Learning the collective dynamics of complex biological systems

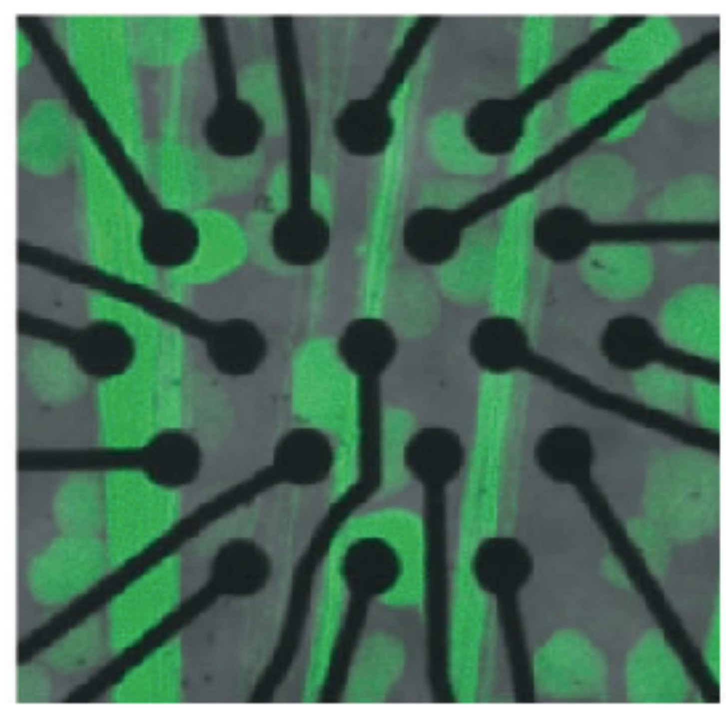
from neurons to animal groups

Thierry Mora

Laboratoire de Physique Statistique
CNRS & École normale supérieure

Università Sapienza Rome
A. Cavagna
I. Giardina
O. Pohl
E. Silvestri
M. Viale

Aberdeen University
F. Ginelli



ENS Paris
A. Walczak

Princeton University
W. Bialek

Vision Institute
S. Deny
O. Marre

emergent collective behaviours in biology

- molecular scale

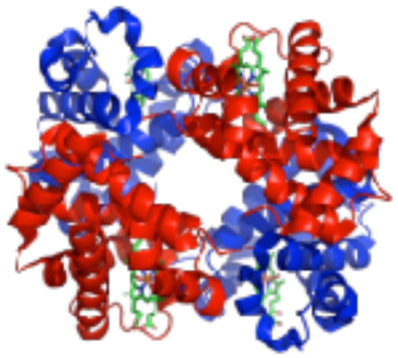
  - the protein folding problem

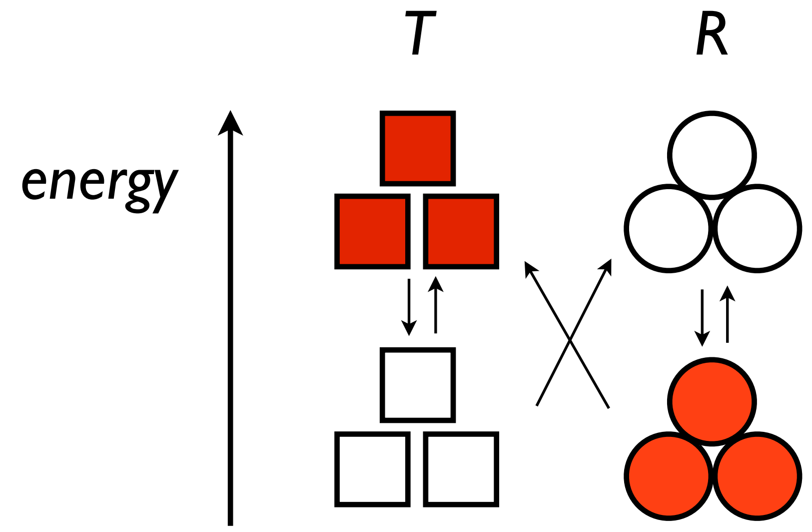
emergent collective behaviours in biology

- molecular scale

  - the protein folding problem

  - allosteric binding of enzymes (MWC model)





emergent collective behaviours in biology

- molecular scale

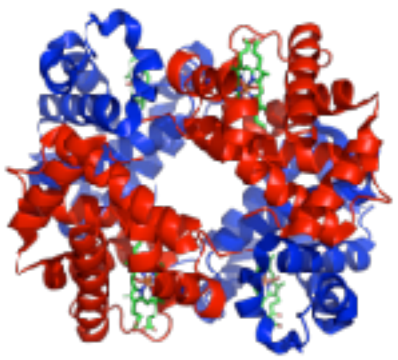
  - the protein folding problem

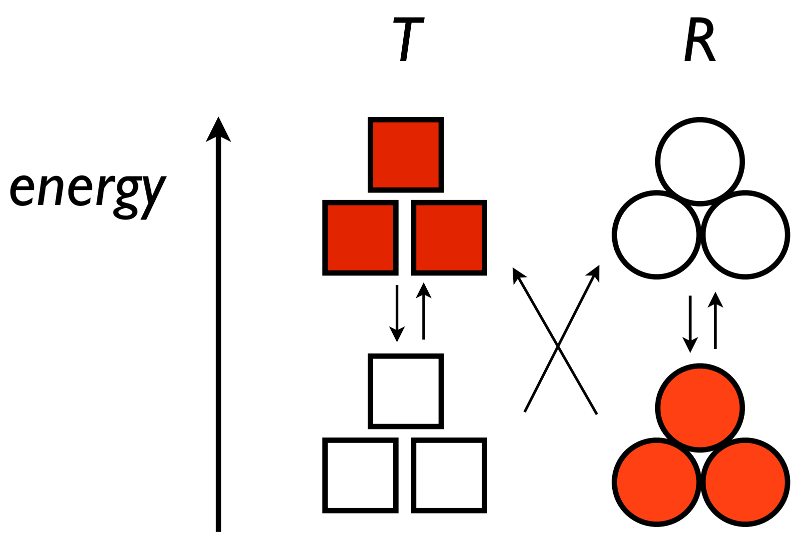
  - allosteric binding of enzymes (MWC model)

- cellular scale

  - multicellularity

  - the brain





emergent collective behaviours in biology

- molecular scale

  - the protein folding problem

  - allosteric binding of enzymes (MWC model)

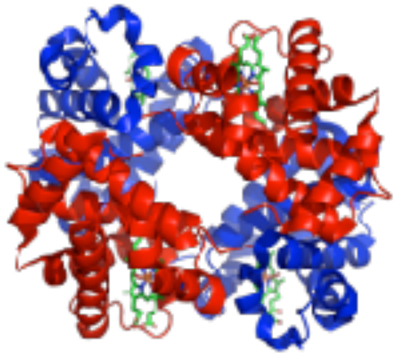
- cellular scale

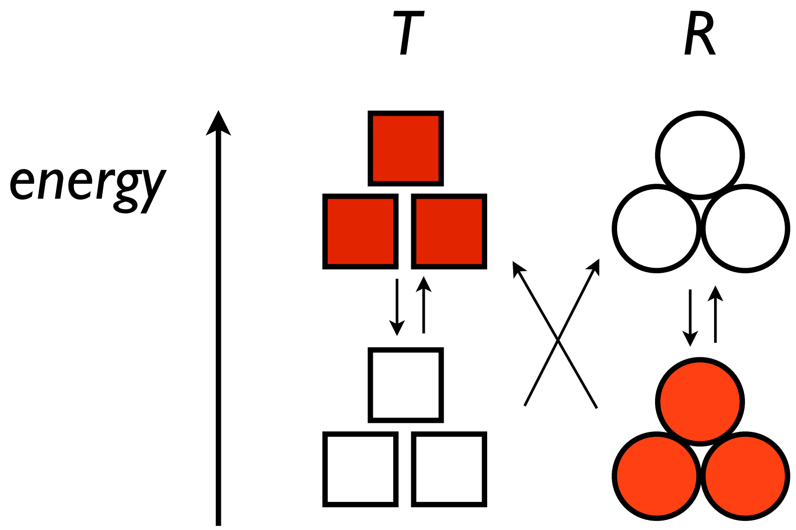
  - multicellularity

  - the brain

- population scale

  - group behaviour





4 August 1972, Volume 177, Number 4047 **SCIENCE**

More Is Different

Broken symmetry and the nature of the hierarchical structure of science.

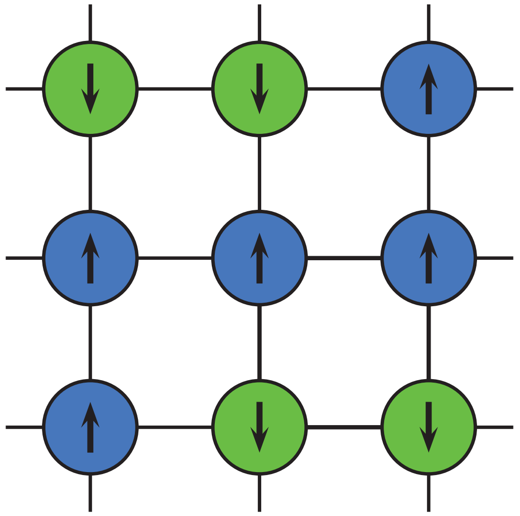
P. W. Anderson

X	Y
solid state or many-body physics	elementary particle physics
chemistry	many-body physics
molecular biology	chemistry
cell biology	molecular biology
•	•
•	•
•	•
psychology	physiology
social sciences	psychology

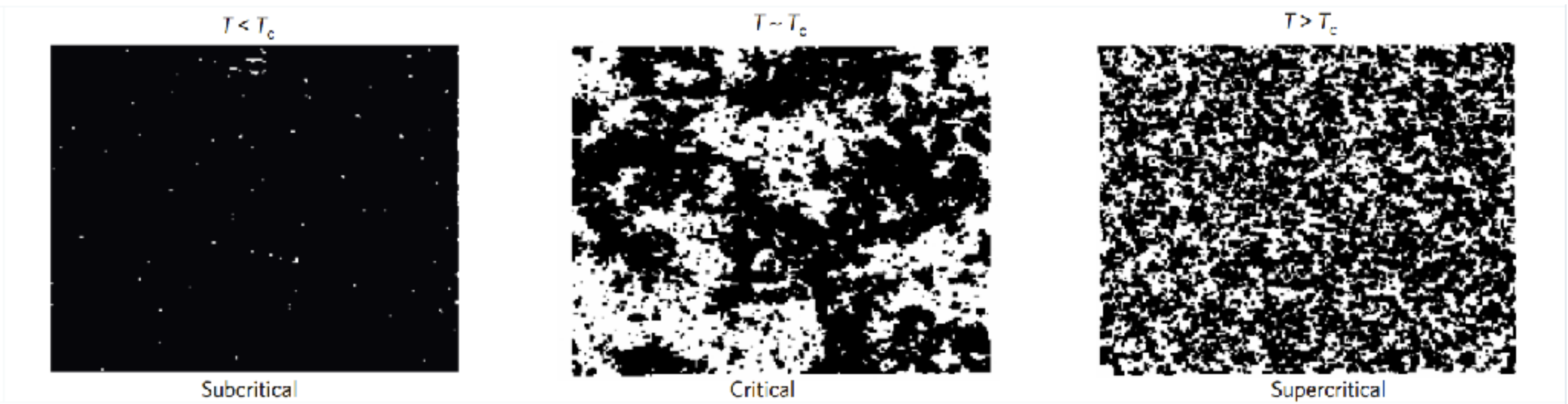
the Ising model

- a very simple example of emergence

$$H = -J \sum_{i,j \text{ neighbours}} s_i s_j \qquad s_i = \pm 1 \text{ (black or white)}$$

