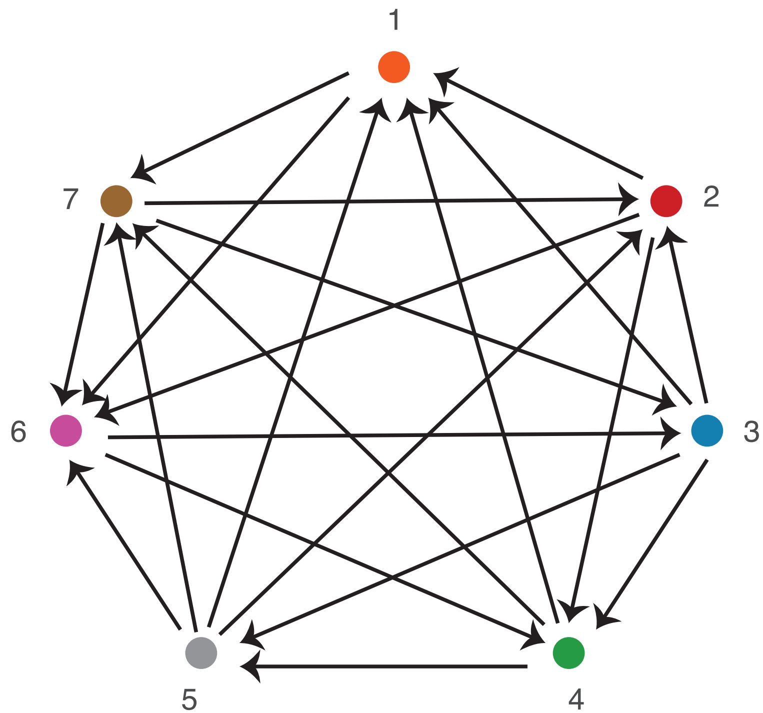
$$\begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 1 & 1 & 1 & 1 & 1 \\ 1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 & 1 & 1 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 0 & 1 & 1 & 1 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 1 & 1 & 0 & 1 & 1 & 0 \end{bmatrix}$$

projection of trajectory



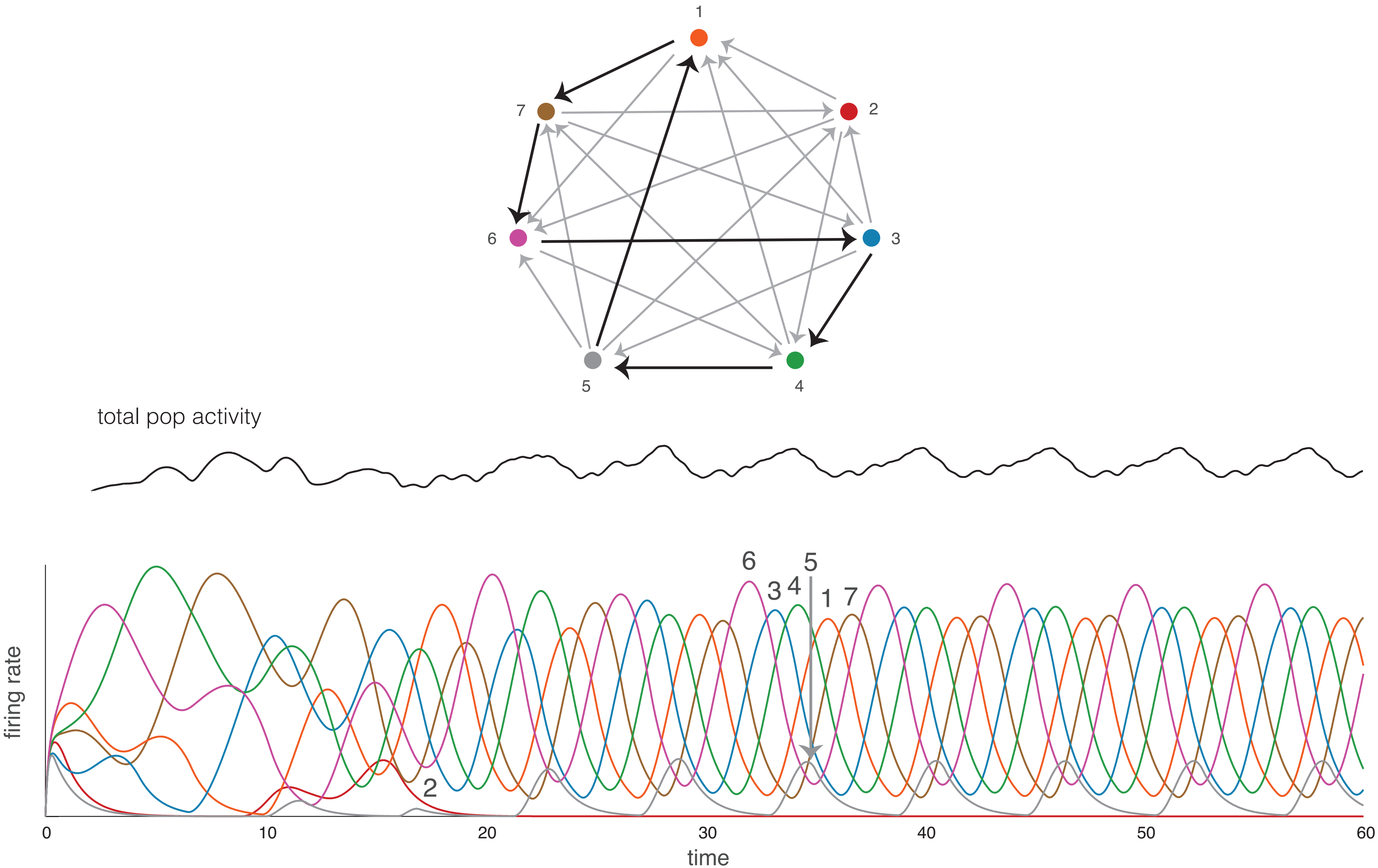
(play song)

# Back to our problem...



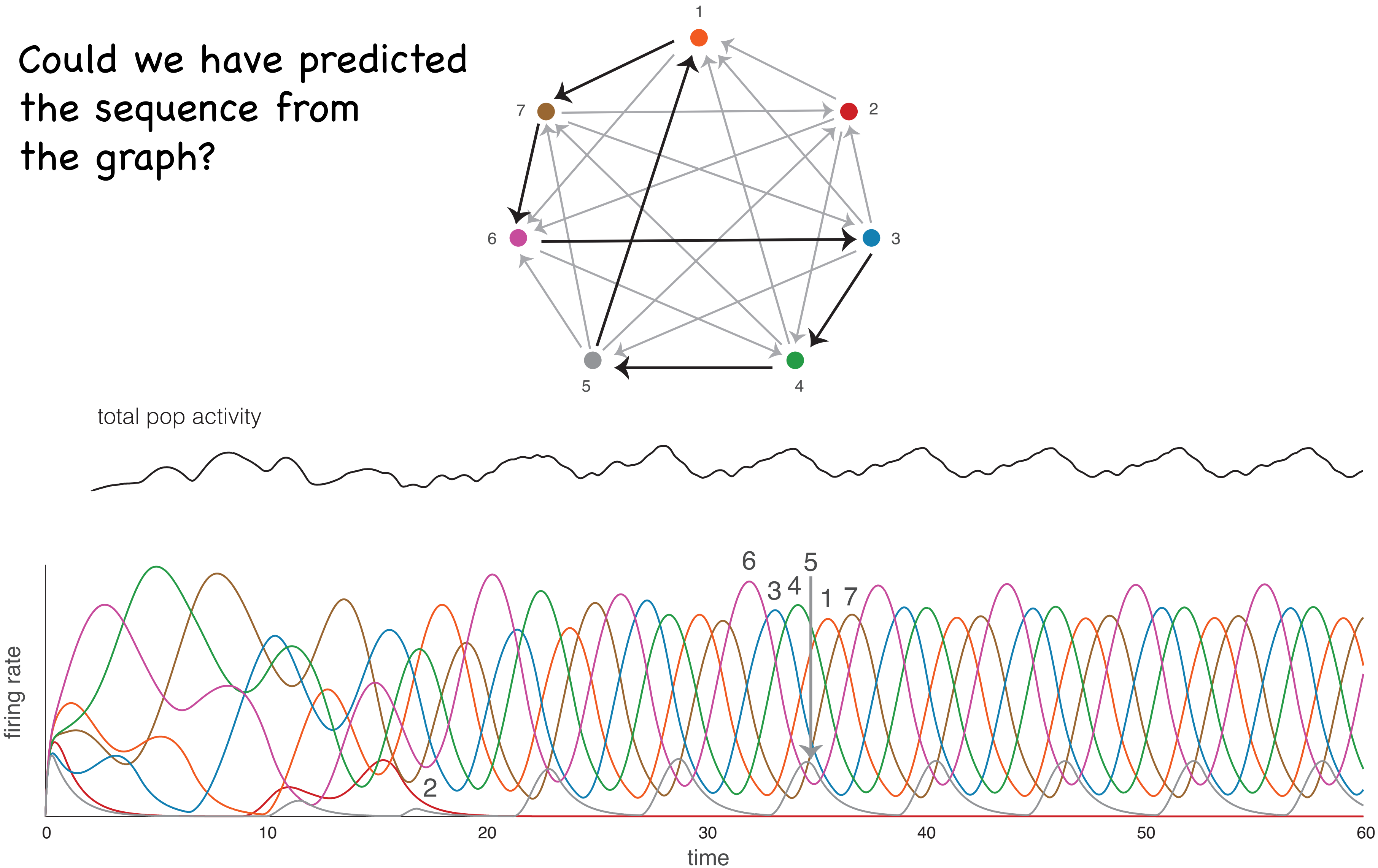

In our toy model, can we figure out what the network is going to do?

# Activity converges to a limit cycle



# Activity converges to a limit cycle

Could we have predicted the sequence from the graph?



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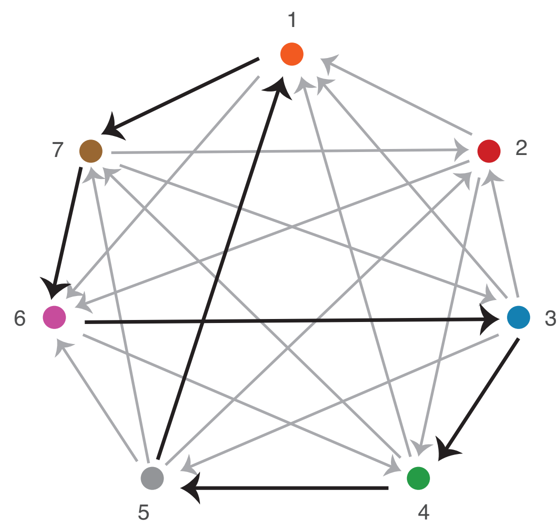
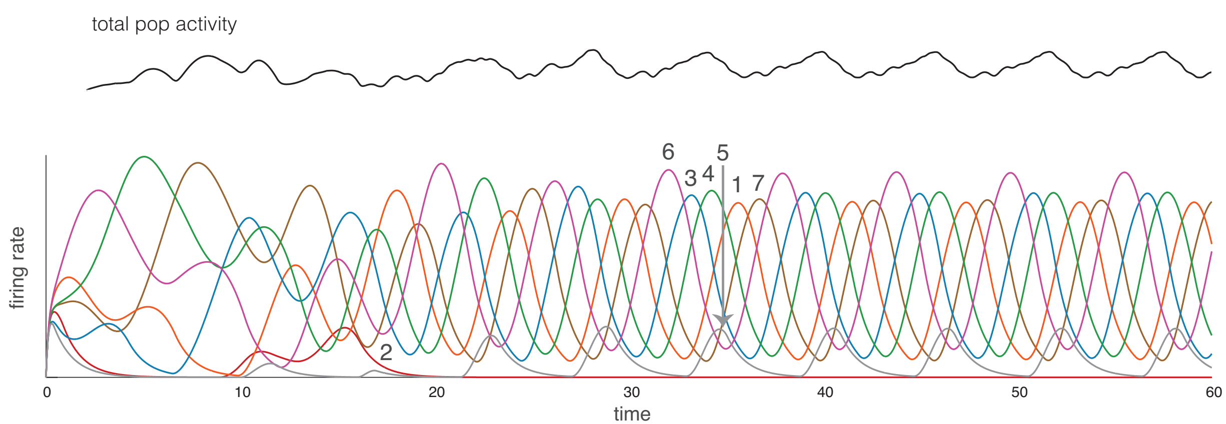
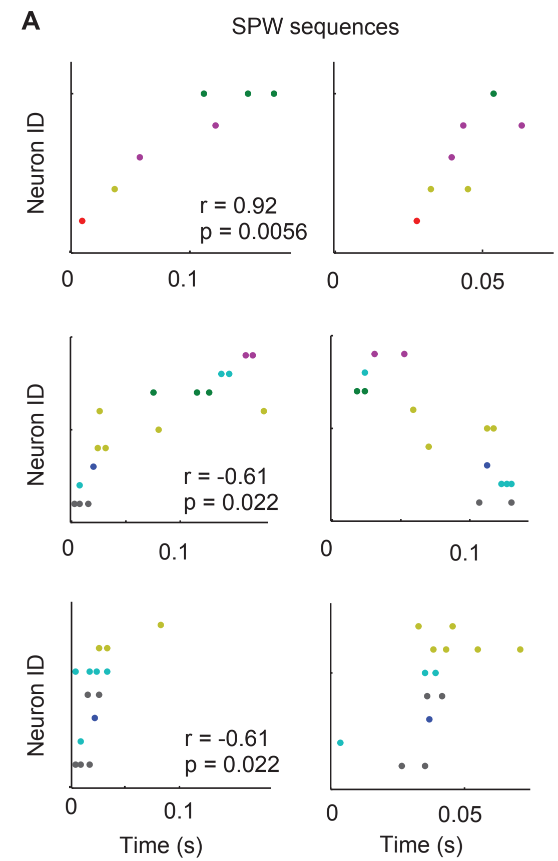