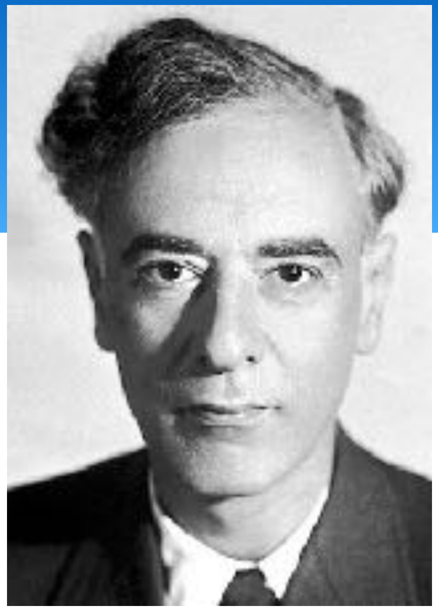


$$P(s_1, \ldots, s_N) = \frac{1}{Z} e^{-H/T}$$



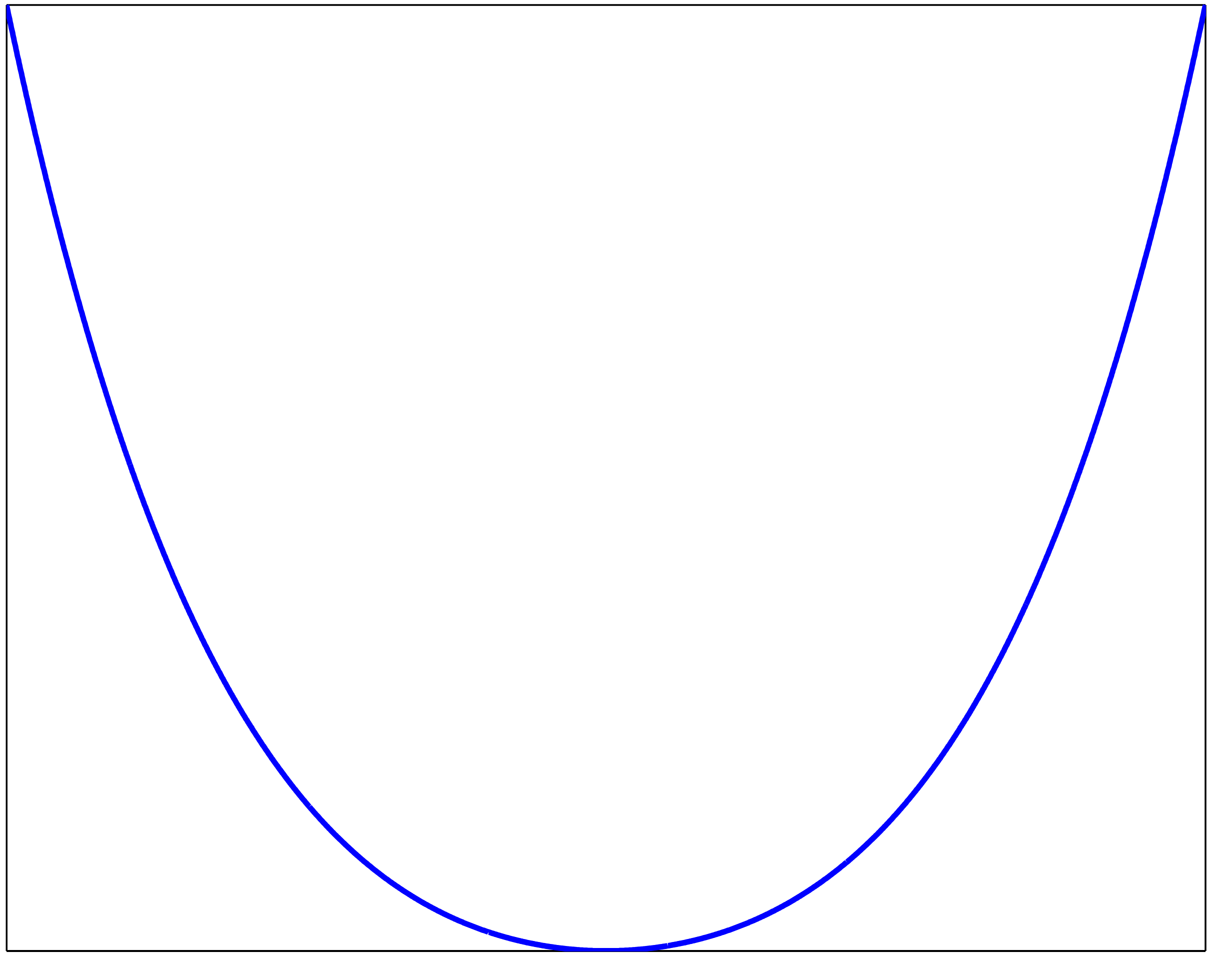
ordered critical disordered

phase transitions



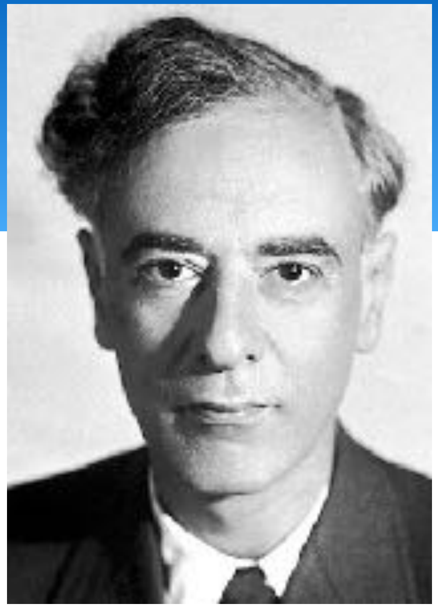
- Laudau's theory

$$H(\phi) = (\nabla\phi)^2 + g(T)\phi^2 + \lambda\phi^4$$



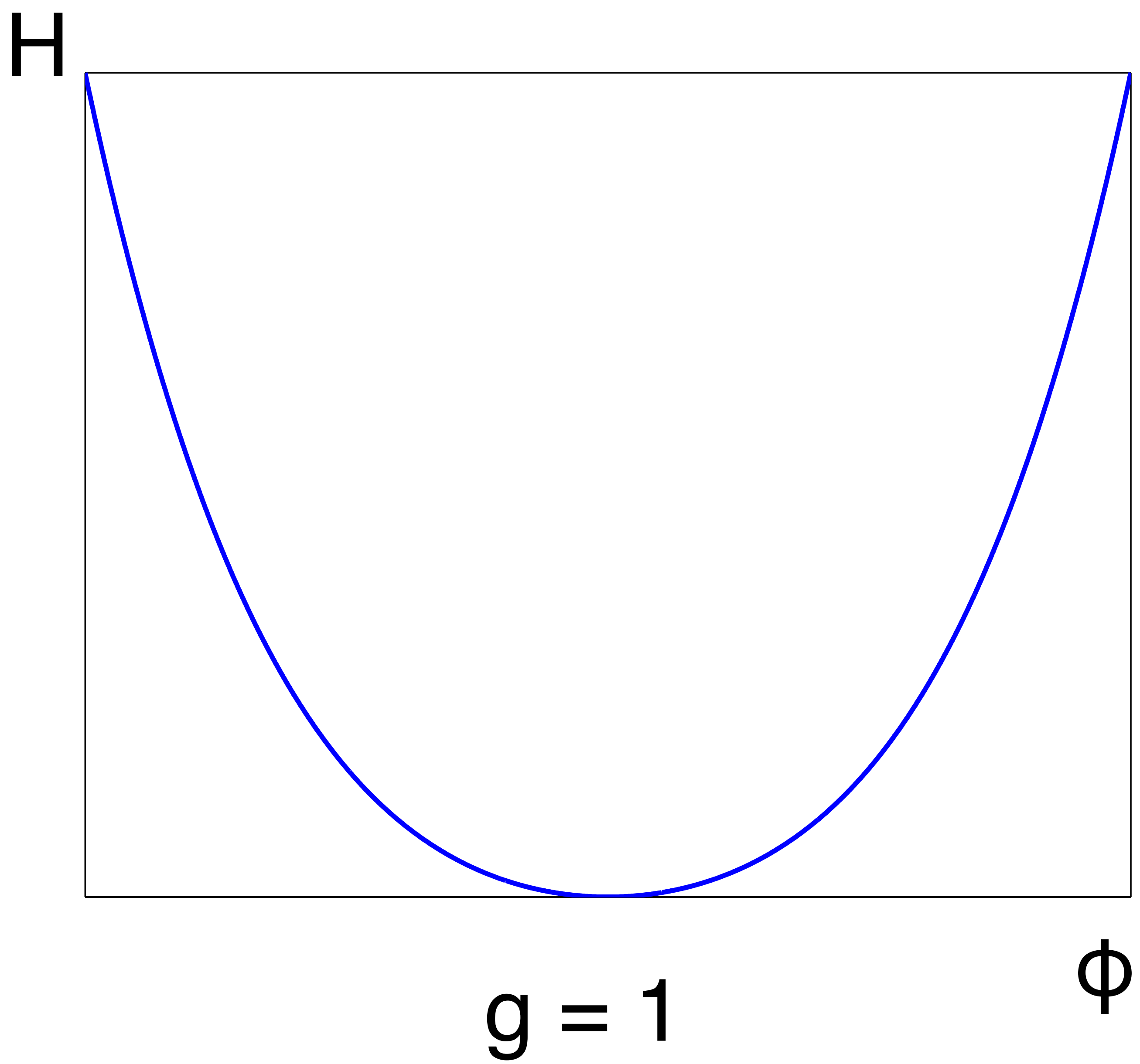
g = 1

phase transitions

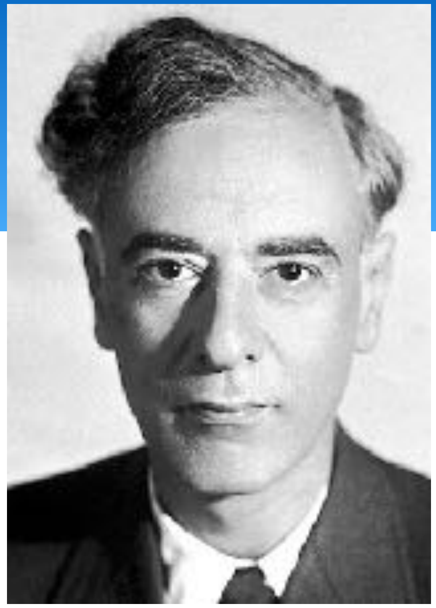


- Laudau's theory

$$H(\phi) = (\nabla\phi)^2 + g(T)\phi^2 + \lambda\phi^4$$

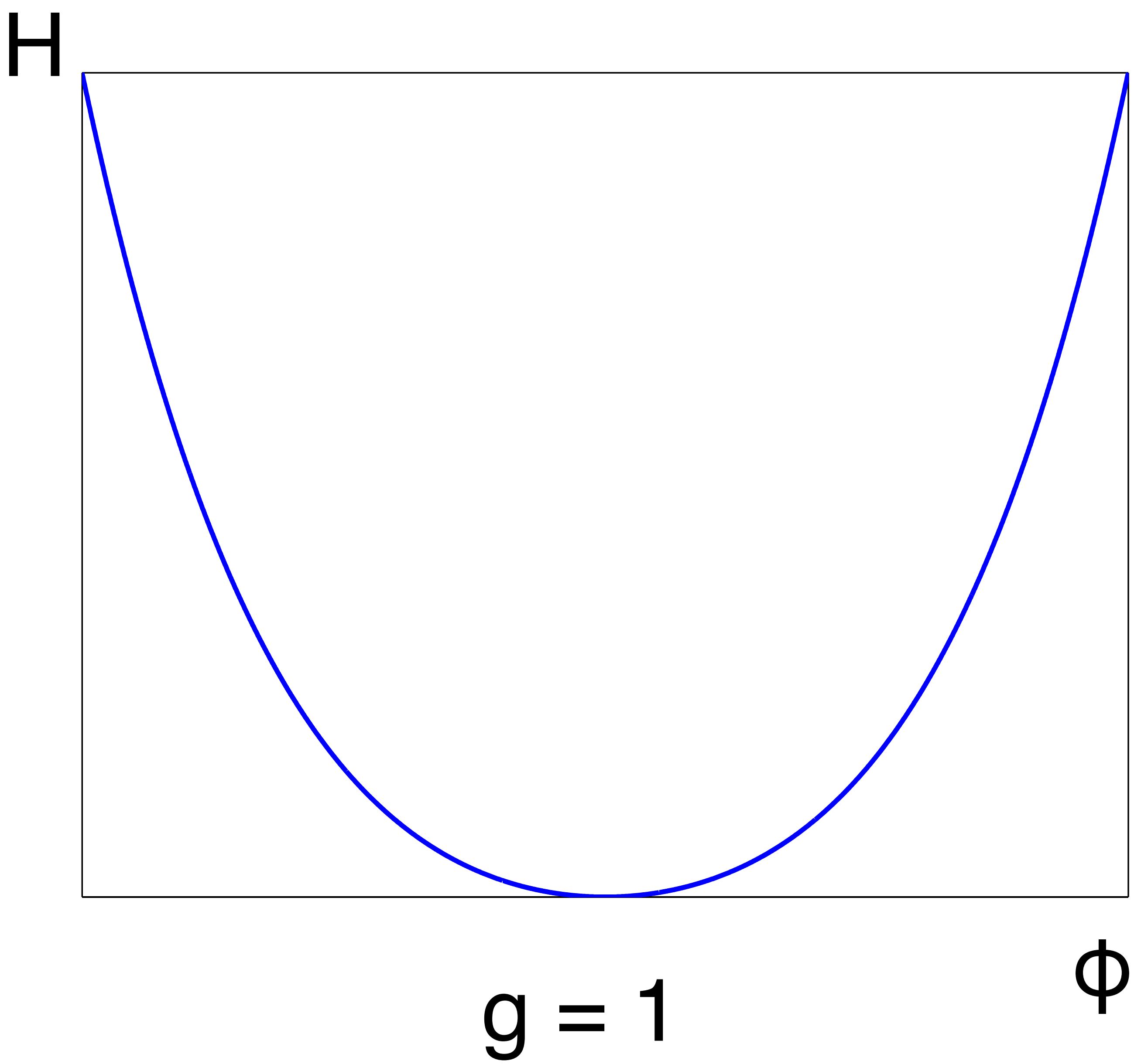


phase transitions

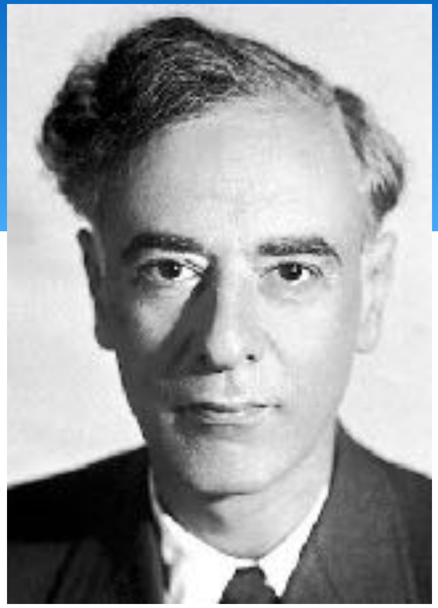


- Laudau's theory (mean field)