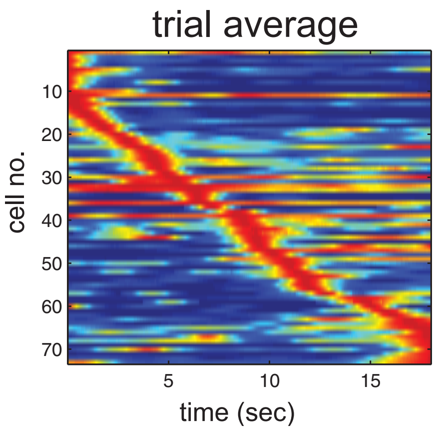

hippocampal ripple sequences



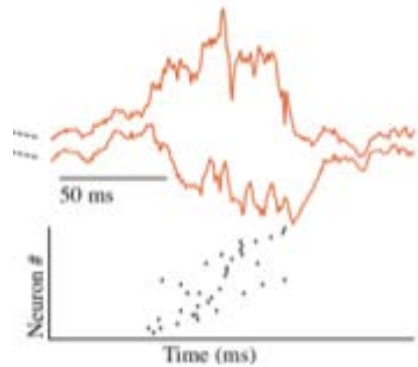

Data from the Pastalkova lab at Janelia

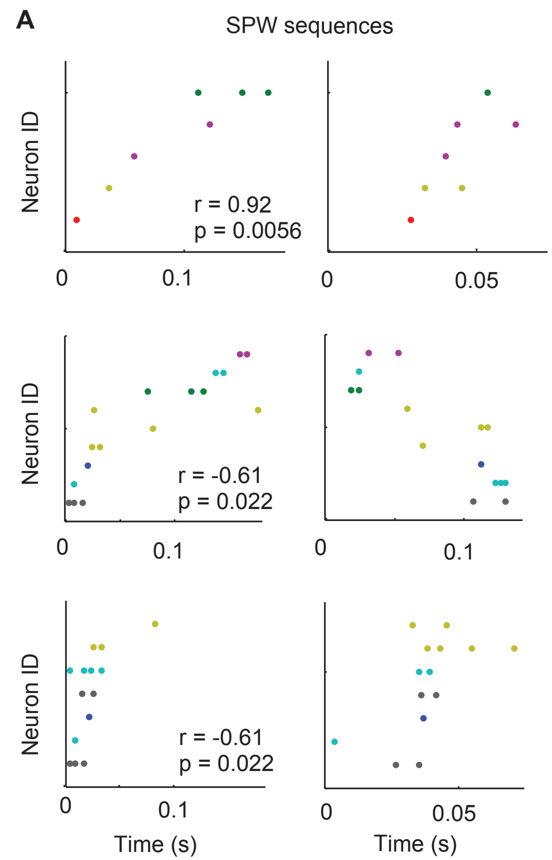
# Diversity of dynamics in hippocampus

## Cell assembly sequences

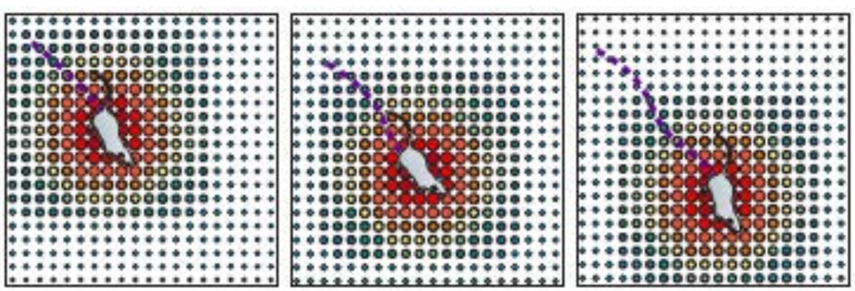



## Ripple sequences (fast)



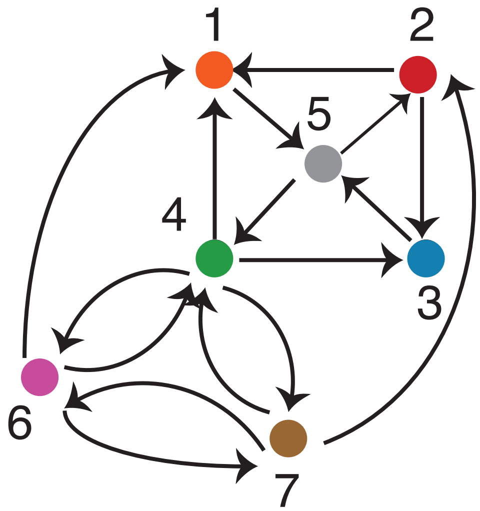

## Associative memory; place coding



McNaughton et. al., Nature Rev. Neurosci. 2006

Data from the Pastalkova lab at Janelia

# Multiple dynamic behaviors in the same network



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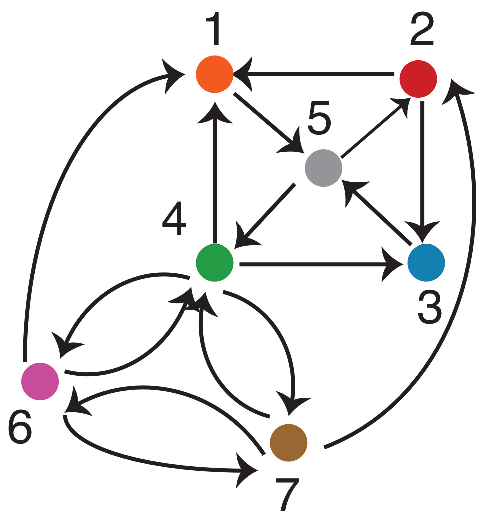


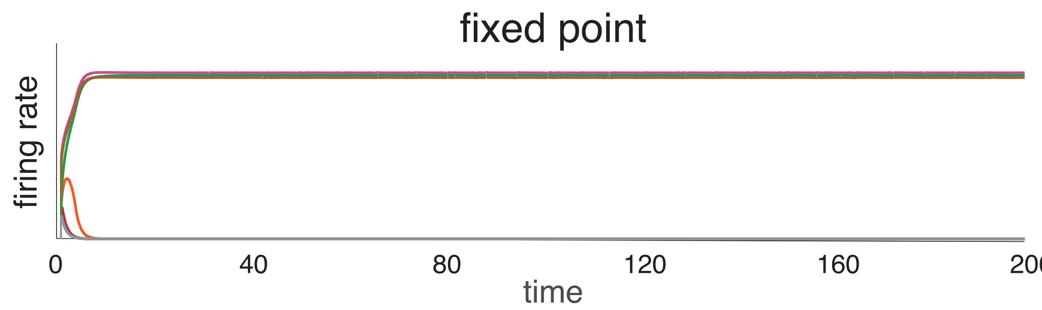

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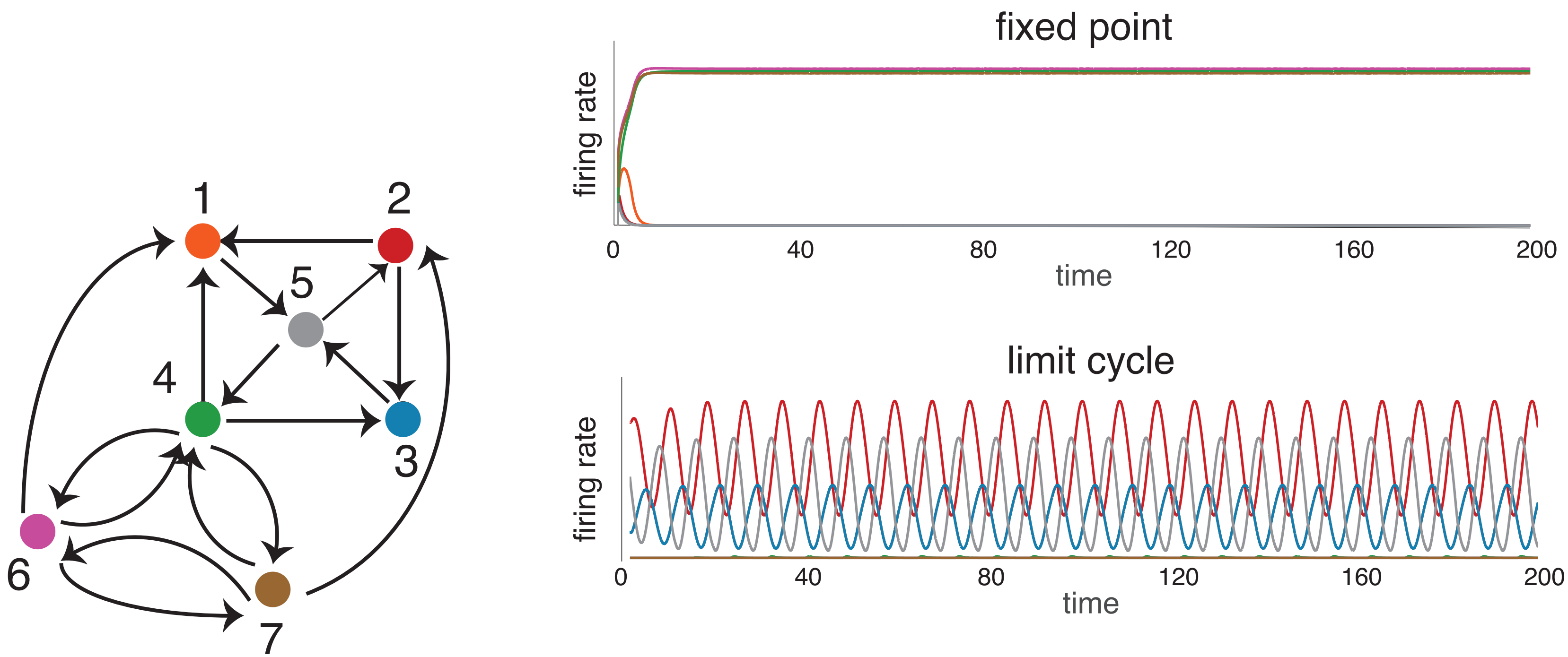