$$H(\phi) = (\nabla\phi)^2 + g(T)\phi^2 + \lambda\phi^4$$

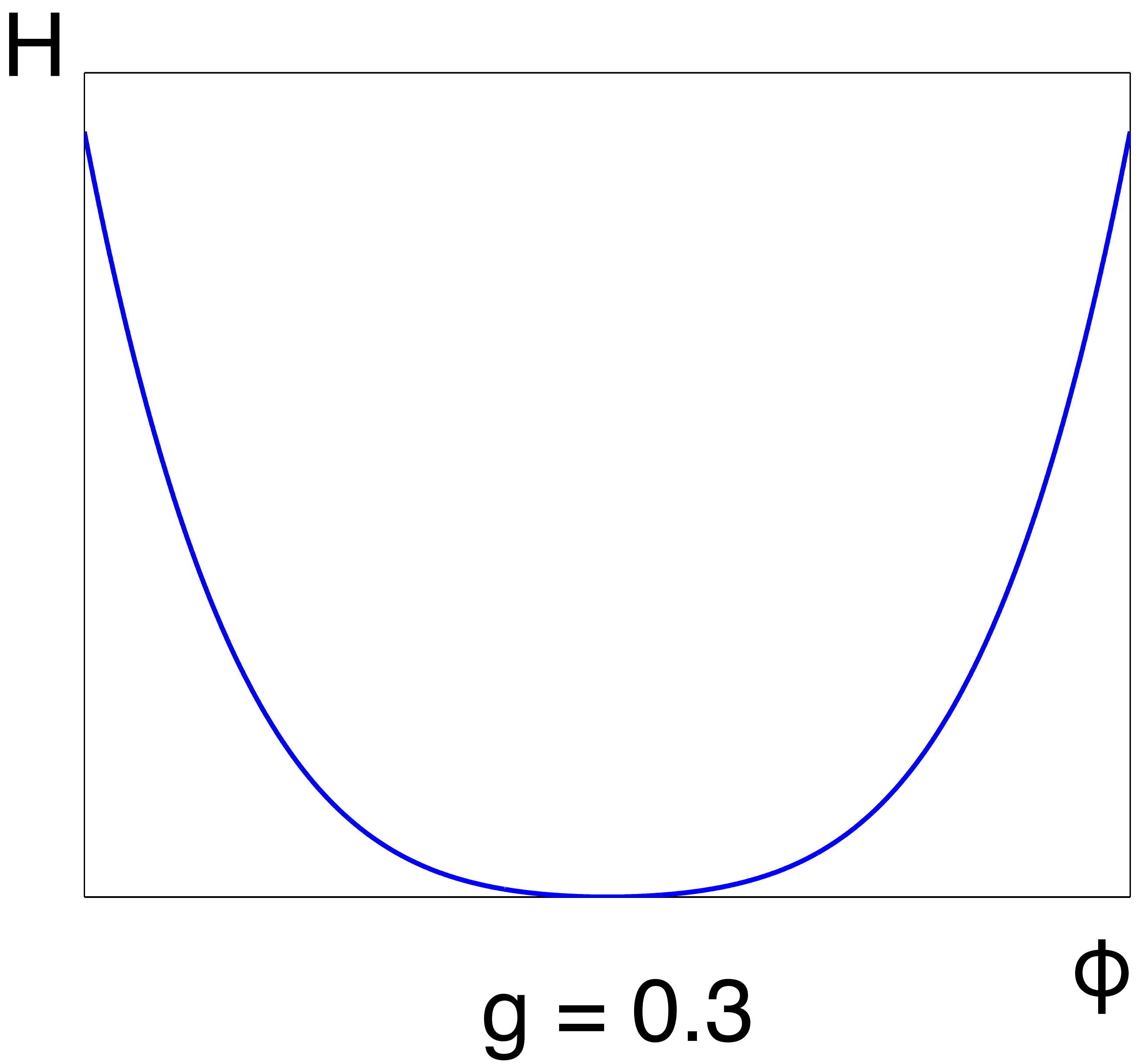


phase transitions

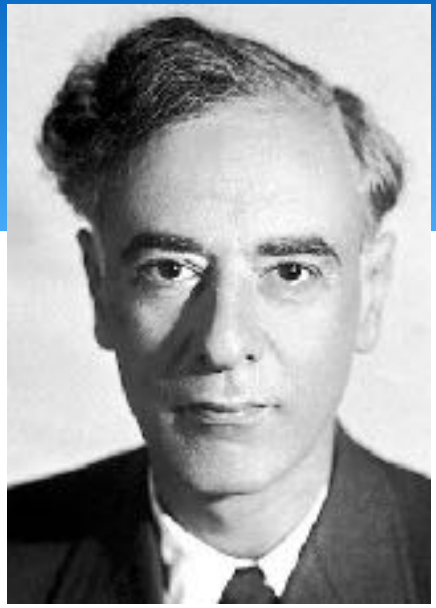


- Laudau's theory (mean field)

$$H(\phi) = (\nabla\phi)^2 + g(T)\phi^2 + \lambda\phi^4$$

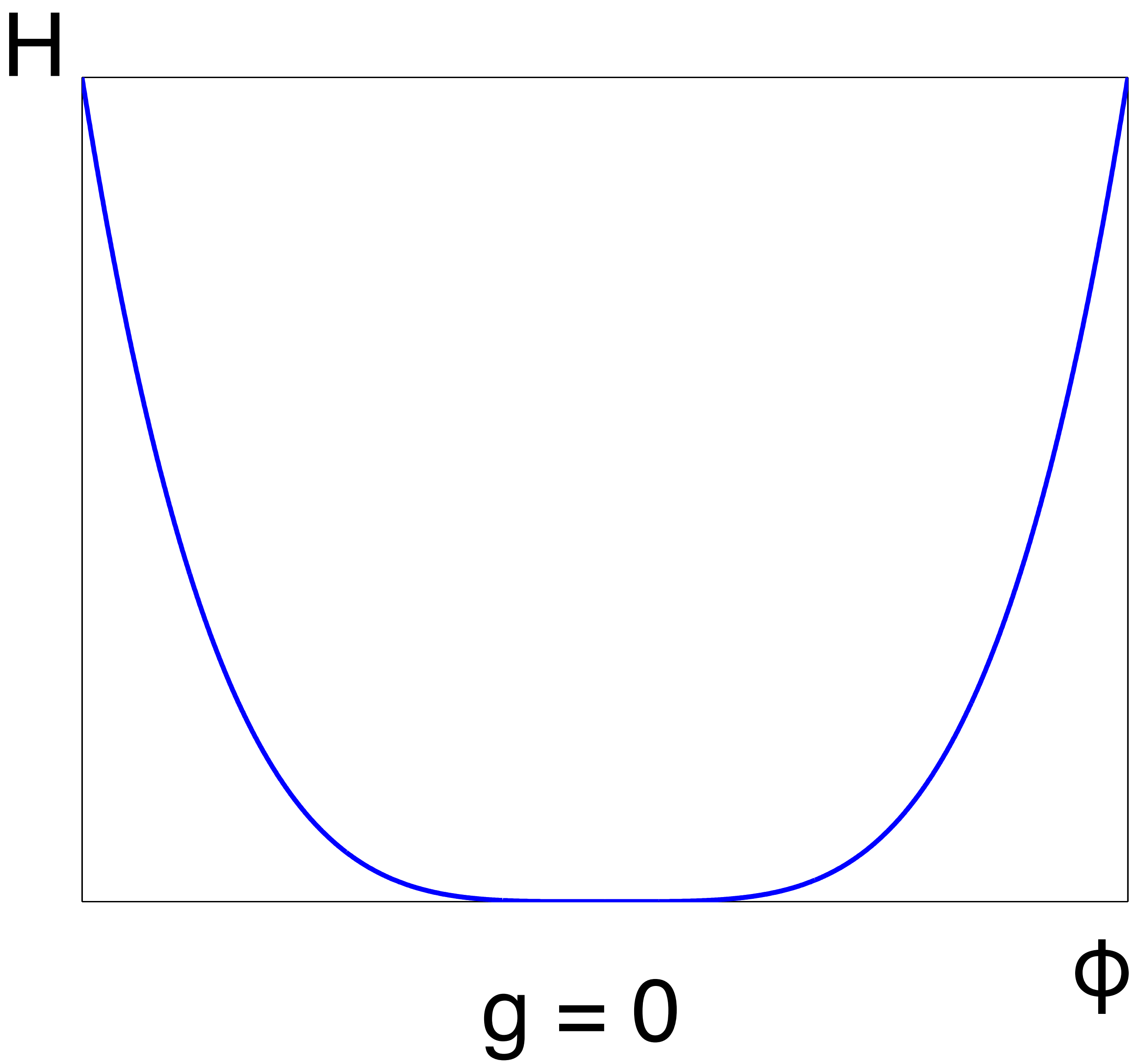


phase transitions

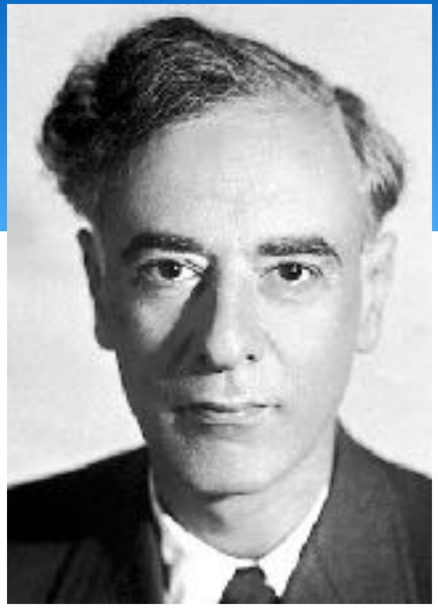


- Laudau's theory (mean field)

$$H(\phi) = (\nabla\phi)^2 + g(T)\phi^2 + \lambda\phi^4$$

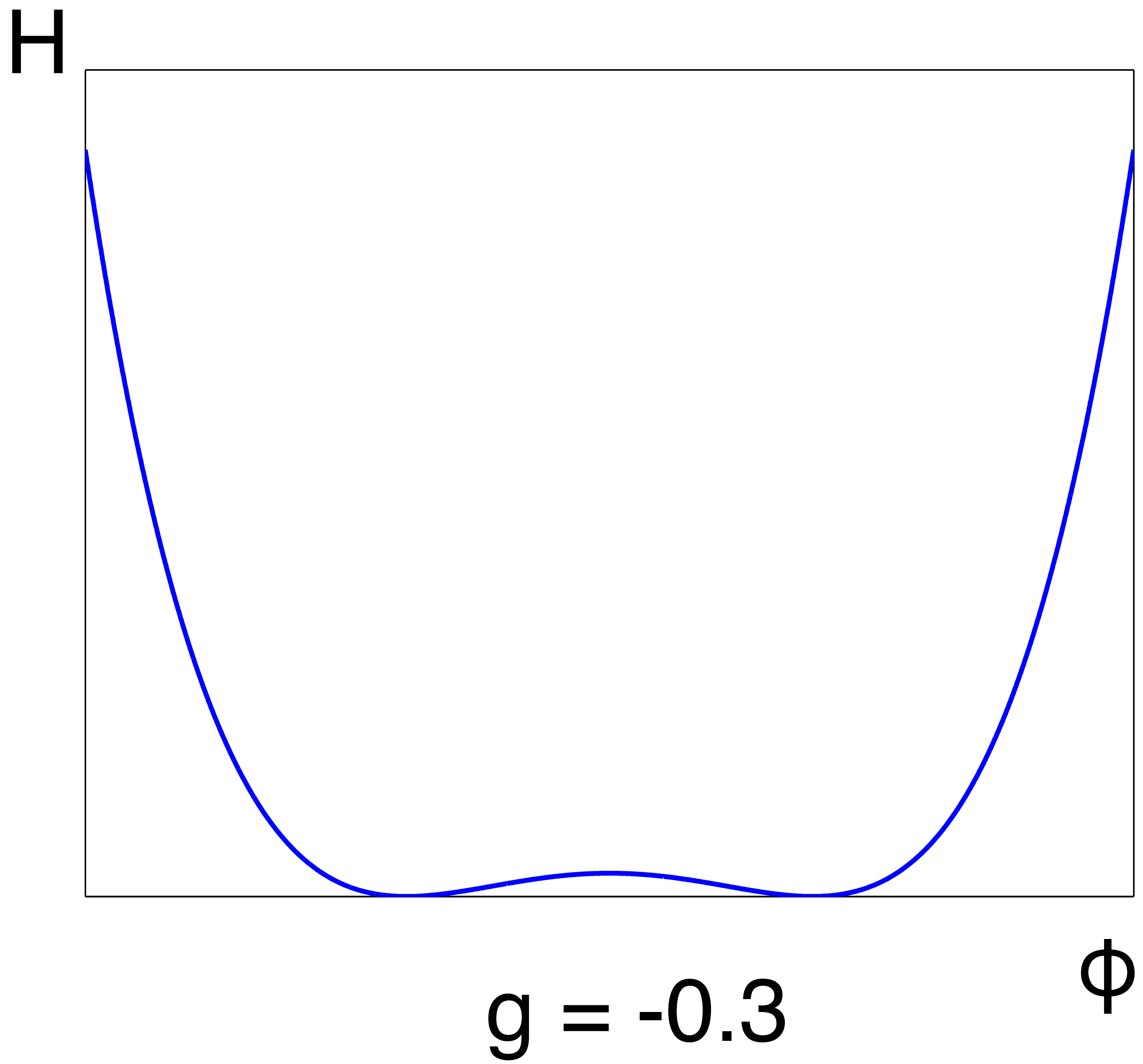


phase transitions

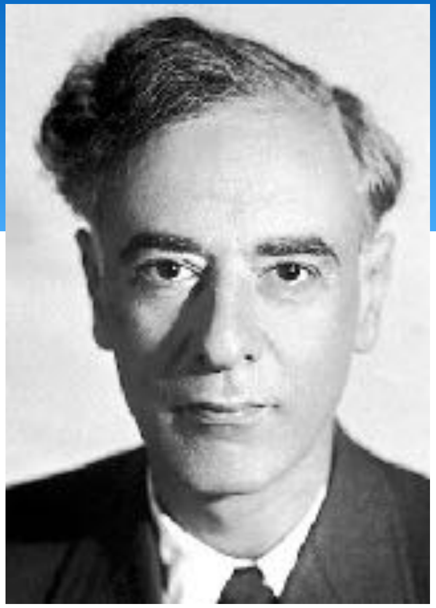


- Laudau's theory (mean field)

$$H(\phi) = \cancel{(\nabla\phi)^2} + g(T)\phi^2 + \lambda\phi^4$$

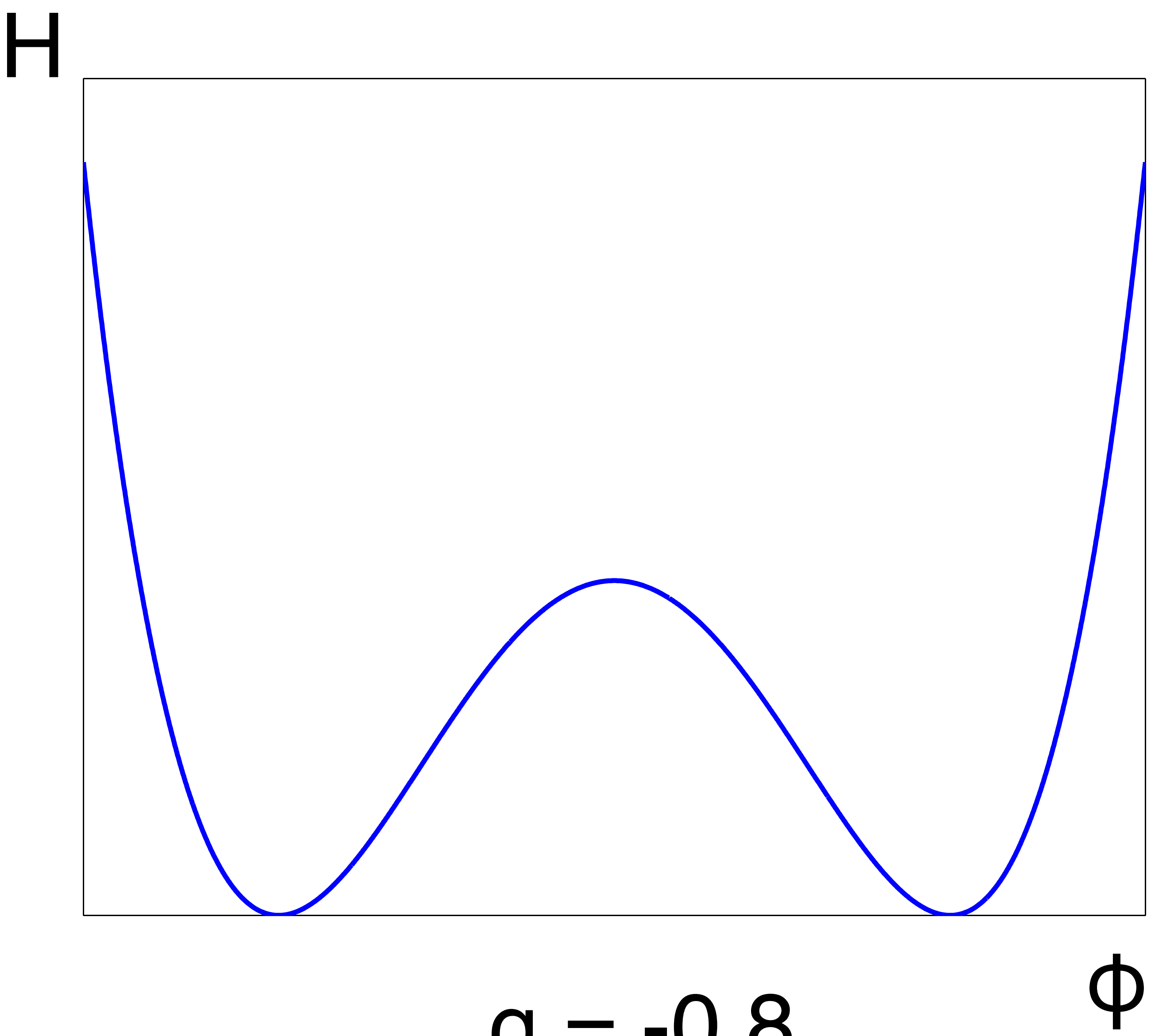


phase transitions



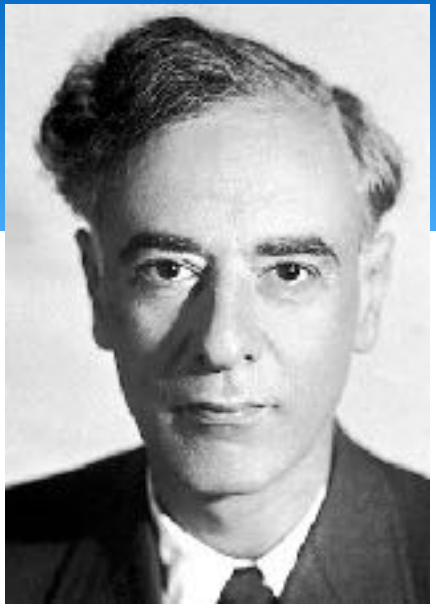
- Laudau's theory (mean field)

$$H(\phi) = (\nabla\phi)^2 + g(T)\phi^2 + \lambda\phi^4$$



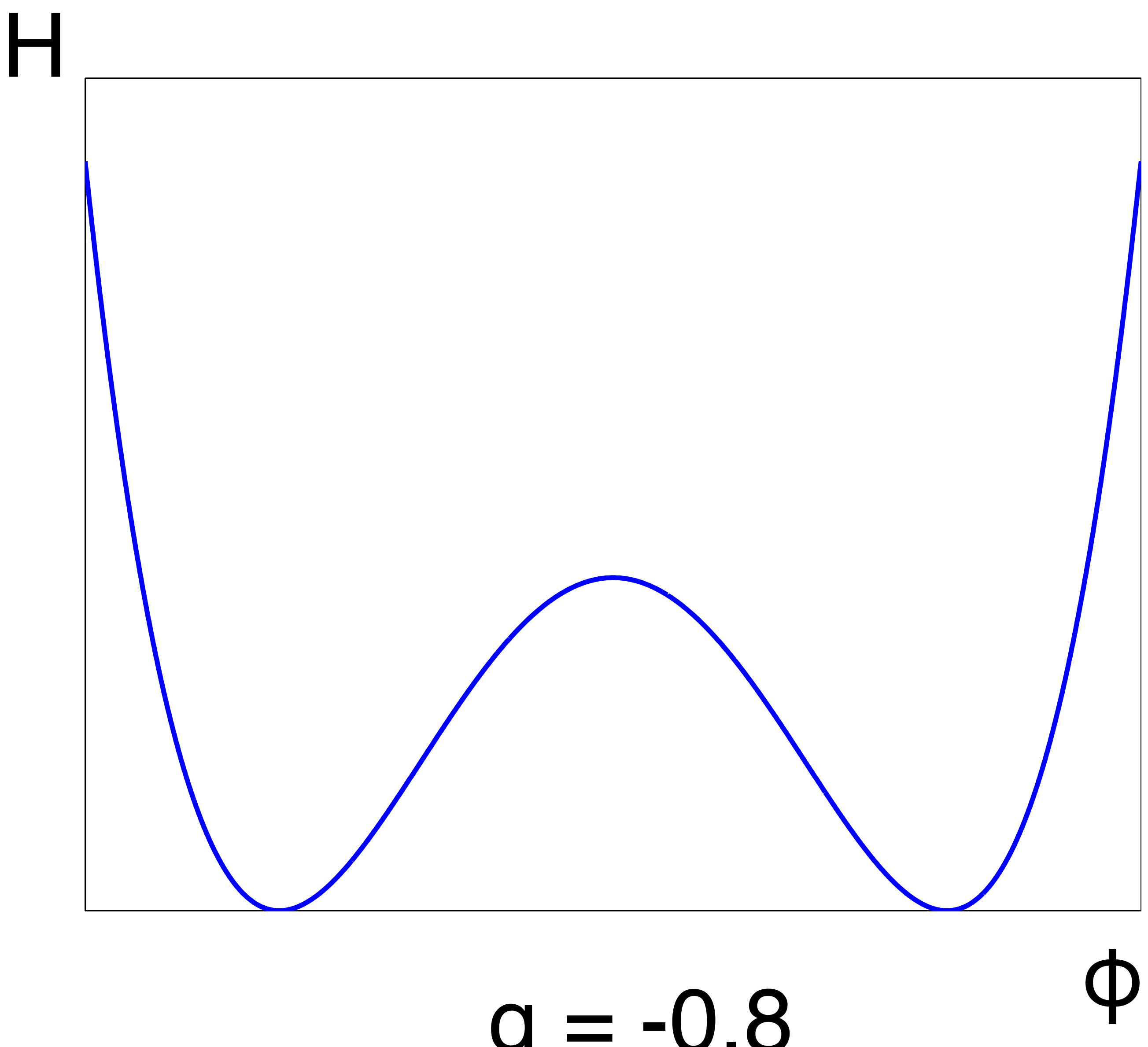
g = -0.8

phase transitions

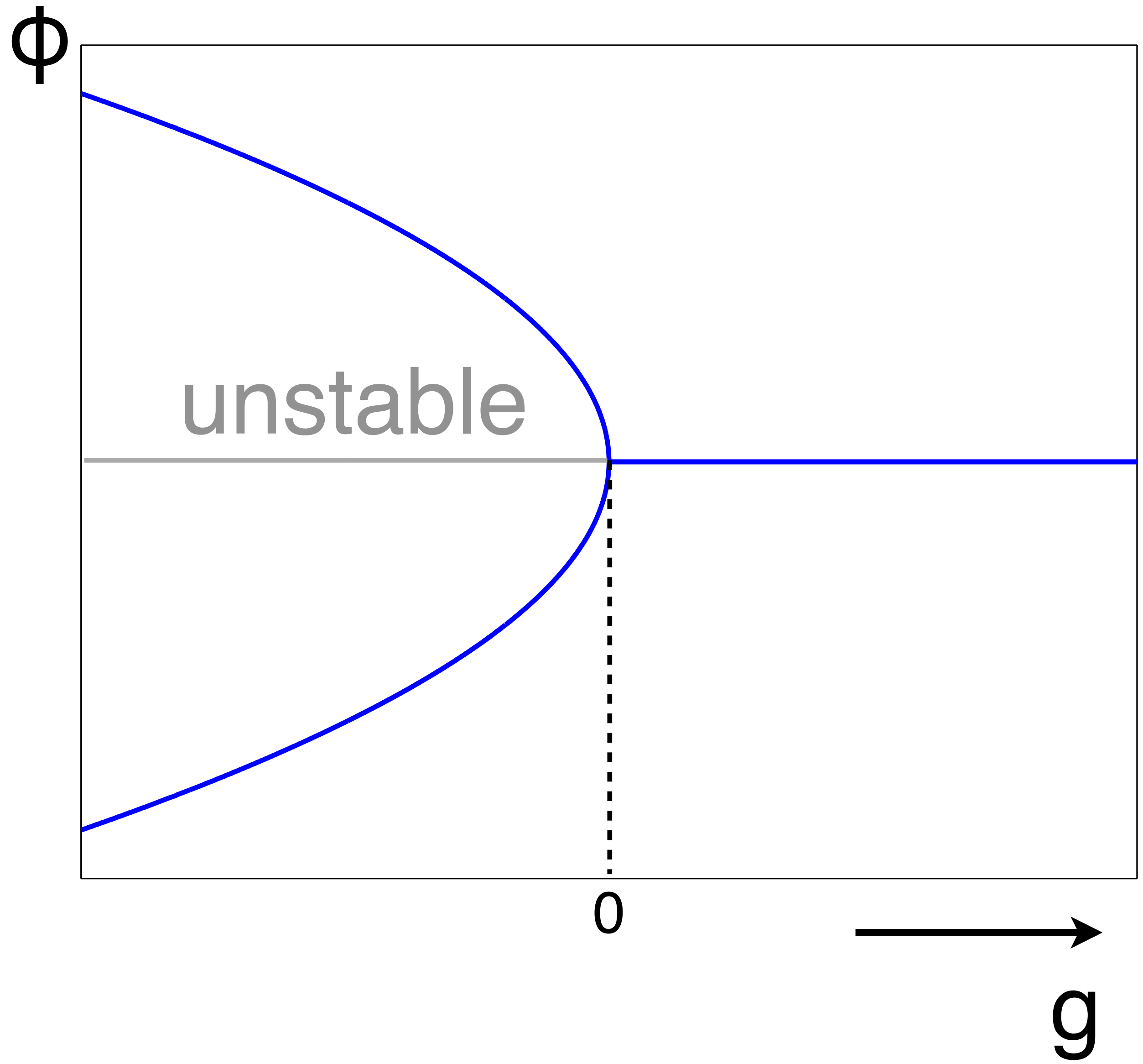


- Laudau's theory (mean field)