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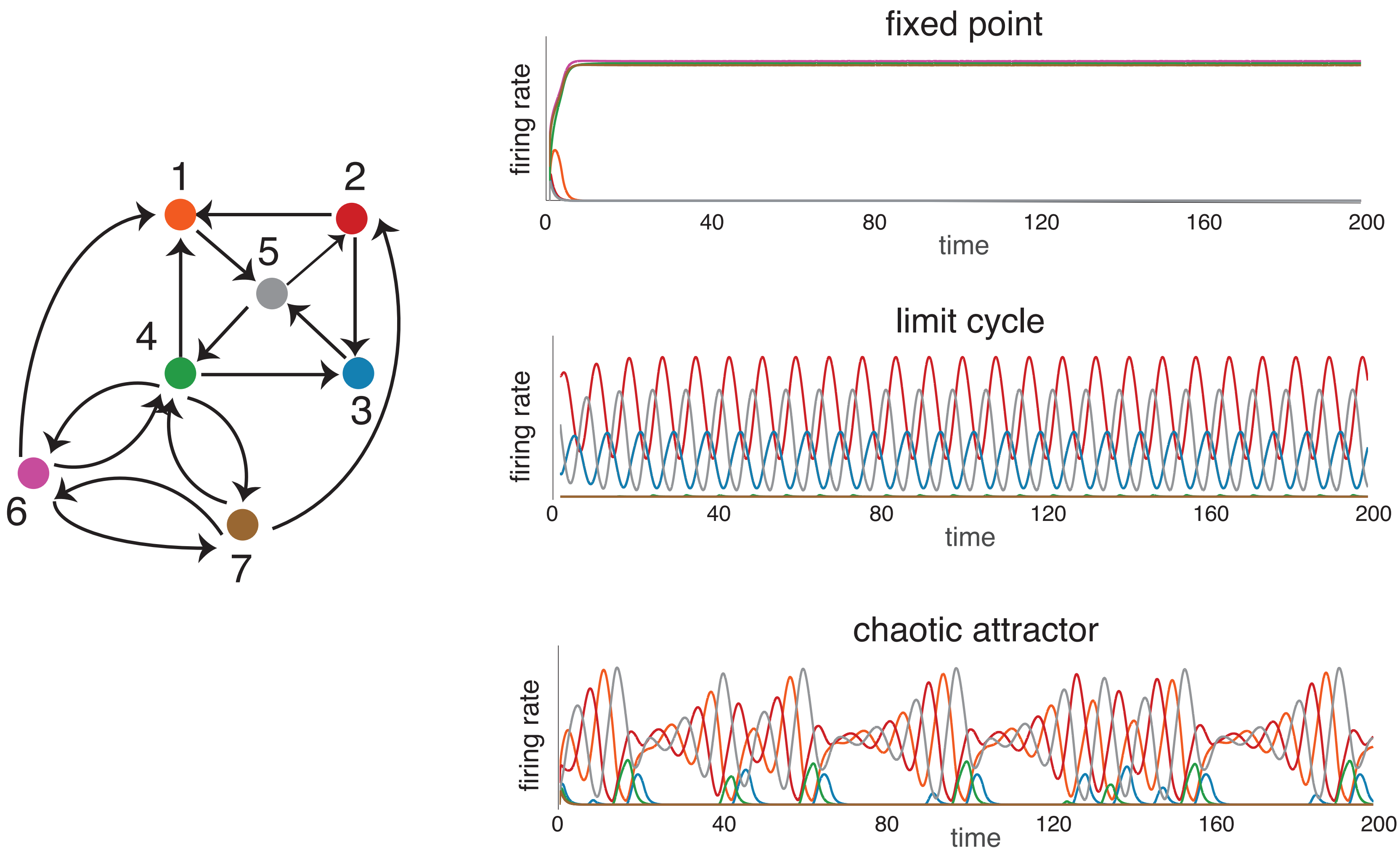


Can we predict these various behaviors from the graph?

# Some mathematical results
# (tractability)

Theorem 1. For any G, a clique is the support of a stable fixed point if and only if it is a target-free clique.

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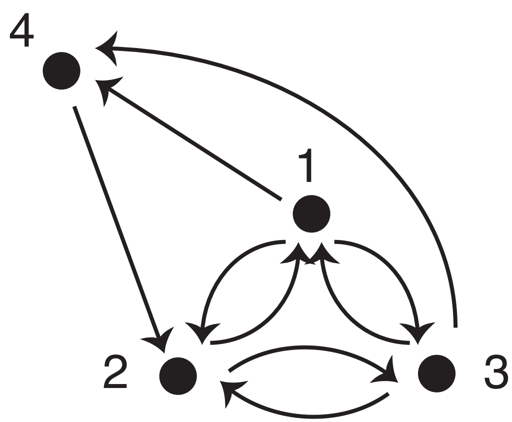
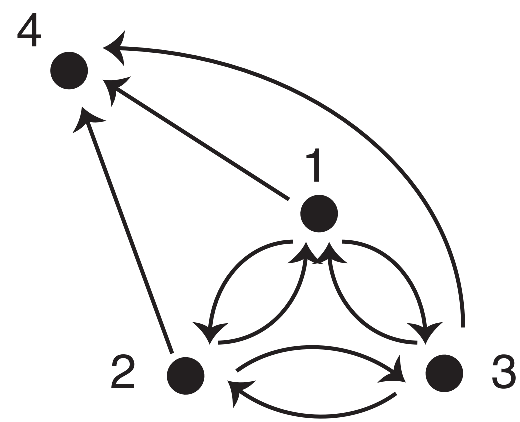



123 is a target-free clique




123 is not target-free

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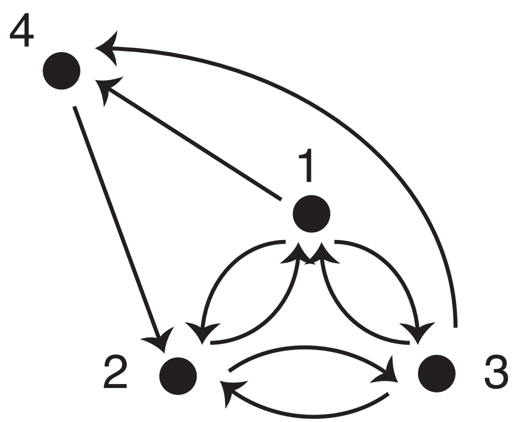


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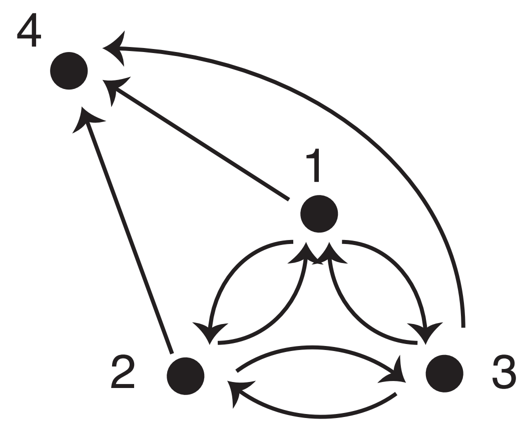
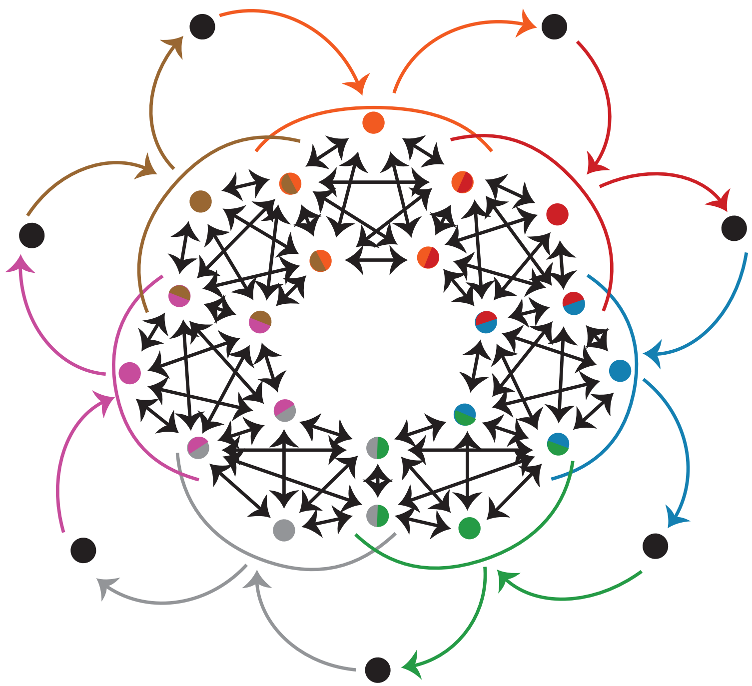
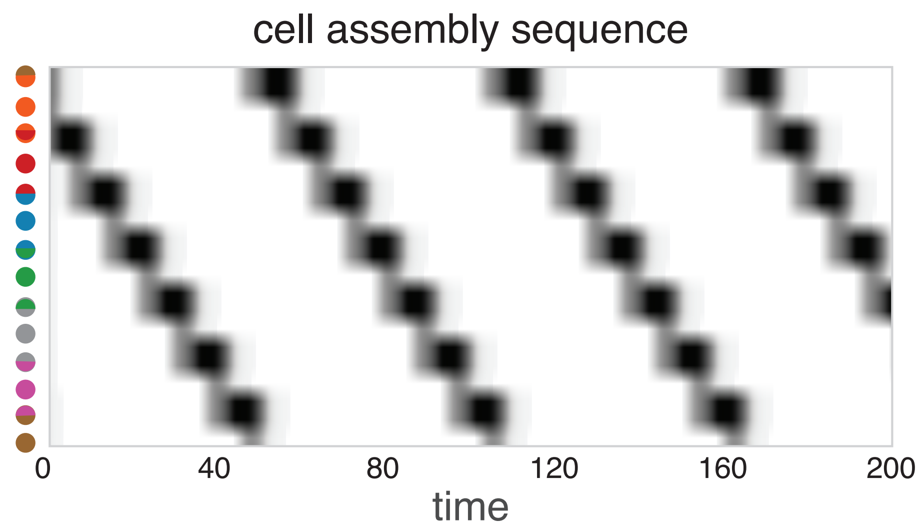



123 is not target-free

Conjecture. A subset of neurons supports a stable fixed point of the dynamics if and only if it is a target-free clique.

# Sequence of overlapping cell assemblies





# Some mathematical results

Theorem 2. If G is an oriented graph with no sinks, then the network has no stable fixed points.

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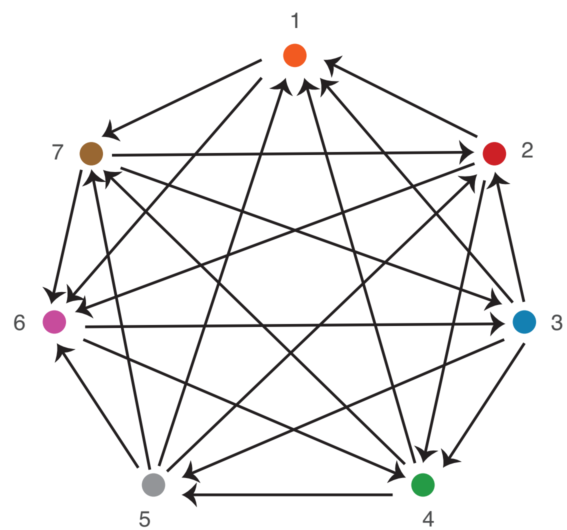
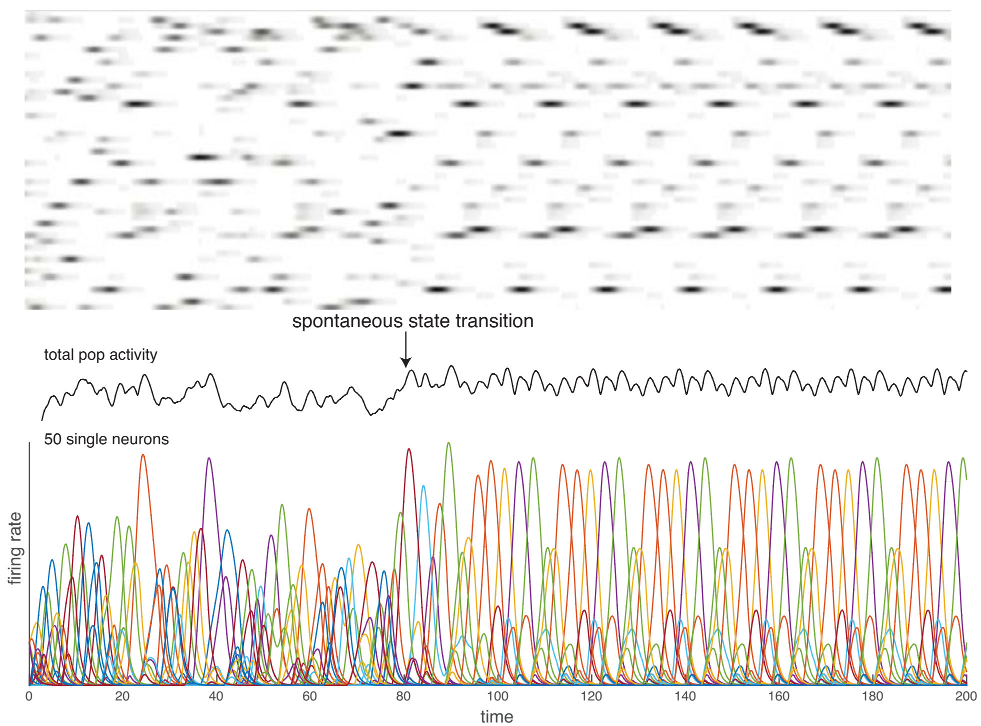



an oriented graph
with no sinks

## Model (50 neurons)

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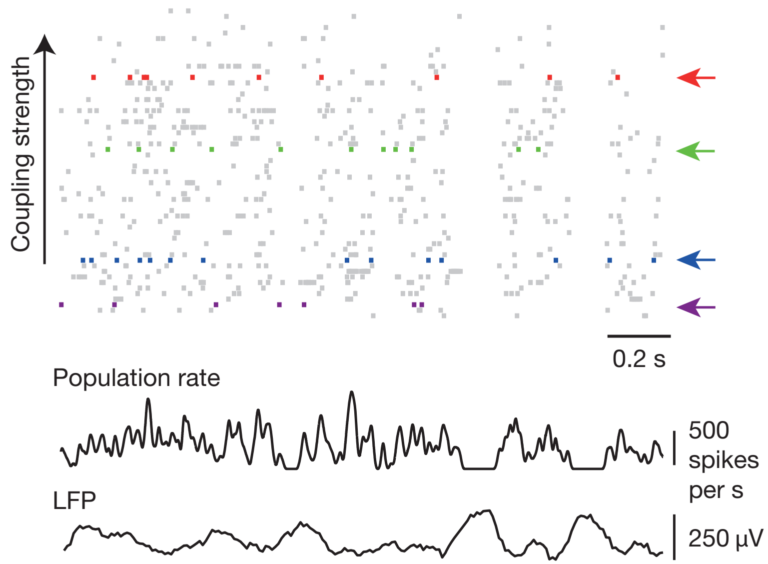



Okun et. al., Nature 2015

# A word on the proofs…

We build on the theory of threshold-linear networks:

X. Xie, R. H. Hahnloser, and H.S. Seung. Selectively grouping neurons in recurrent networks of lateral inhibition. Neural Computation, 2002.