$$H(\phi) = \cancel{(\nabla\phi)^2} + g(T)\phi^2 + \lambda\phi^4$$

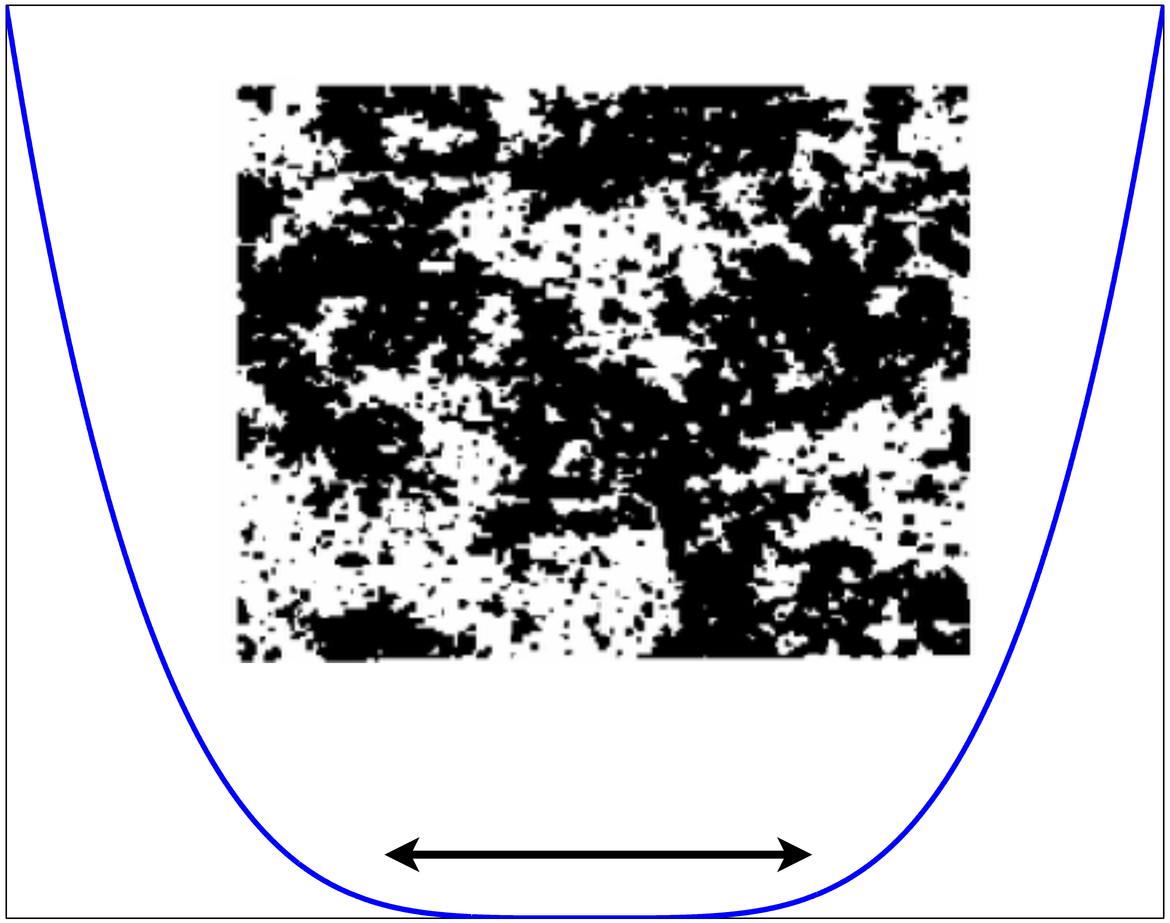


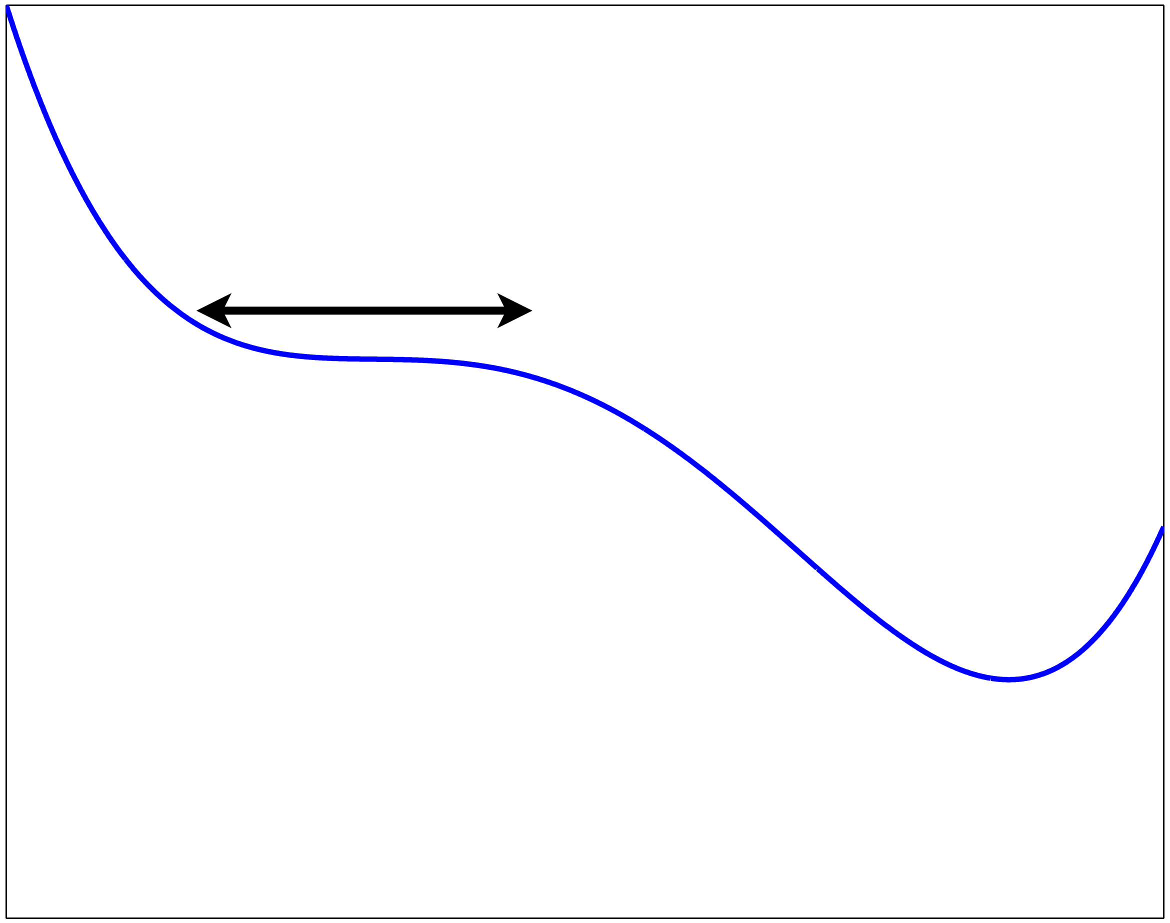
second order transition



critical point

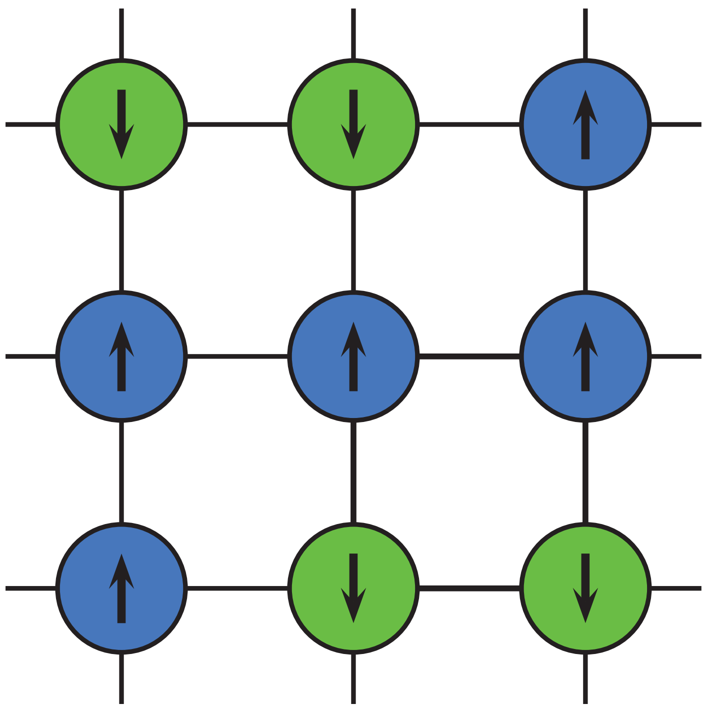
- the variance explodes
- divergence of correlation length – fractal structure
- critical slowing down





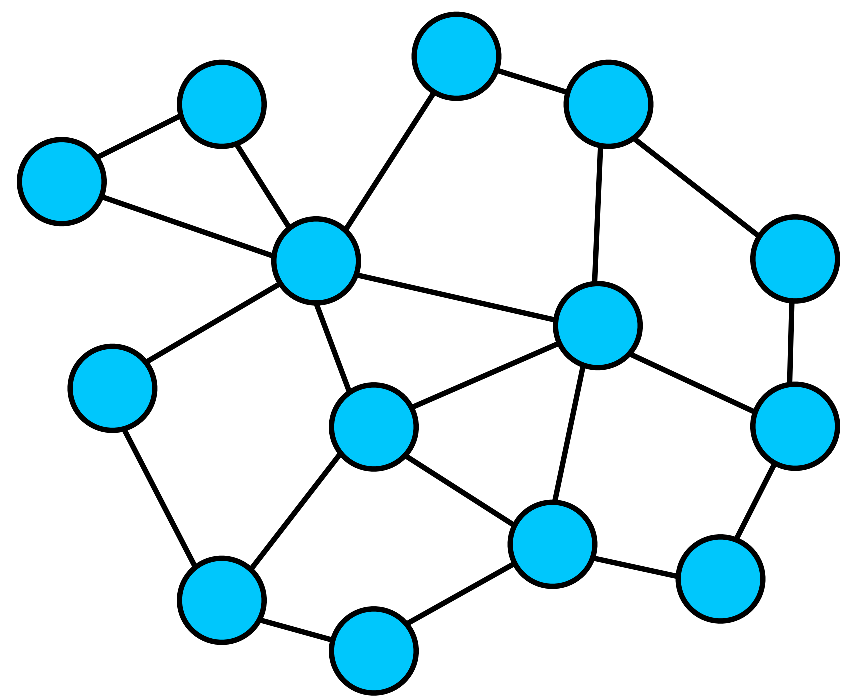
statistical mechanics as a tool to bridge scales

interacting spins



spontaneous magnetization

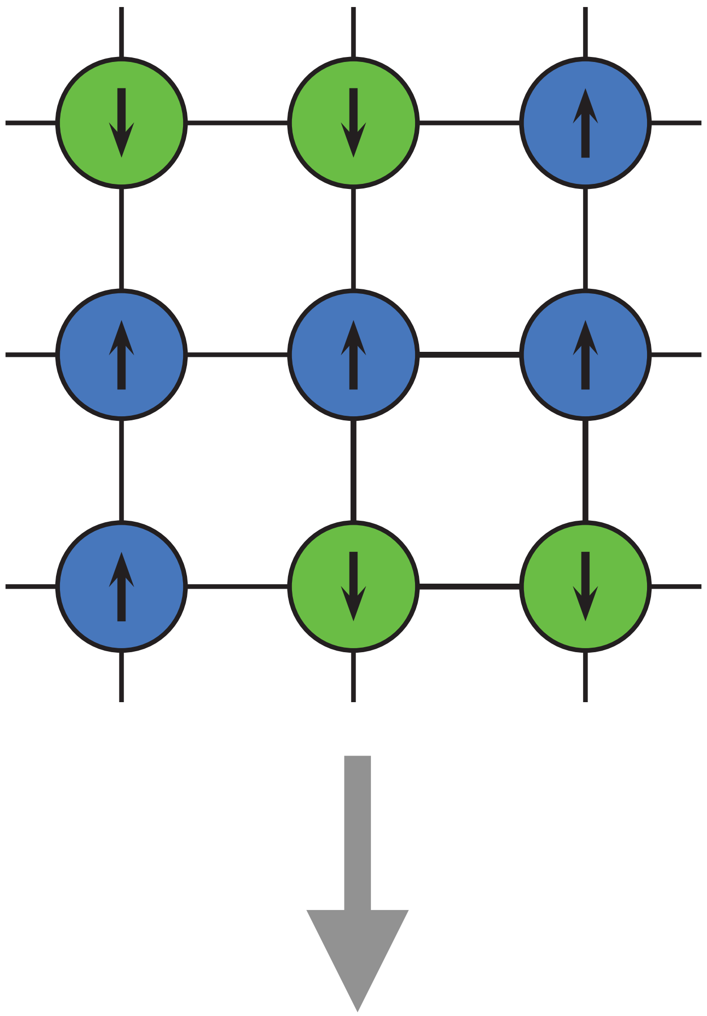
(any) interacting agents



collective behaviour

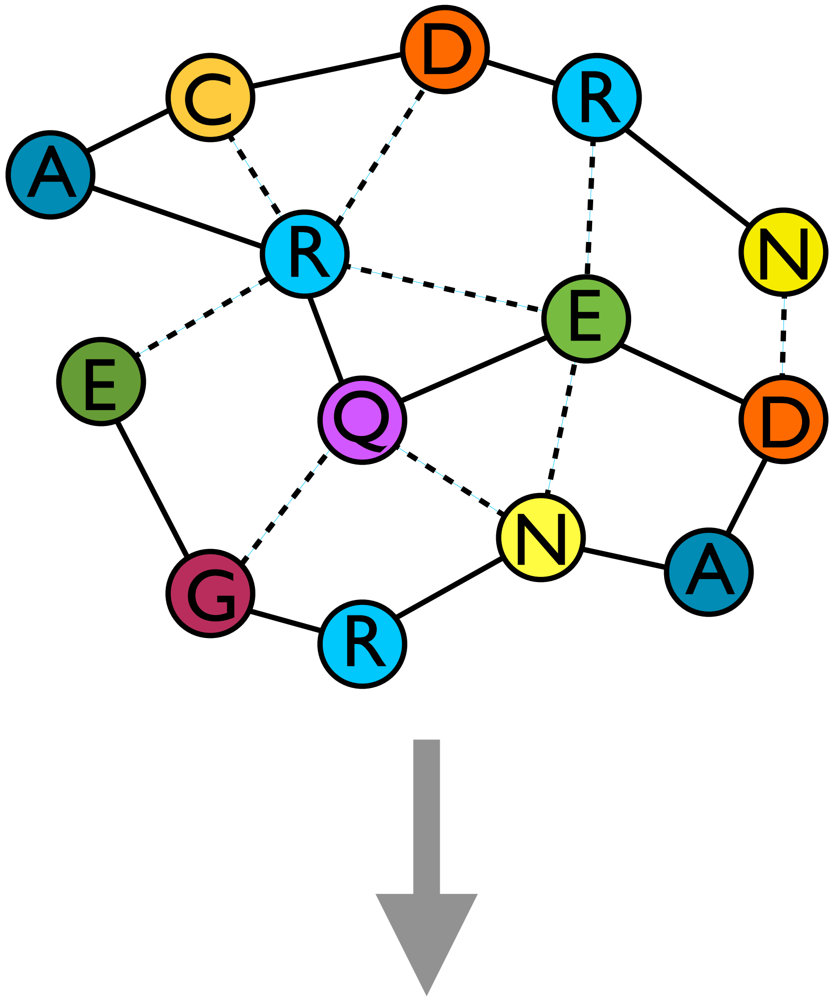
statistical mechanics as a tool to bridge scales

interacting spins



spontaneous magnetization

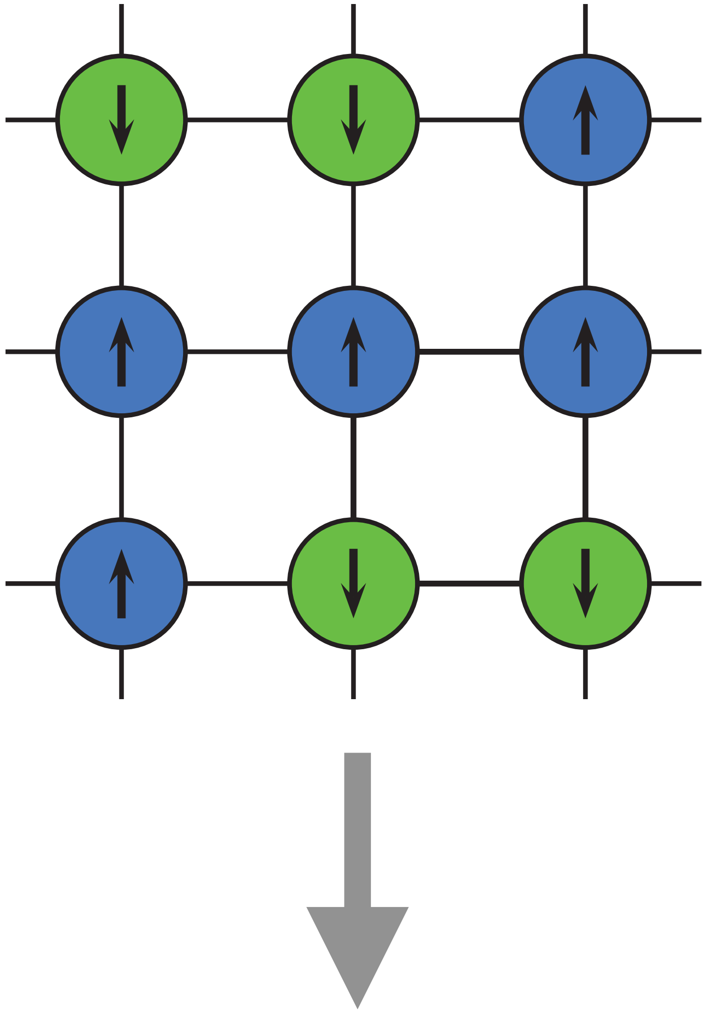
(any) interacting agents



collective behaviour

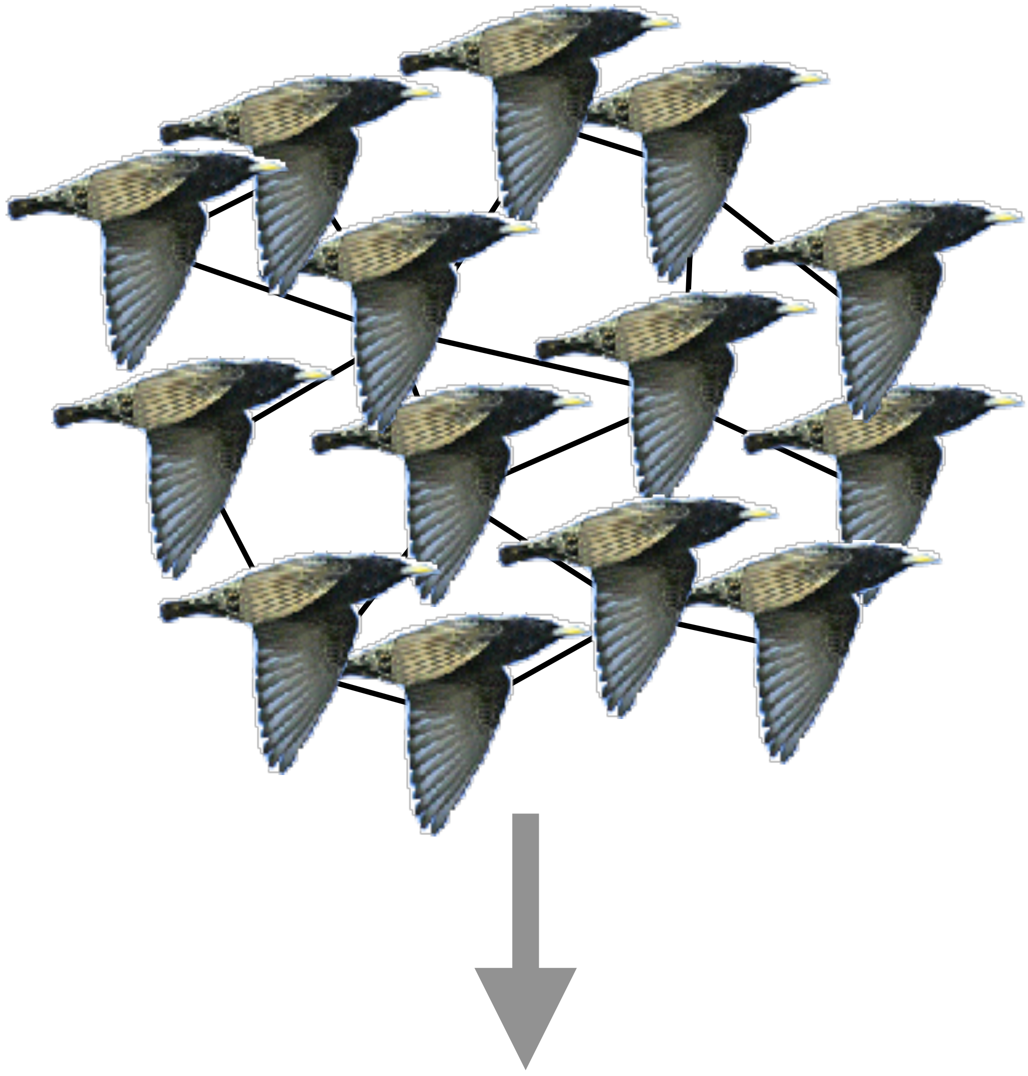
statistical mechanics as a tool to bridge scales

interacting spins



spontaneous magnetization

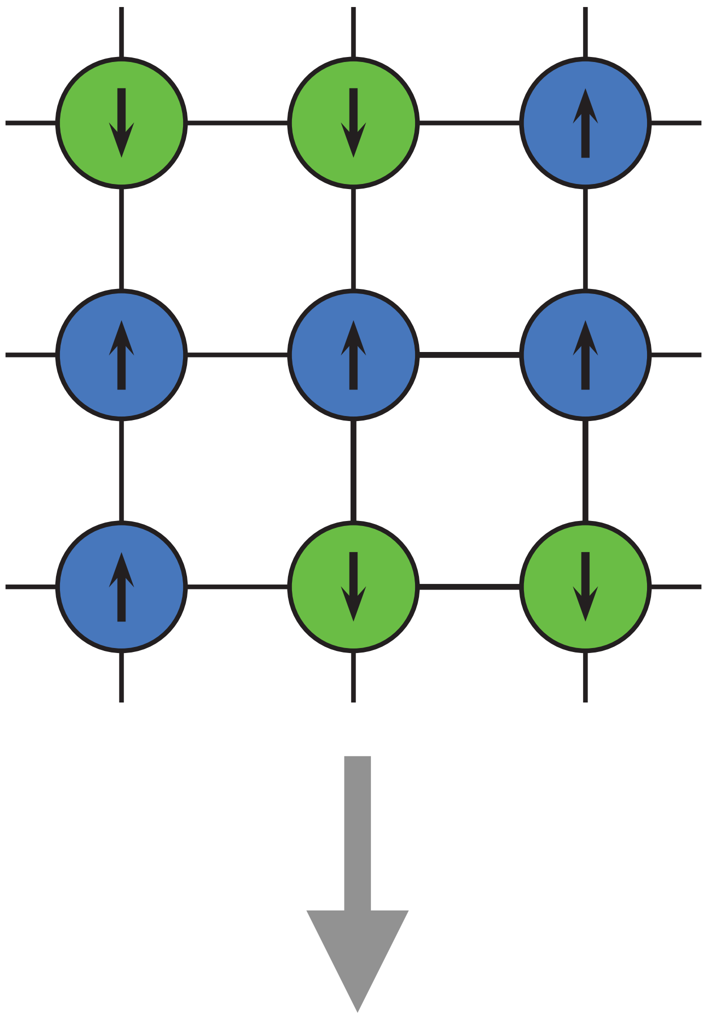
(any) interacting agents



collective behaviour

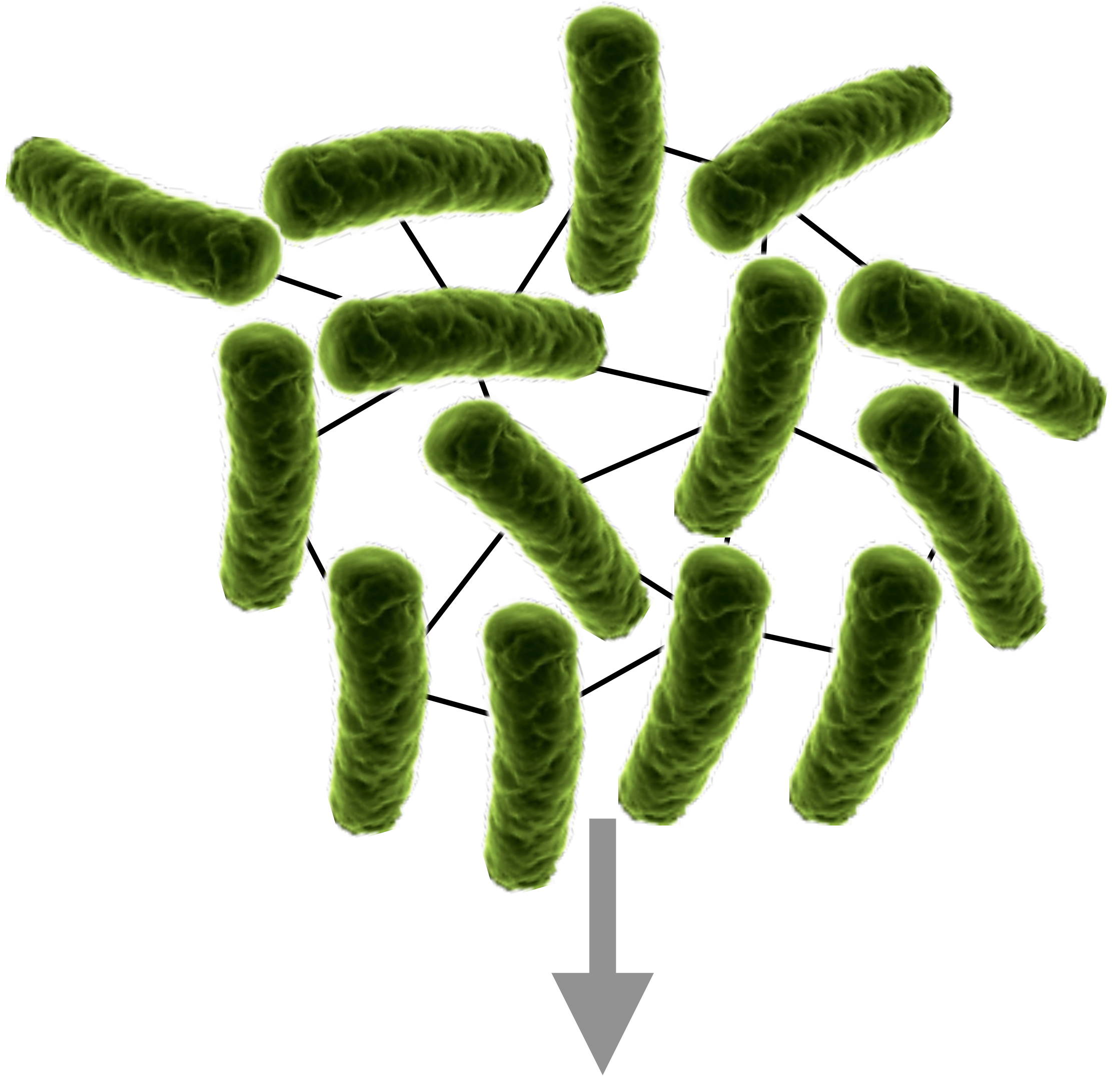
statistical mechanics as a tool to bridge scales