R. H. Hahnloser, H.S. Seung, and J.J. Slotine. Permitted and forbidden sets in symmetric threshold-linear networks. Neural Computation, 2003.

C. Curto, A. Degeratu, and V. Itskov. Flexible memory networks. Bull. Math. Biol., 2012.

C. Curto, A. Degeratu, and V. Itskov. Encoding binary neural codes in networks of threshold-linear neurons. Neural Computation, 2013.

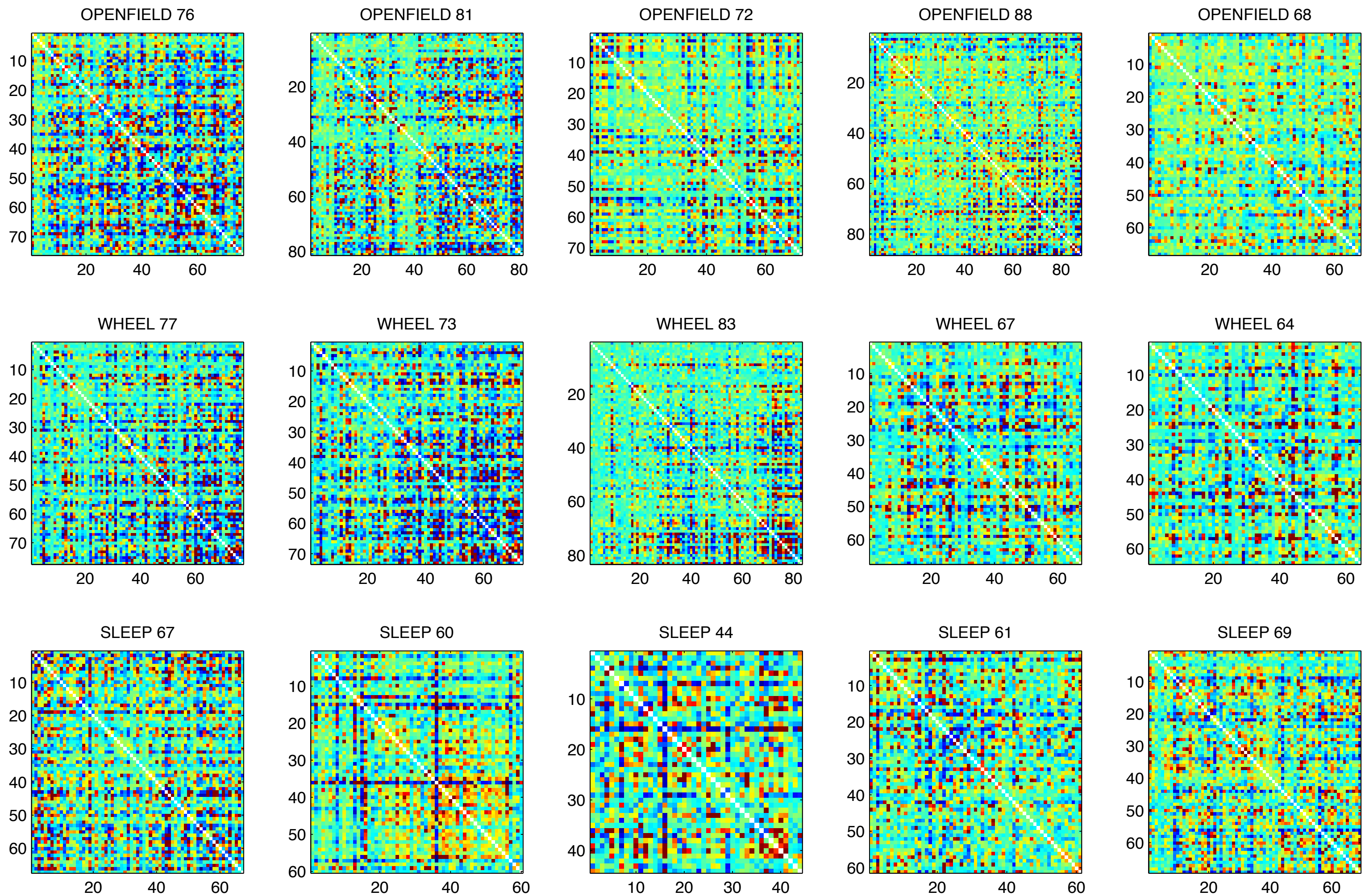
C. Curto and K. Morrison. Pattern completion in threshold-linear networks. In prep.

Some mathematical ingredients of this theory:

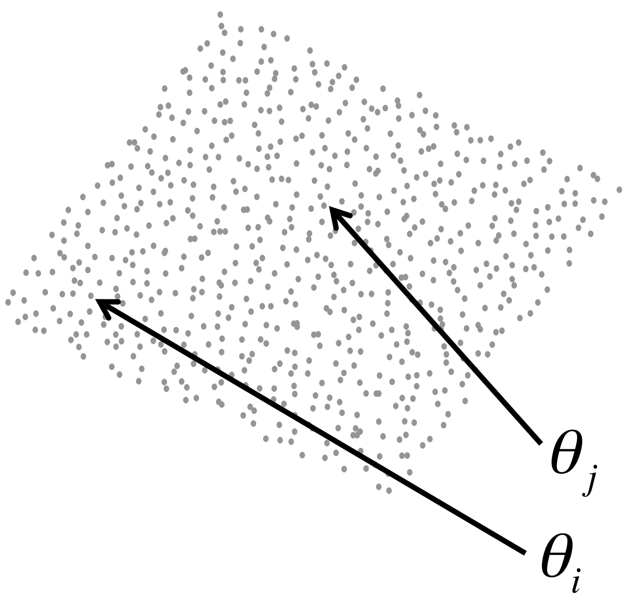
Combinatorics + matrix theory
Distance geometry (Cayley-Menger determinants)

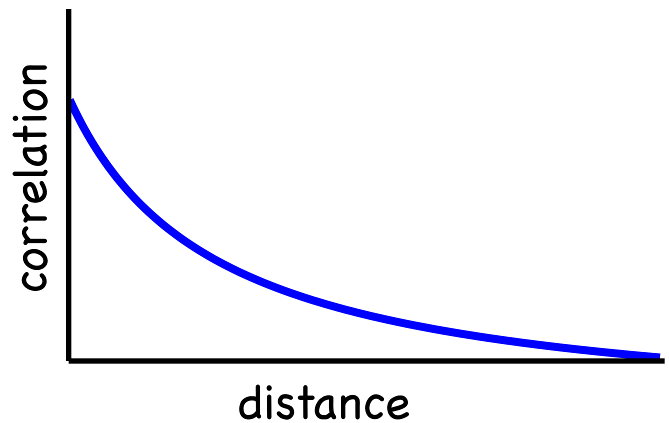
# Part II: data analysis

# Hunting for structure in pairwise correlations



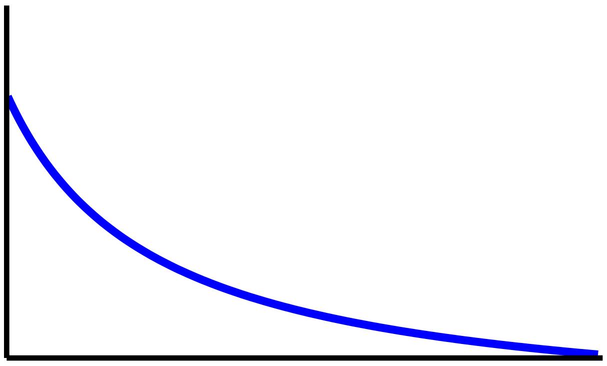
# Geometric structure of correlations

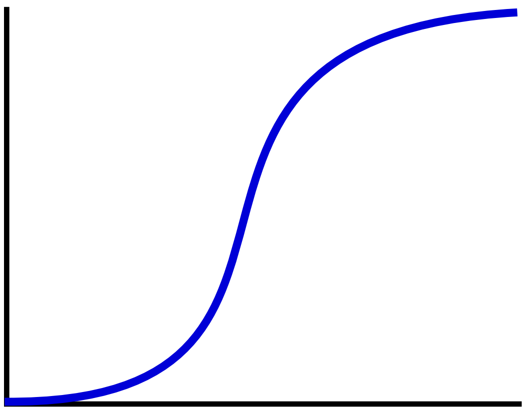



Each neuron has a position in a “*feature space.*”

# Why hunting for structure is hard...

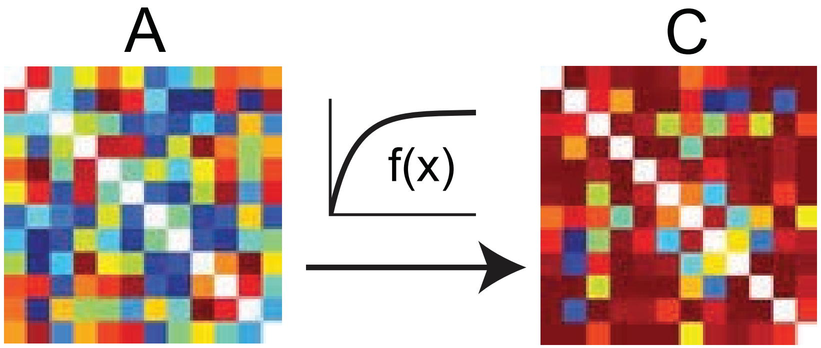




There is often a nonlinear relationship between observed variables and underlying “structured” variables.