interacting spins



spontaneous magnetization

(any) interacting agents

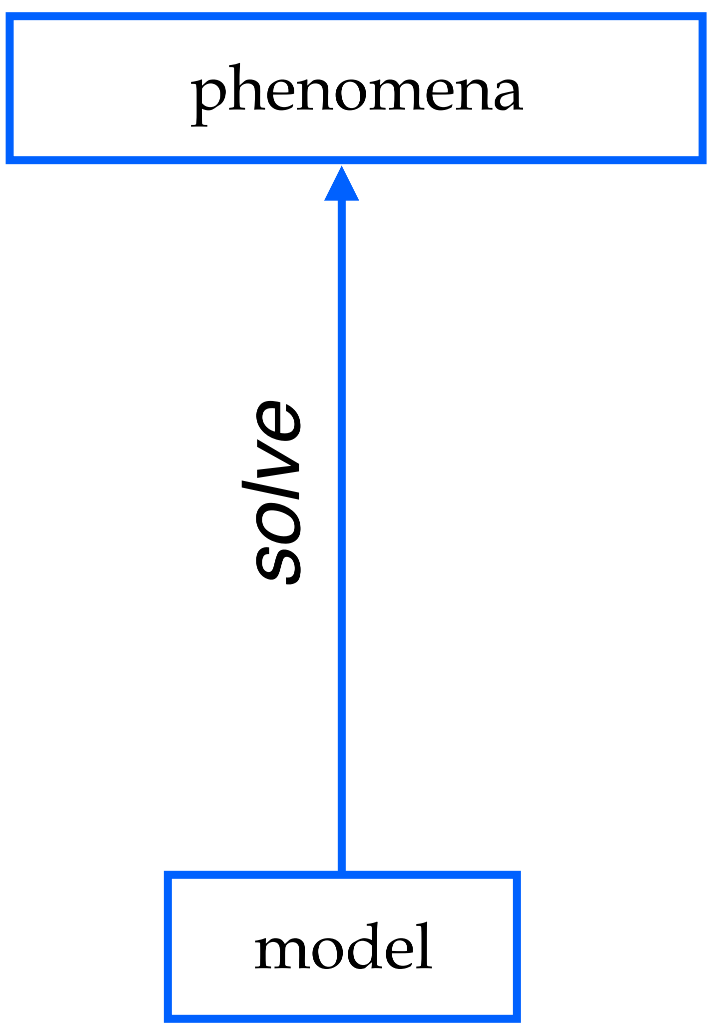


collective behaviour

two modeling approaches

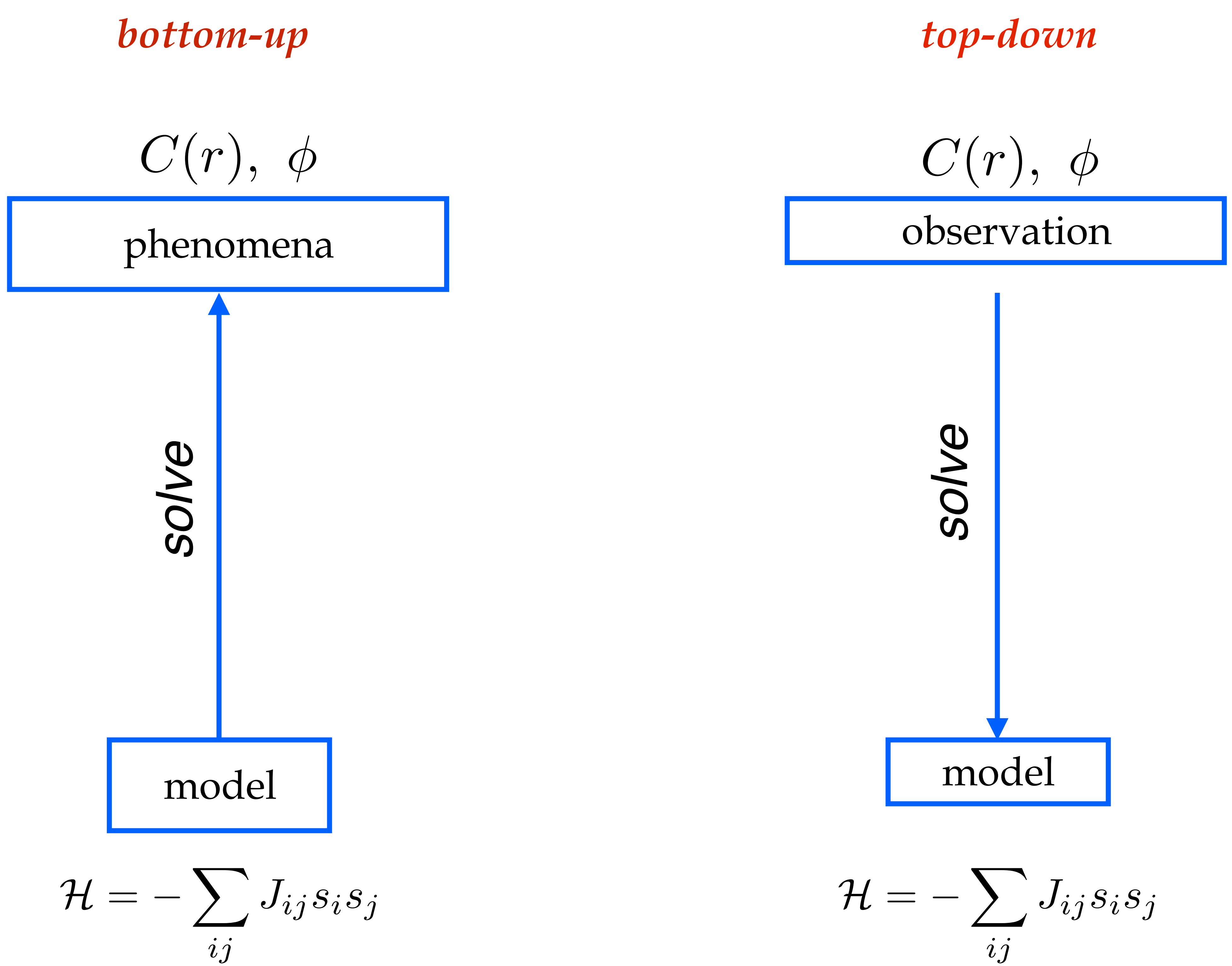
bottom-up

$$C(r), \;\; \phi$$

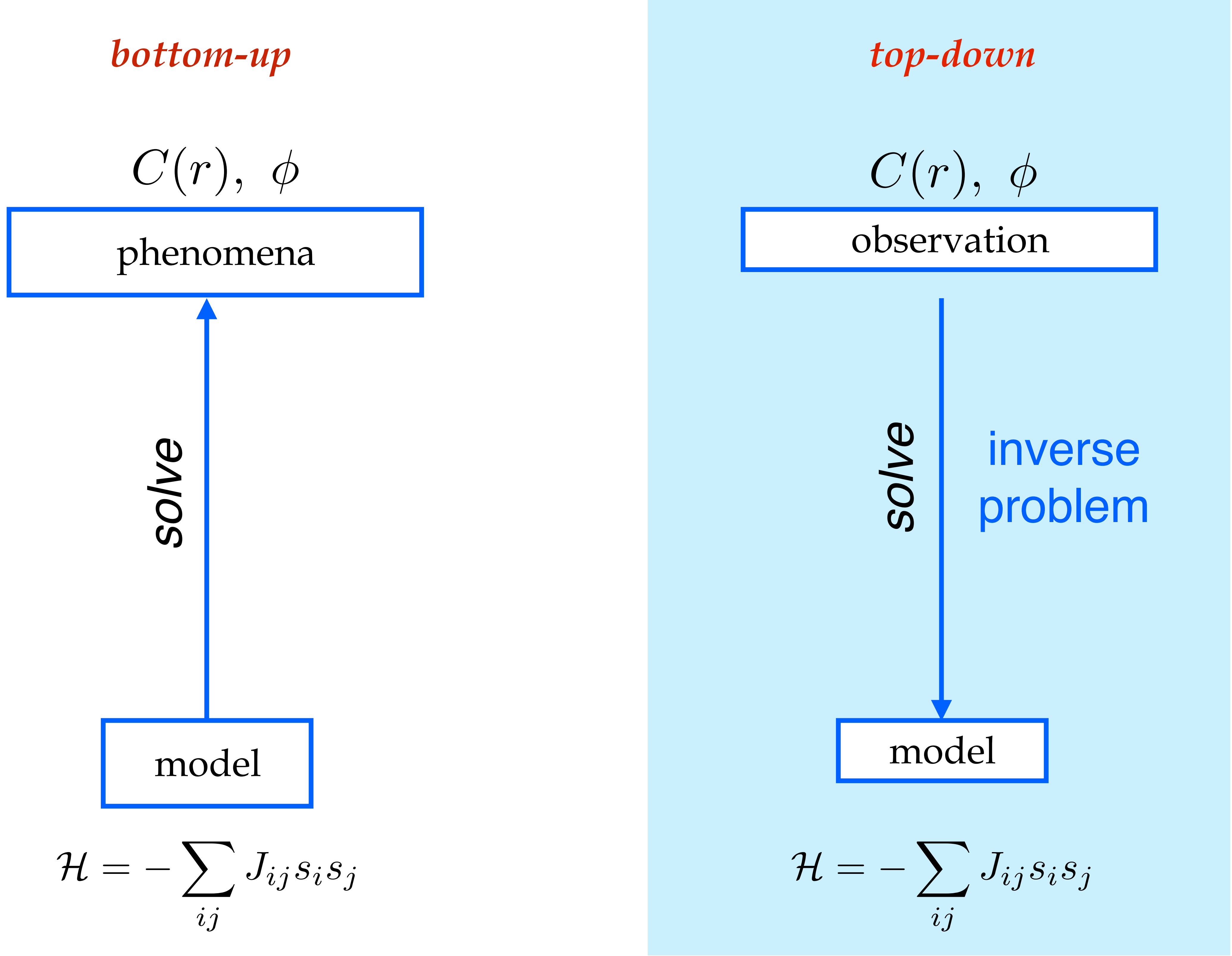


$$\mathcal{H} = -\sum_{ij} J_{ij} s_i s_j$$

two modeling approaches

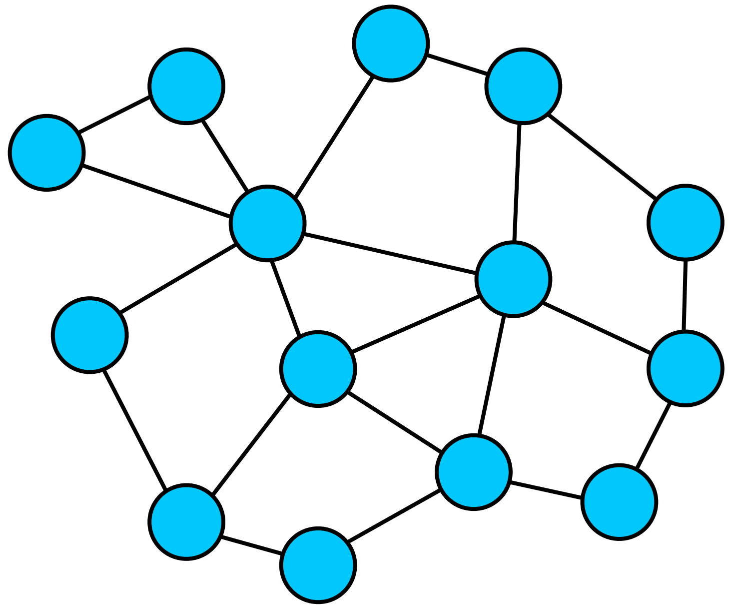


two modeling approaches



how to fit model to data – maximum entropy

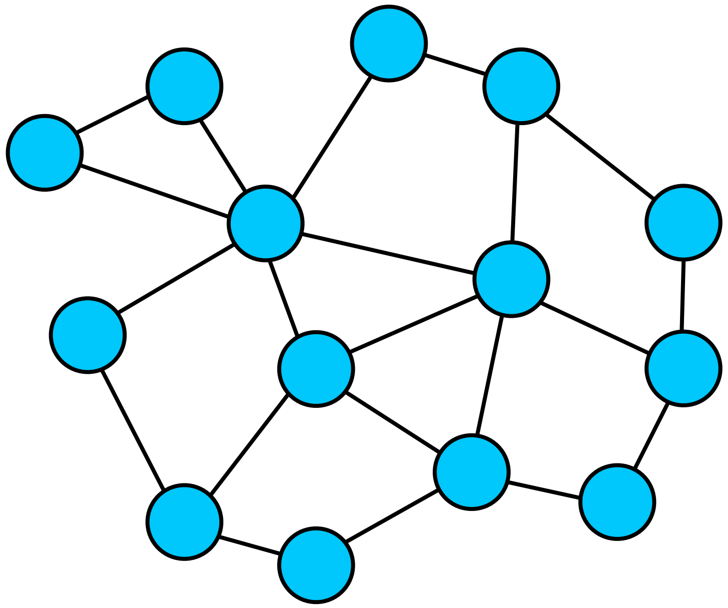
$$\boldsymbol{\sigma} = (\sigma_1, \sigma_2, \ldots, \sigma_N)$$



how to fit model to data – maximum entropy

- N agents / units described by a variable σ

$$\boldsymbol{\sigma} = (\sigma_1, \sigma_2, \ldots, \sigma_N)$$

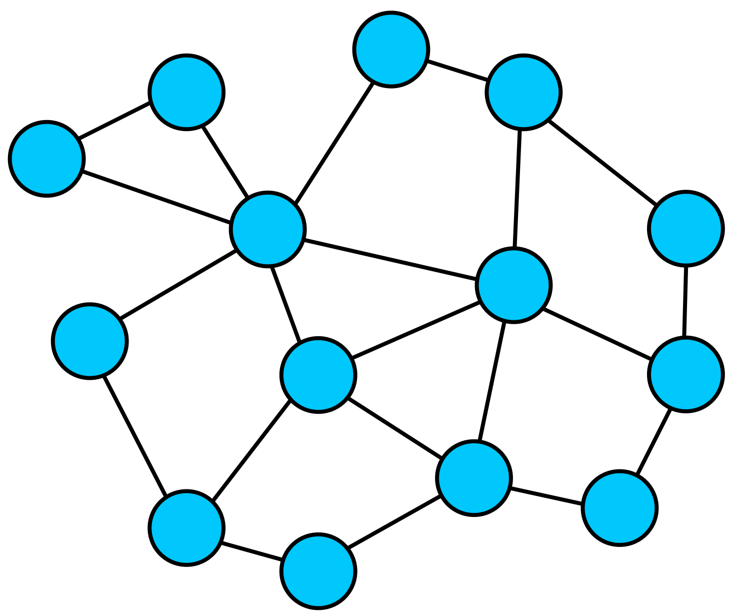


how to fit model to data – maximum entropy

- N agents / units described by a variable σ

$$\boldsymbol{\sigma} = (\sigma_1, \sigma_2, \ldots, \sigma_N)$$

- Maximize the entropy $S = -\sum_{\boldsymbol{\sigma}} P(\boldsymbol{\sigma}) \log P(\boldsymbol{\sigma})$



how to fit model to data – maximum entropy

- N agents / units described by a variable σ

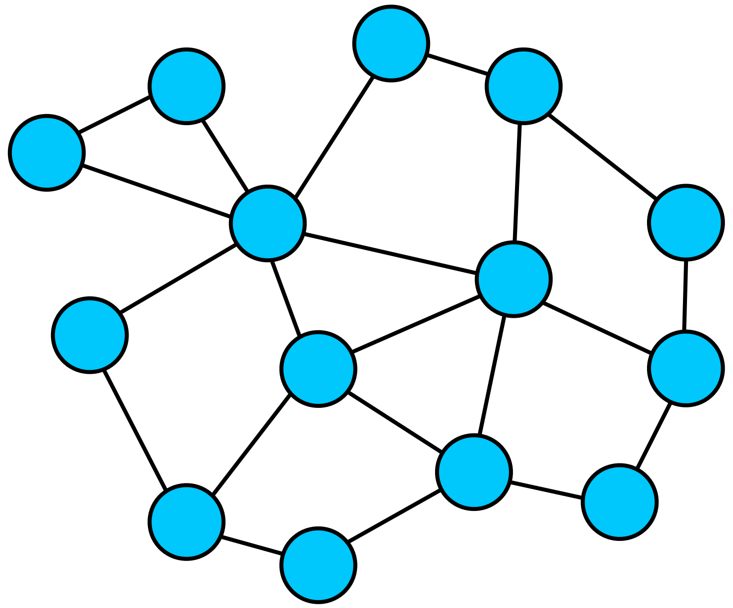
$$\boldsymbol{\sigma} = (\sigma_1, \sigma_2, \ldots, \sigma_N)$$