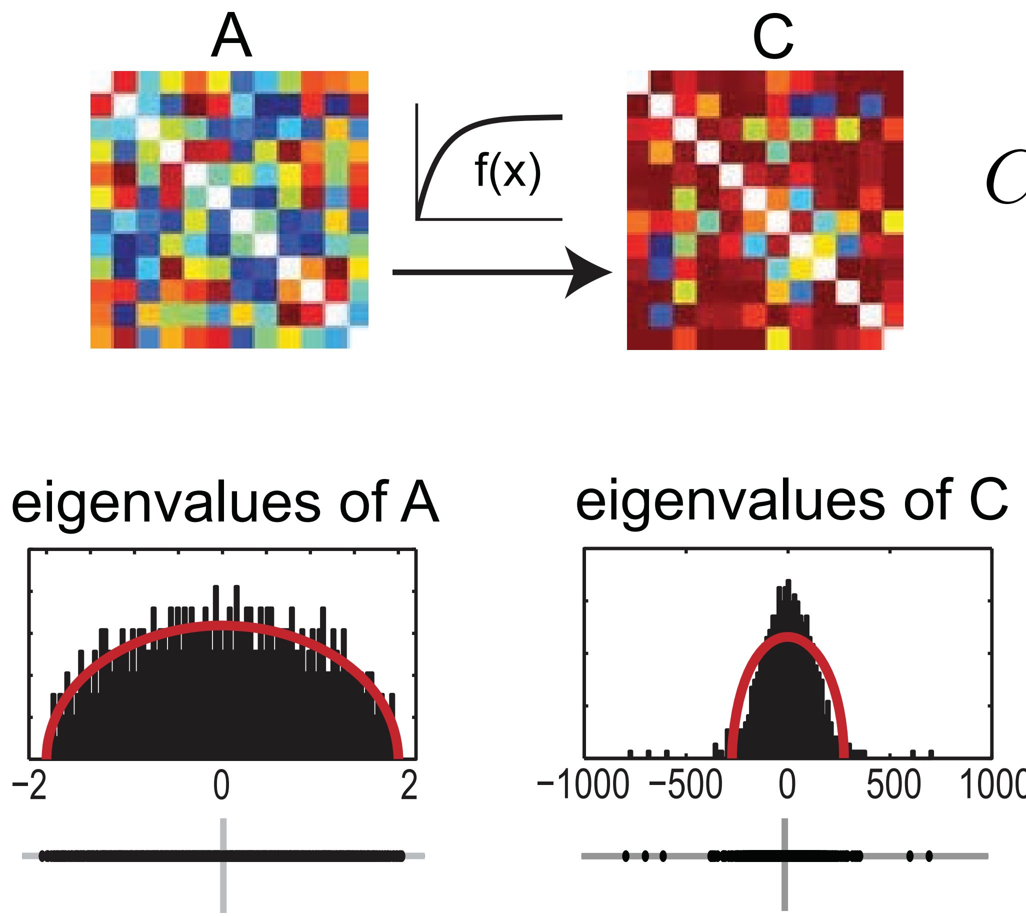
But, this relationship is typically monotonic.

Goal: to detect random or geometric structure that is invariant under monotone transformations



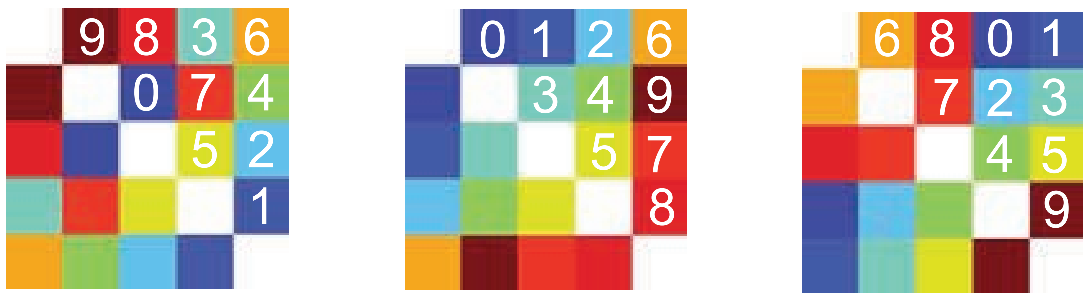

$$C_{ij} = f(A_{ij})$$

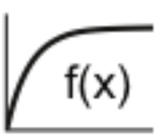
# What isn't invariant: eigenvalues




$$C_{ij} = f(A_{ij})$$

# What is invariant: the ordering of matrix entries

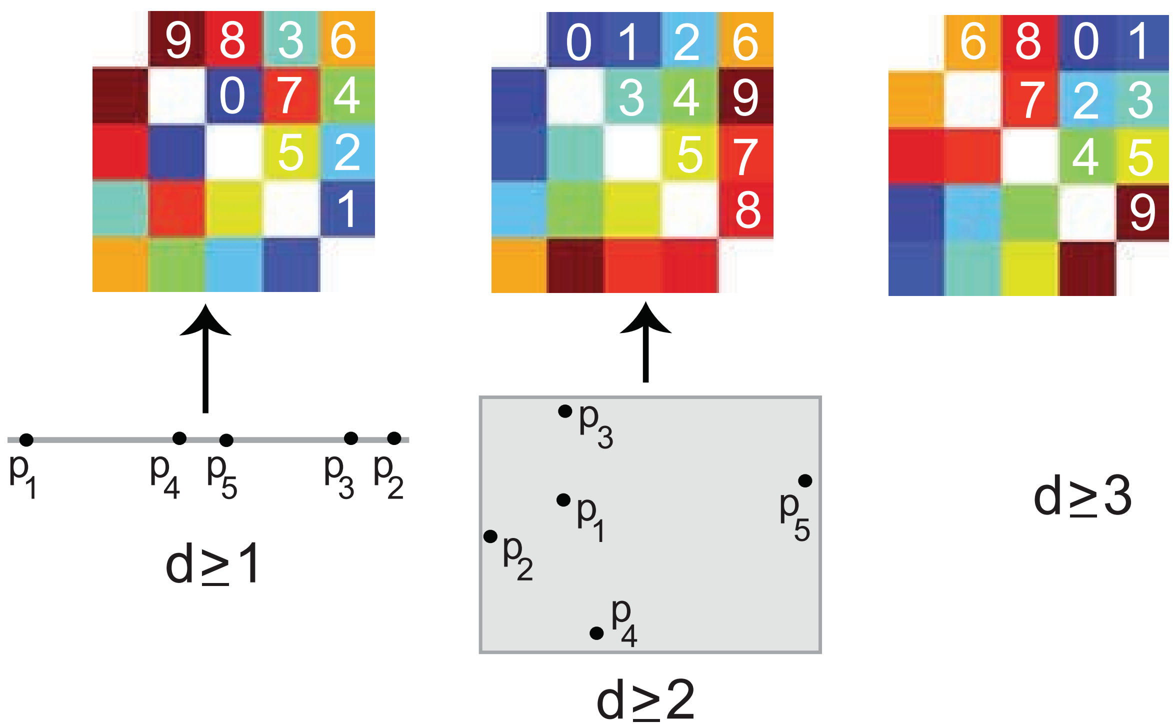



$$C_{ij} = f(A_{ij})$$

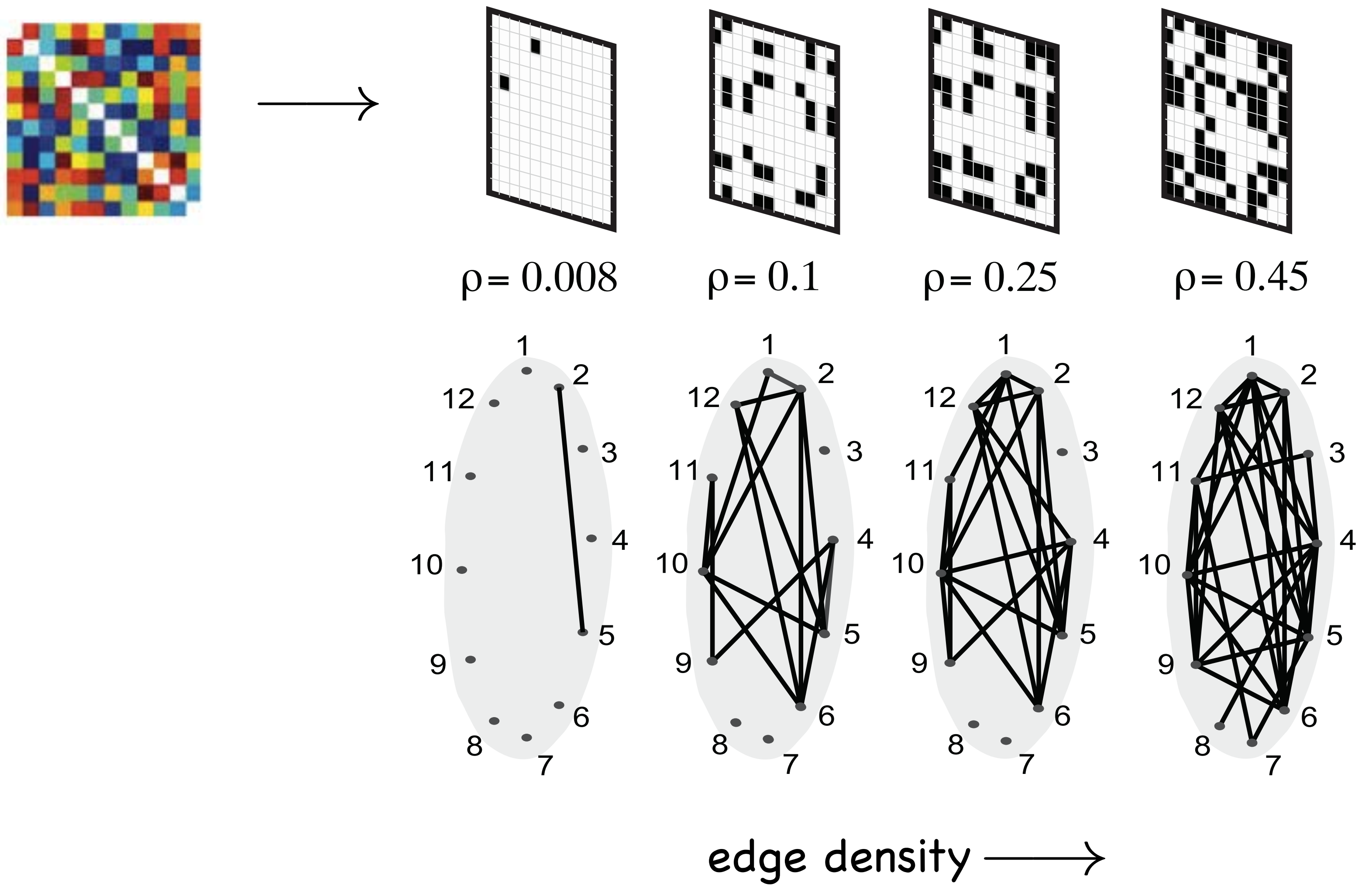
$$C_{ij} < C_{k\ell} \Leftrightarrow A_{ij} < A_{k\ell}$$

# Maybe surprising: geometric structure is encoded in the ordering of matrix entries

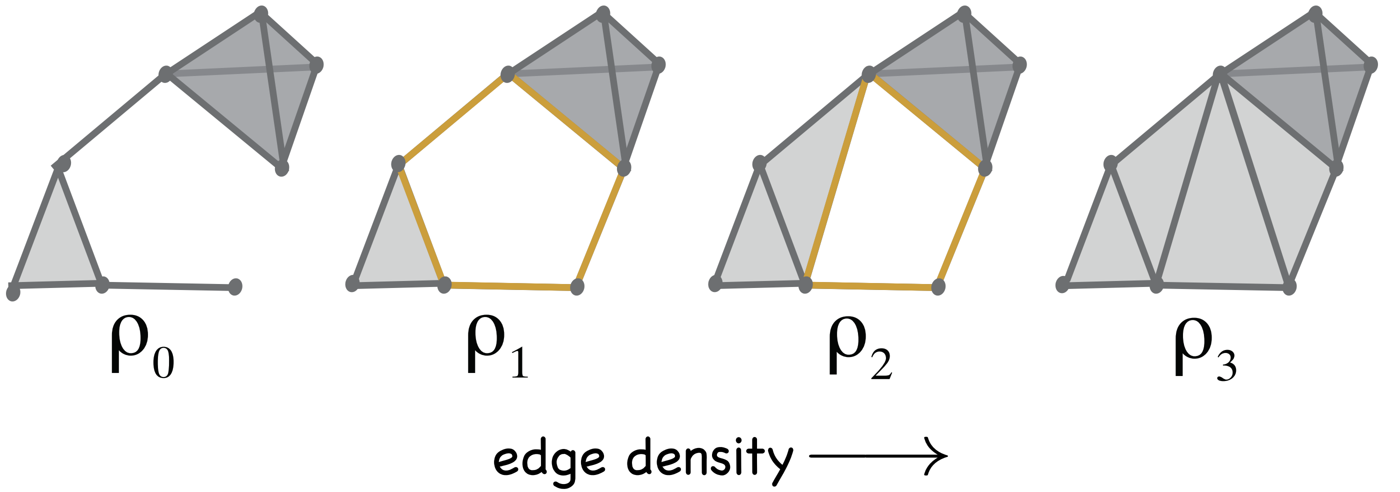


# Repackaging the matrix ordering data...

$$G_0 \subset G_1 \subset \ldots \subset G_{\binom{n}{2}}$$

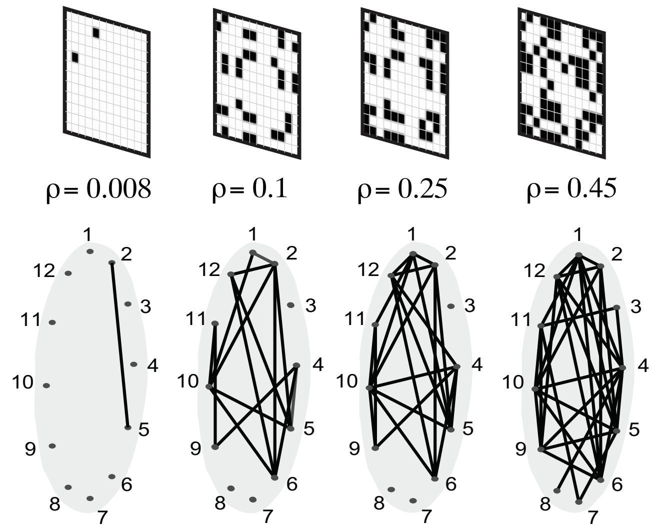


Idea: measure the organization of cliques across the sequence of graphs



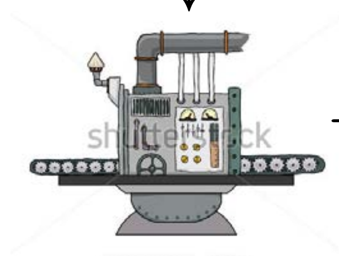

Intuition: geometric structure in the matrix causes the holes to fill in more quickly

# Idea: measure the organization of cliques across the sequence of graphs



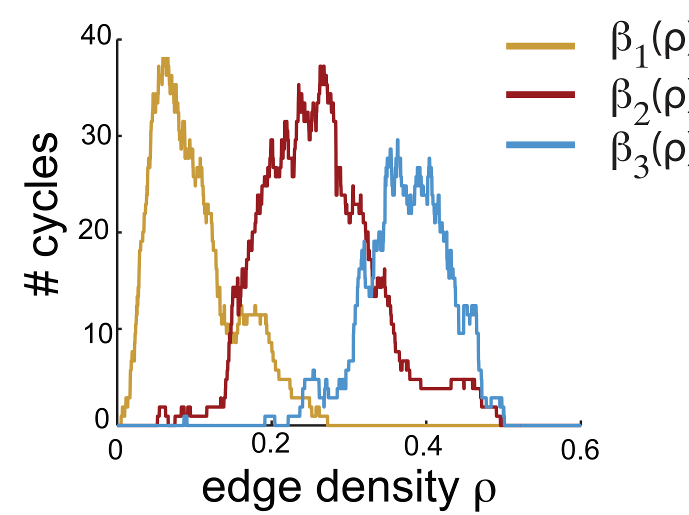

Persistent homology

Computational algebraic topology




Topological machine

## Betti curves

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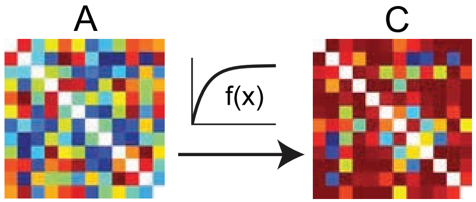
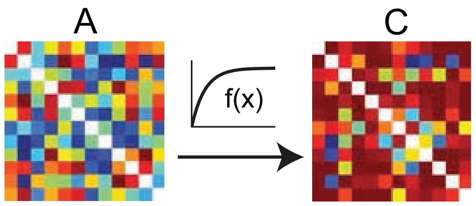
Betti curves are invariant under monotone transformations...



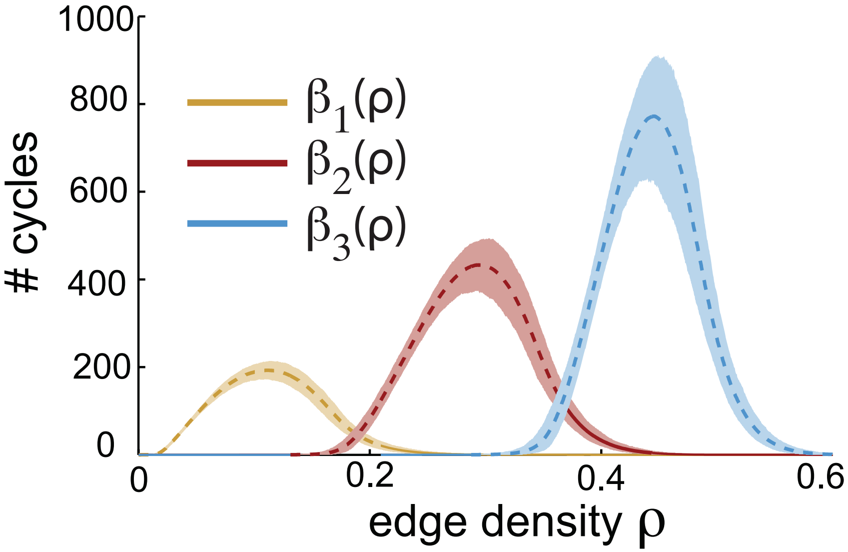
Betti curves are invariant under monotone transformations...




But can they be used to detect random or geometric structure?

# Betti curves of random and geometric matrices

## random

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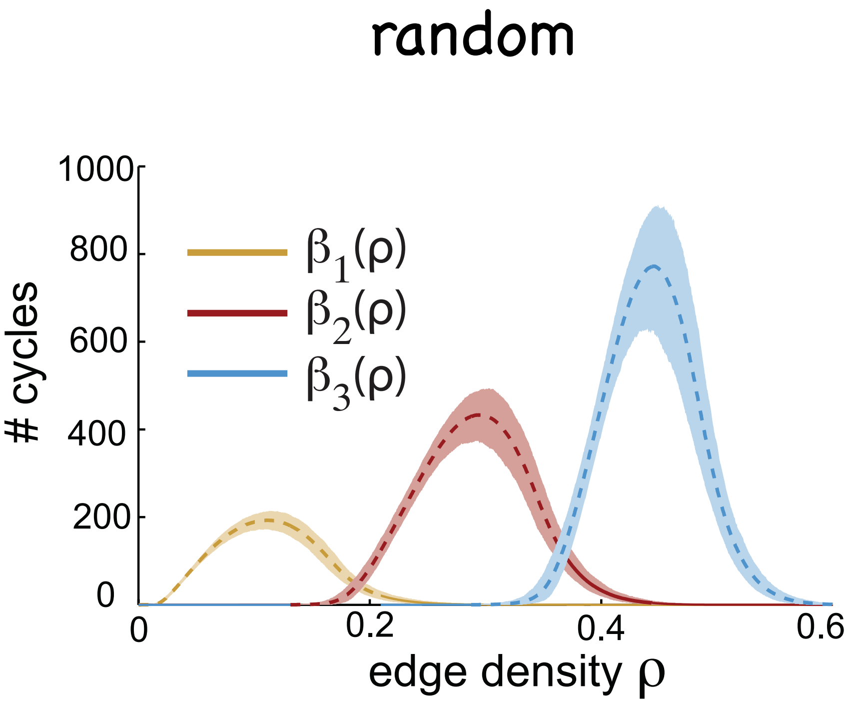
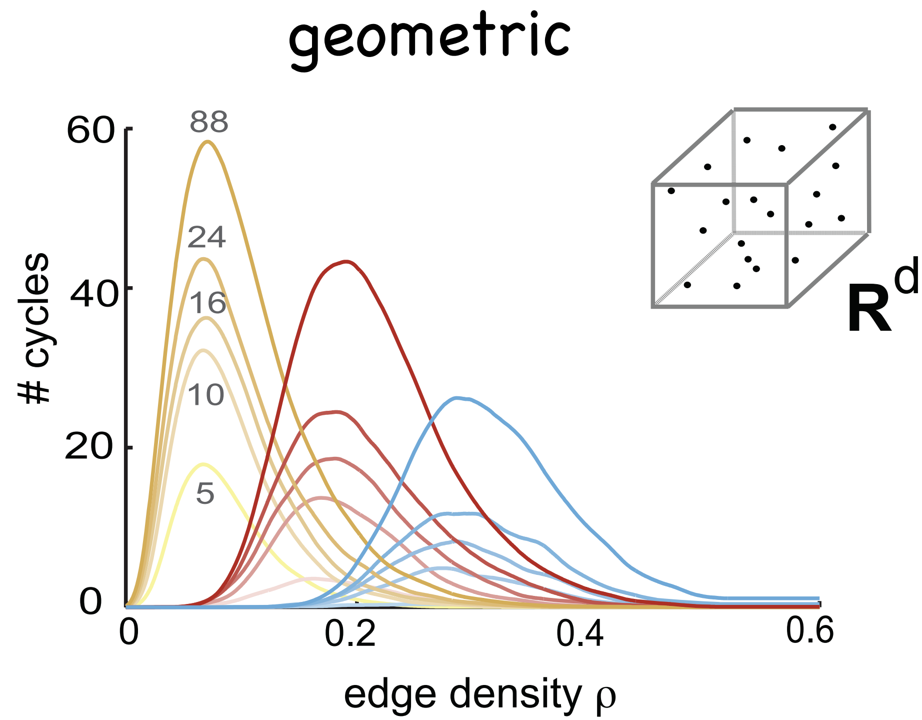
# Betti curves of random and geometric matrices

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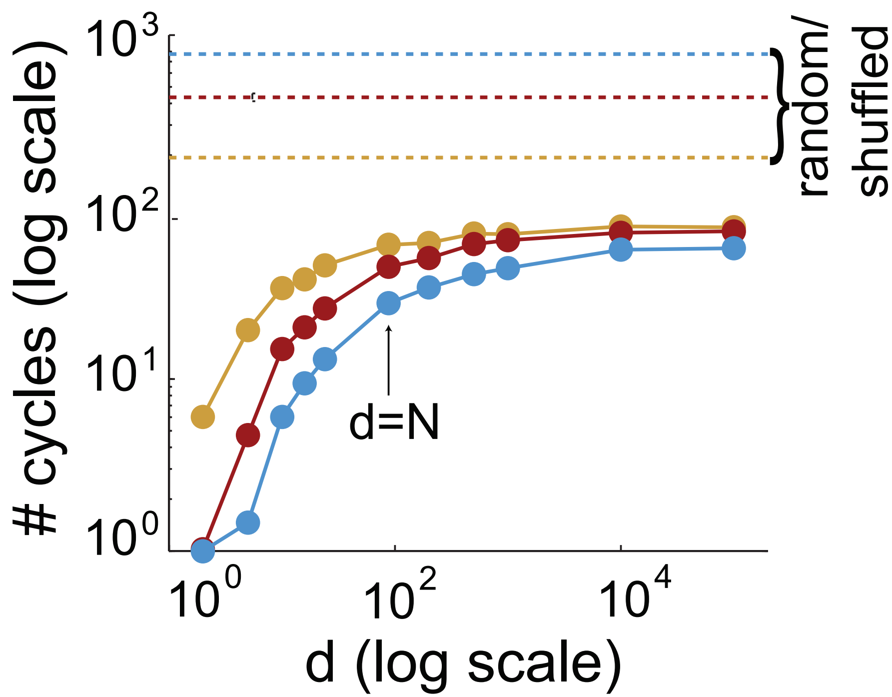
# Betti curves of random and geometric matrices

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# Software for computing Betti curves for symmetric matrices

- Custom-made software for generating clique complexes (Chad Giusti).

- **Perseus** software for computing homology groups of clique complexes. Vidit Nanda (while a student of Konstantin Mischaikow).

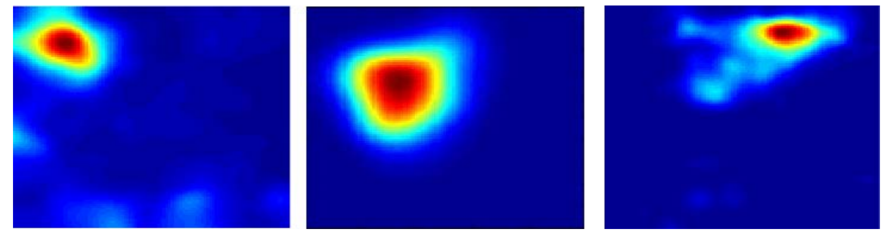
- **Software** on GitHub:

  `https://github.com/nebneuron/clique-top`

# What happens when we feed in real data?

place cell

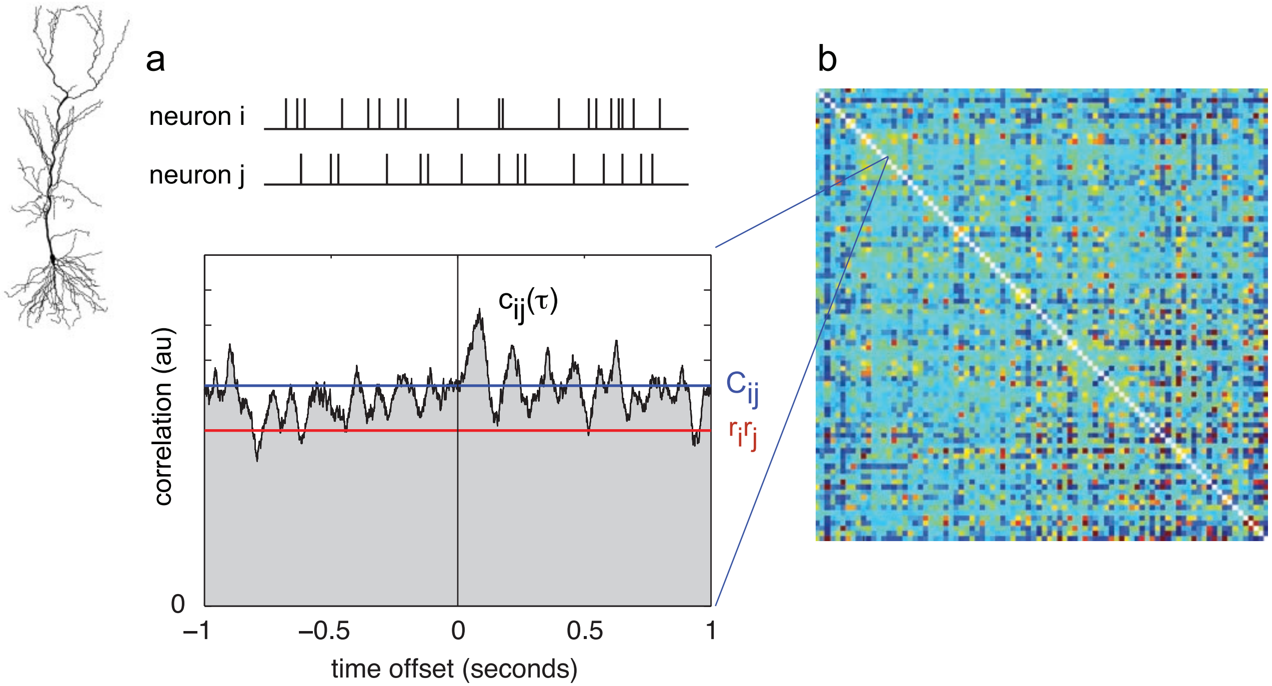
place fields



We used multi-unit electrophysiological recordings of CA1 pyramidal cells in rat hippocampus during open field exploration.

Data provided by Eva Pastalkova’s lab at Janelia Research Campus, HHMI.

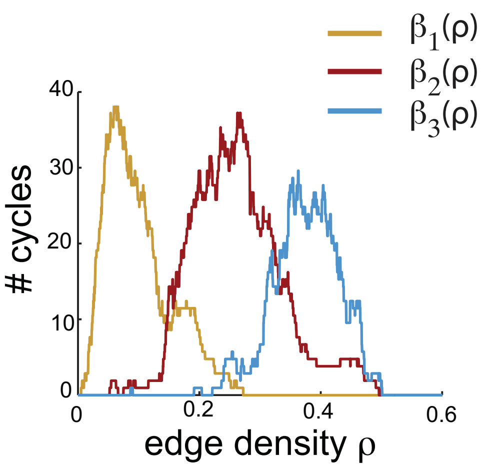
# Pairwise correlations for place cells (open field)



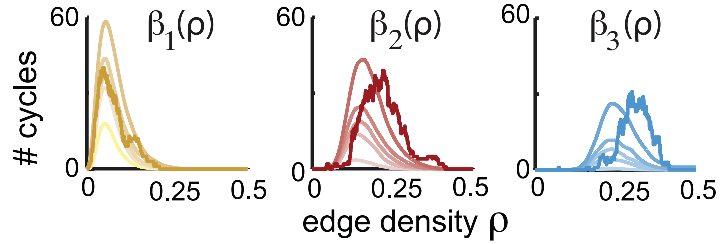

$$c_{ij}(\tau) = \frac{1}{T}\int_0^T f_i(t) f_j(t+\tau)\mathrm{d}t$$

# Betti curves for open field data

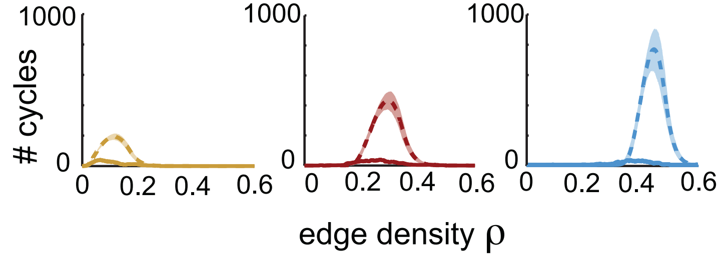
place cell data

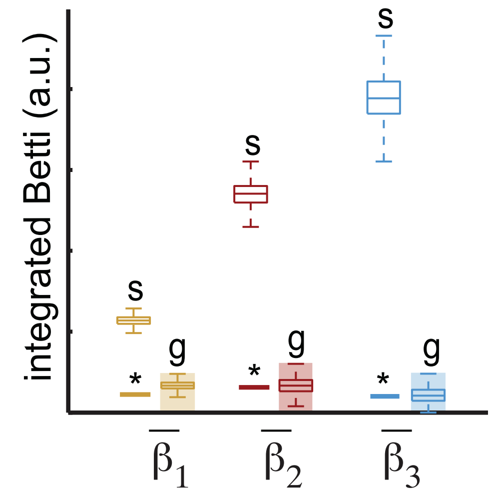



data vs. geometric




data vs. shuffled

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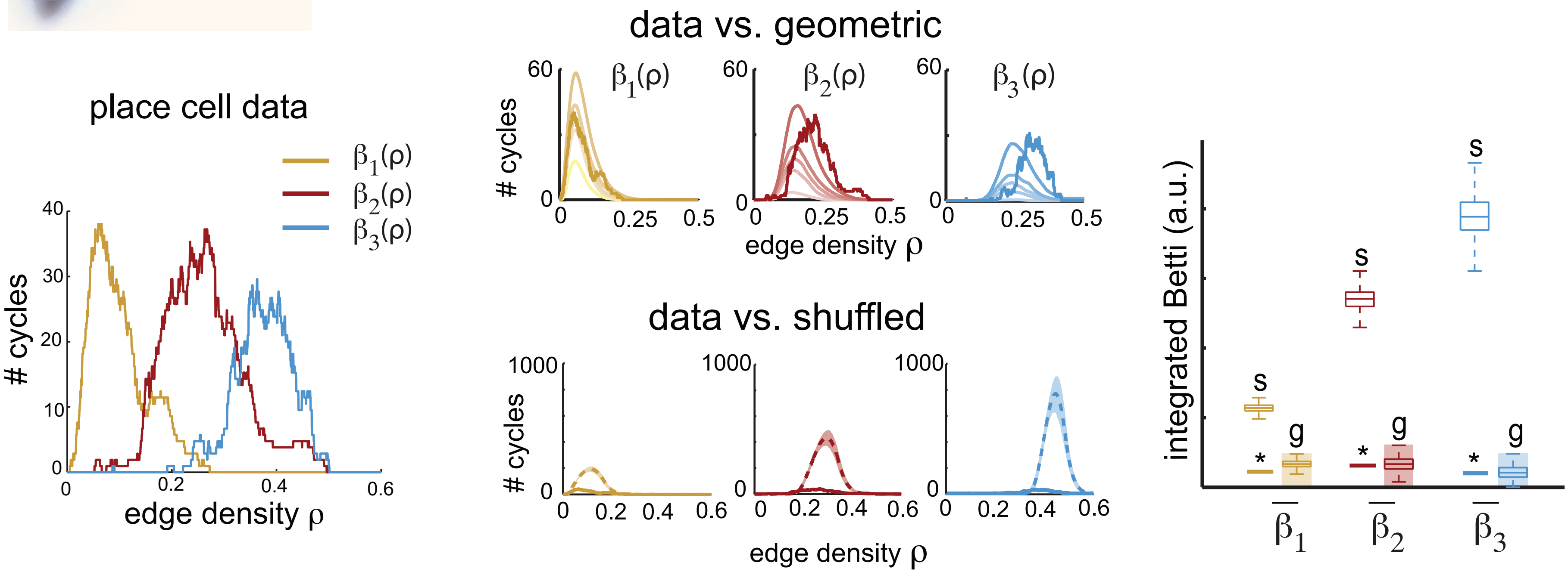
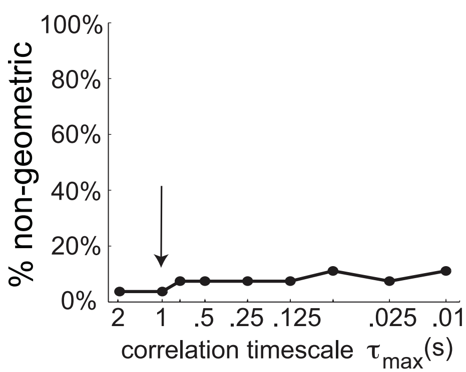
# Betti curves for open field data




Results are consistent across data sets, and correlation timescales

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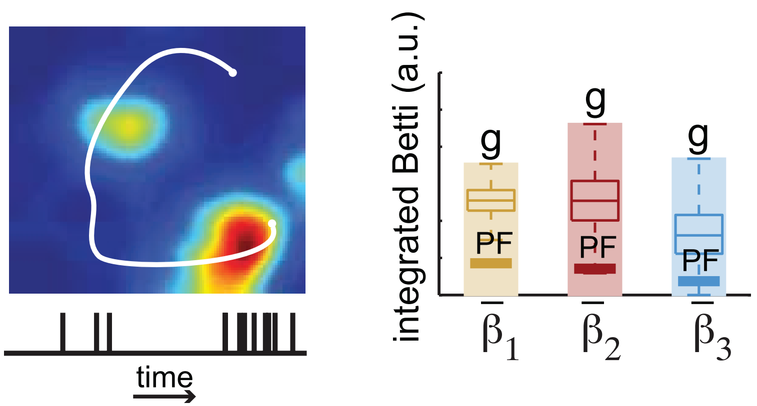
# Simulated data from a simple PF model

place field model

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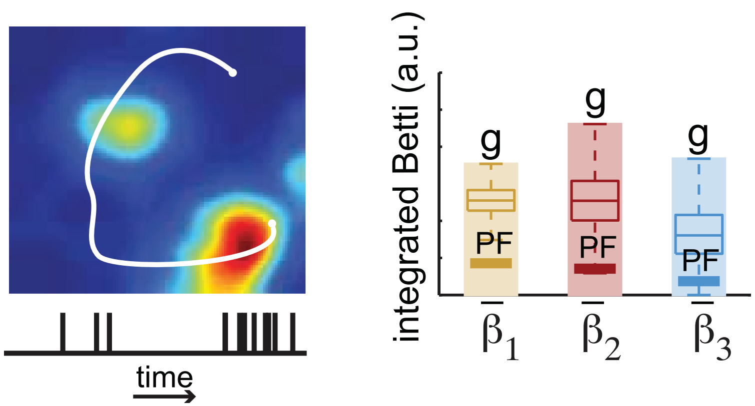
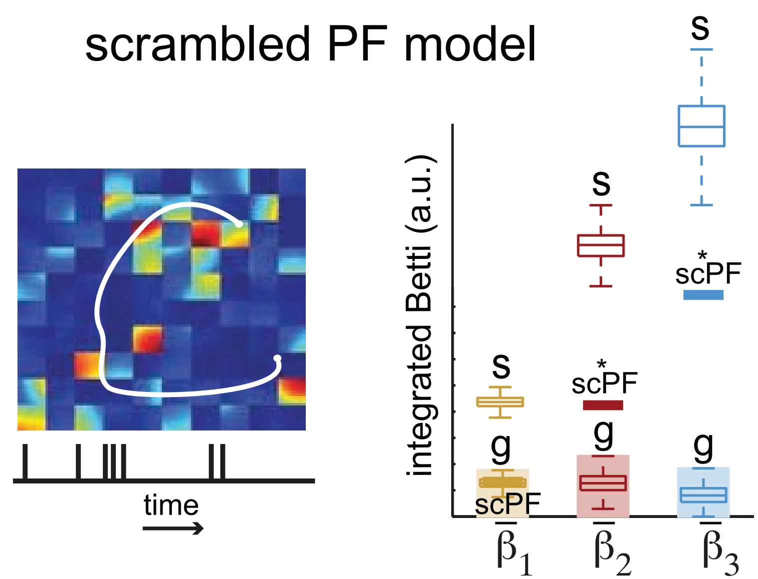
# Simulated data from a simple PF model

place field model




scrambled PF model

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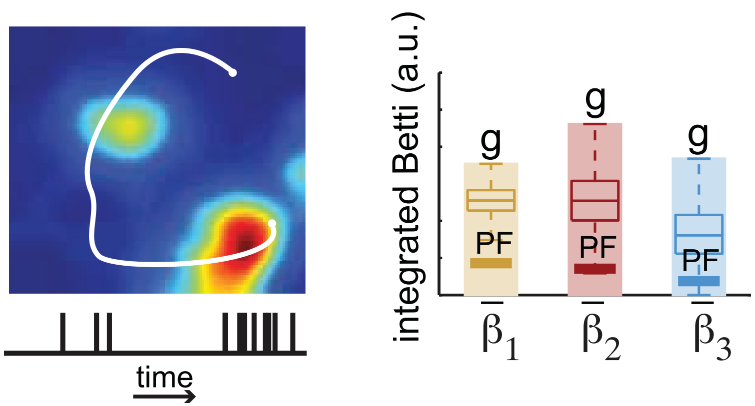
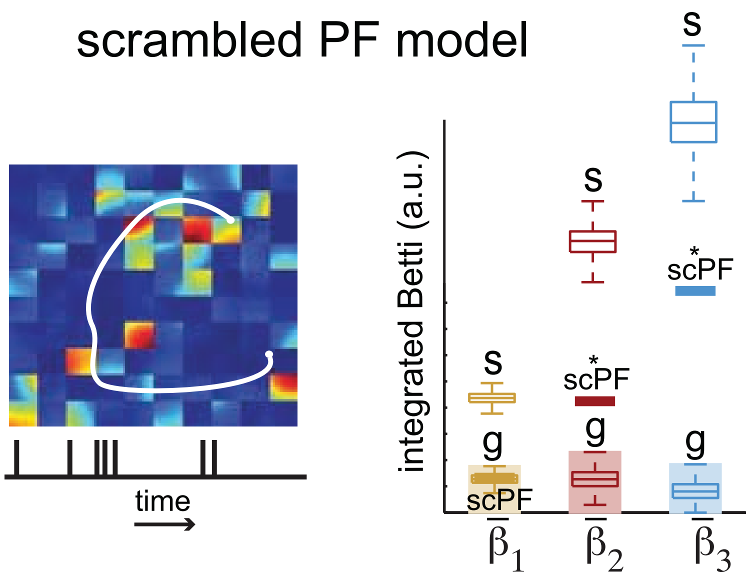
# Simulated data from a simple PF model

place field model




scrambled PF model




Geometric structure of correlations can be explained by place fields alone, but not if they are scrambled and non-geometric.

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# Thanks!

Collaborators on this work:
Katie Morrison (University of Northern Colorado)
Anda Degeratu (Freiberg)
Chad Giusti (former postdoc at UNL, now at UPenn)
Vladimir Itskov (Penn State)
Eva Pastalkova (Janelia Research Campus, HHMI)

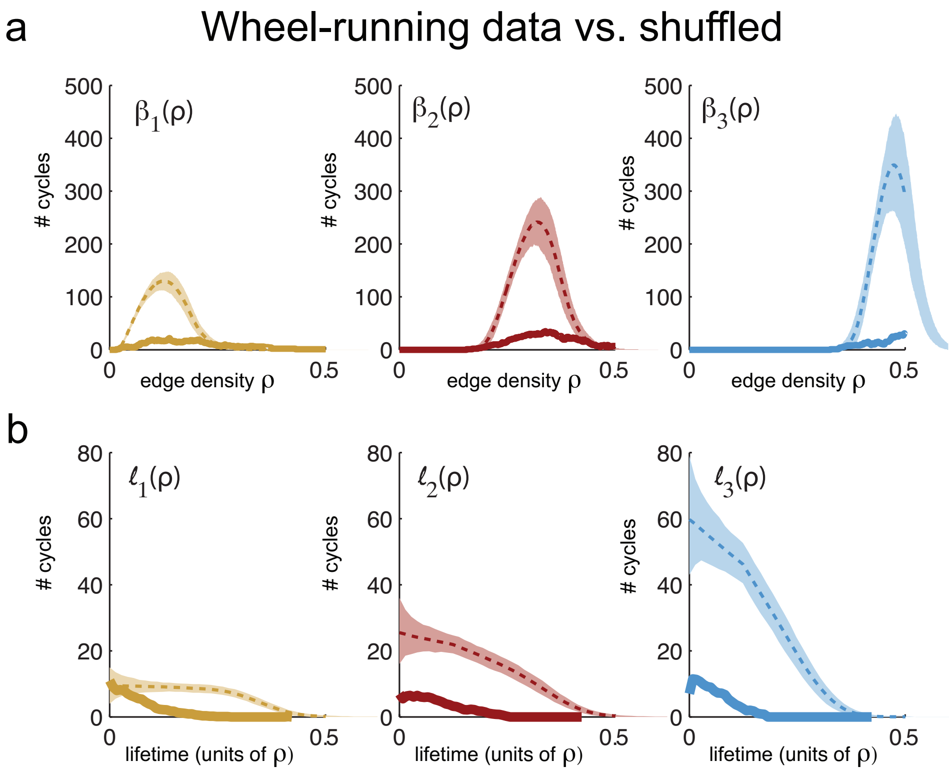
Funding: NSF DMS, Sloan Foundation, Janelia Visitor Program

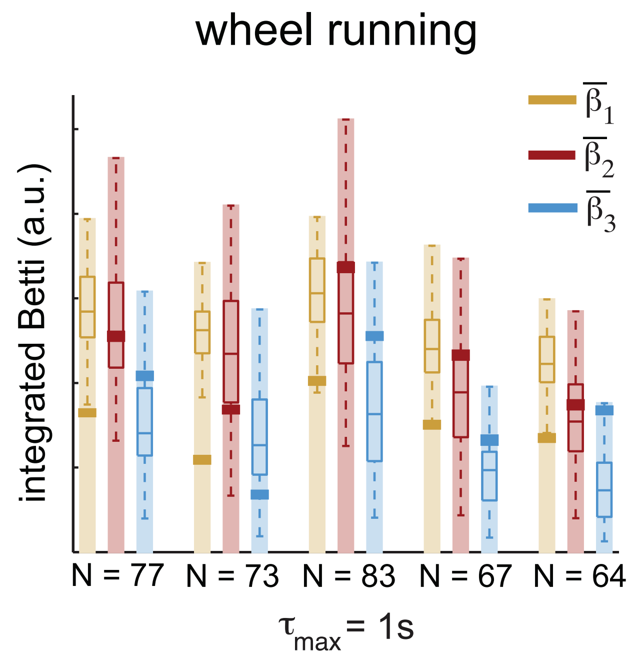
# What about non-spatial behaviors?

running wheel

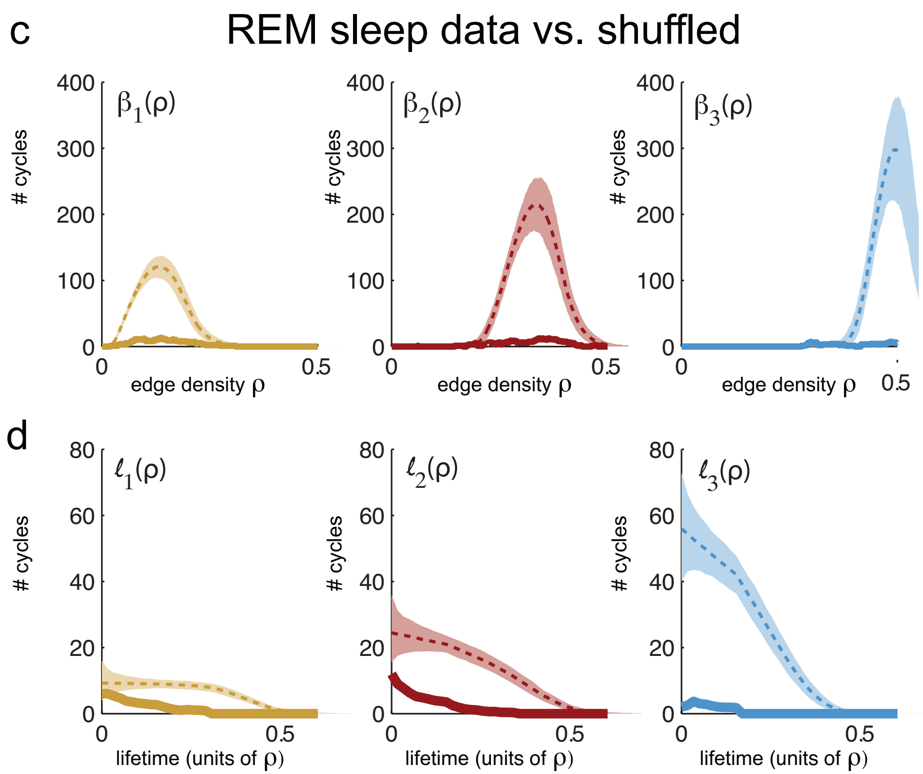
REM sleep

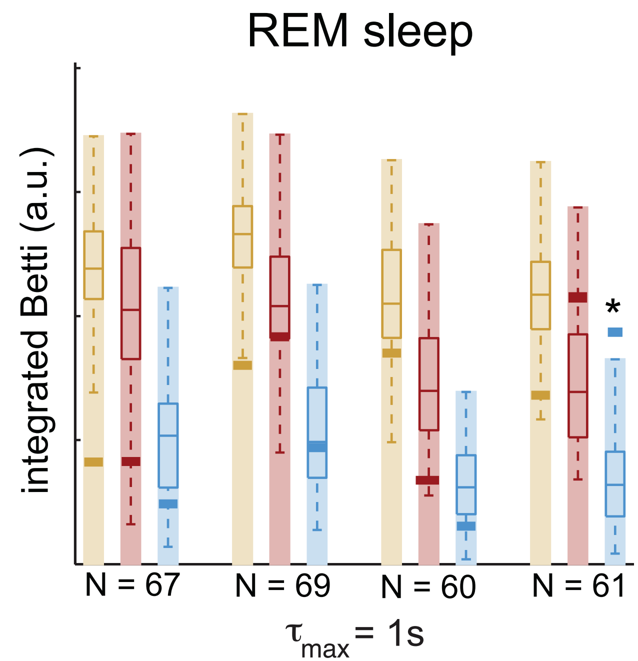
# Betti curves: wheel running vs. controls



# Betti curves: REM sleep vs. controls



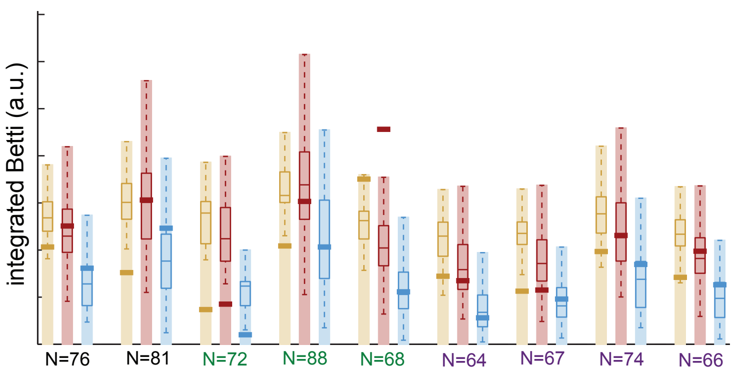



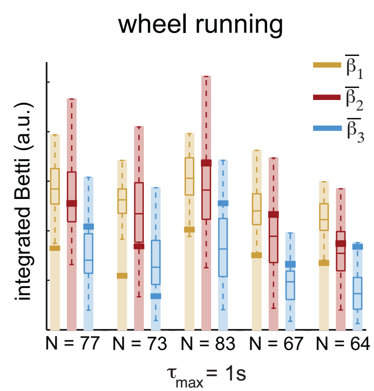
# The results look very similar across behavioral conditions…

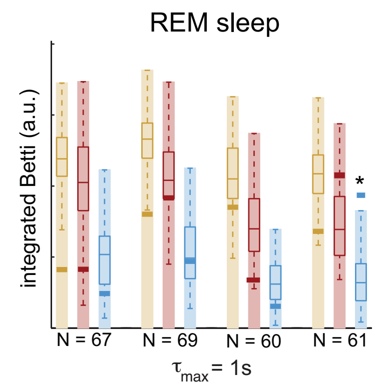
open field

wheel running

REM sleep




## Conclusion:

The “geometric” correlation structure appears to be a property of the network, not just of the inputs.

# The results look very similar across behavioral conditions...

open field

wheel running

REM sleep