- Maximize the entropy $S = -\sum_{\boldsymbol{\sigma}} P(\boldsymbol{\sigma}) \log P(\boldsymbol{\sigma})$
- under the constraint that observables $\mathcal{O}_1, \mathcal{O}_2, \ldots$

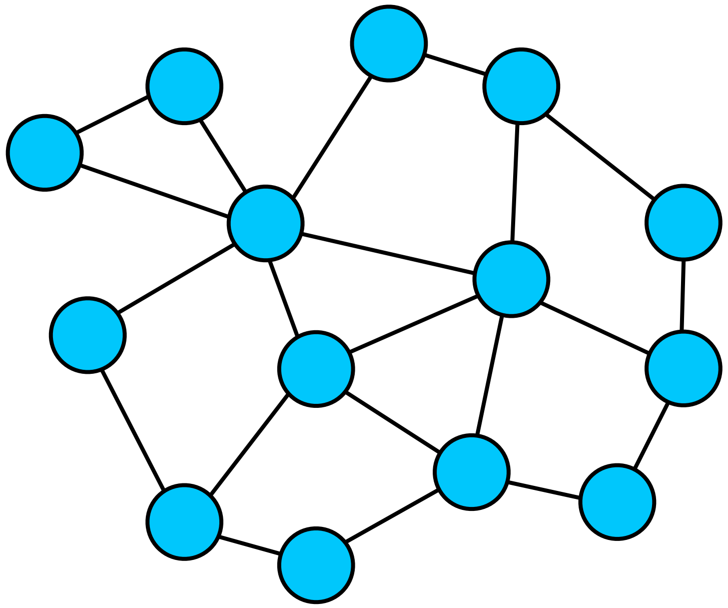
  have the same average as the data

$$\langle \mathcal{O}_a \rangle_{\text{model}} = \langle \mathcal{O}_a \rangle_{\text{data}}$$

$\langle \mathcal{O}_a \rangle$ is typically a moment, e.g. $\langle \sigma_i \rangle, \langle \sigma_i \sigma_j \rangle$



how to fit model to data – maximum entropy



- N agents / units described by a variable σ

$$\boldsymbol{\sigma} = (\sigma_1, \sigma_2, \ldots, \sigma_N)$$

- Maximize the entropy $\quad S = -\sum_{\boldsymbol{\sigma}} P(\boldsymbol{\sigma}) \log P(\boldsymbol{\sigma})$
- under the constraint that observables $\quad \mathcal{O}_1, \mathcal{O}_2, \ldots$

have the same average as the data

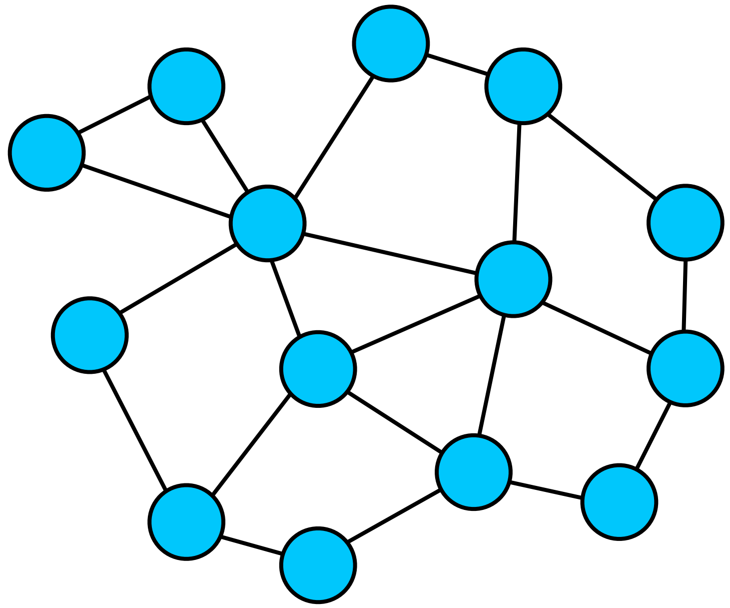
$$\langle \mathcal{O}_a \rangle_{\text{model}} = \langle \mathcal{O}_a \rangle_{\text{data}}$$

$\langle \mathcal{O}_a \rangle$ is typically a moment, e.g. $\langle \sigma_i \rangle, \langle \sigma_i \sigma_j \rangle$

$$P(\boldsymbol{\sigma}) = \frac{1}{Z} \exp \Bigg[\underbrace{\sum_a J_a \mathcal{O}_a(\boldsymbol{\sigma})}_{-E/k_B T} \Bigg]$$

e.g. $\quad P(\boldsymbol{\sigma}) = \frac{1}{Z} e^{\sum_i h_i \sigma_i + \sum_{ij} J_{ij} \sigma_i \sigma_j}$

how to fit model to data – maximum entropy



- N agents / units described by a variable σ

$$\boldsymbol{\sigma} = (\sigma_1, \sigma_2, \ldots, \sigma_N)$$

- Maximize the entropy $S = -\sum_{\boldsymbol{\sigma}} P(\boldsymbol{\sigma}) \log P(\boldsymbol{\sigma})$
- under the constraint that observables $\mathcal{O}_1, \mathcal{O}_2, \ldots$

  have the same average as the data

$$\langle \mathcal{O}_a \rangle_{\text{model}} = \langle \mathcal{O}_a \rangle_{\text{data}}$$

$\langle \mathcal{O}_a \rangle$ is typically a moment, e.g. $\langle \sigma_i \rangle, \langle \sigma_i \sigma_j \rangle$

$$P(\boldsymbol{\sigma}) = \frac{1}{Z} \exp \Big[\underbrace{\sum_a J_a \mathcal{O}_a(\boldsymbol{\sigma})}_{-E/k_B T} \Big]$$

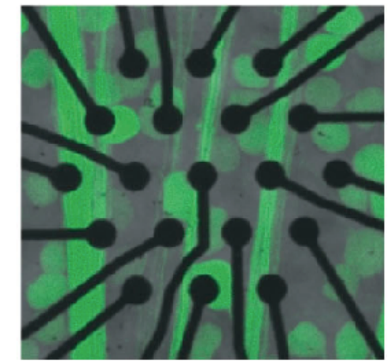
e.g. $$P(\boldsymbol{\sigma}) = \frac{1}{Z} e^{\sum_i h_i \sigma_i + \sum_{ij} J_{ij} \sigma_i \sigma_j}$$

(disordered) Ising model!

maximum entropy in biology

- collective activity of neural populations

  Schneidman et al. Nature 2006
  Shlens et al J. Neuroscience 2006
  Tang et al J. Neuroscience 2008
  Tkacik et al PLoS CP 2014



- co-variations in protein families $\Rightarrow$ contact prediction

  Weigt et al. PNAS 2009; Morcos et al. PNAS 2011
  Marks et al PLoS ONE 2012; Sulkowska et al PNAS 2012

- diversity of antibody repertoires in the immune system

  Mora Walczak Callan Bialek PNAS 2010

- DNA motifs of transcription factor binding sites

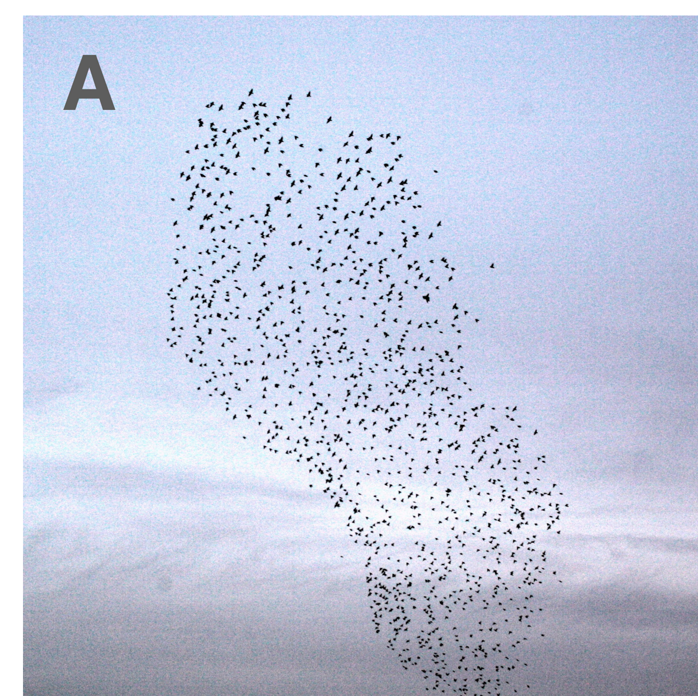
  Santolini Mora Hakim Plos ONE 2014

- collective behaviour of mice

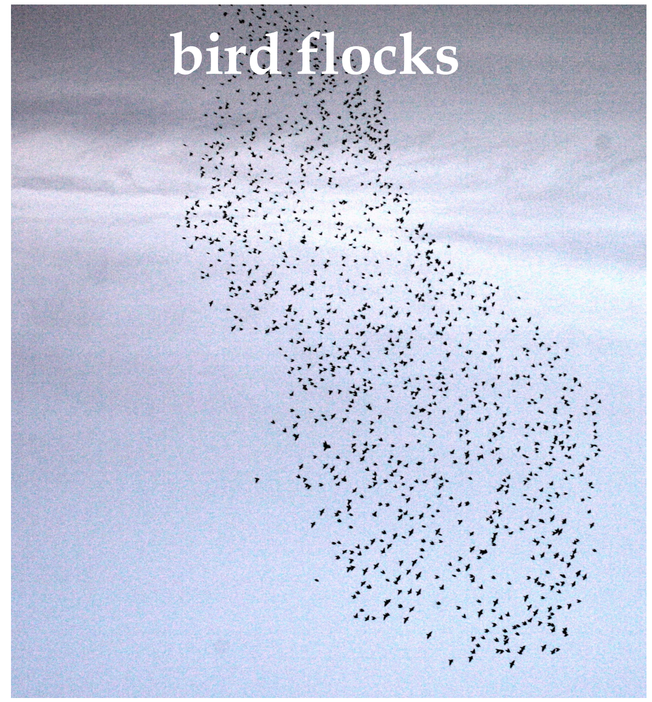
  Shemesh et al. eLife 2013

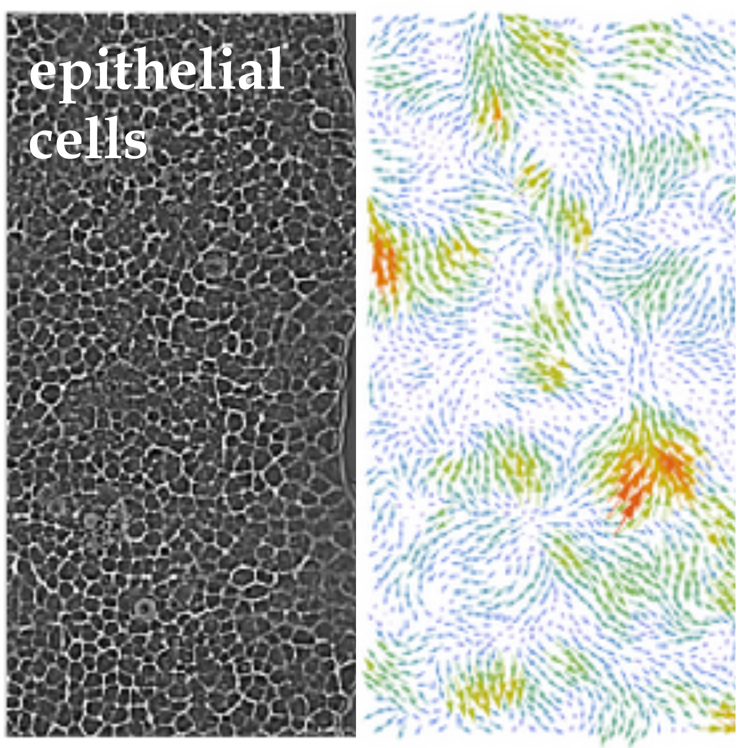
- collective behaviour of bird flocks

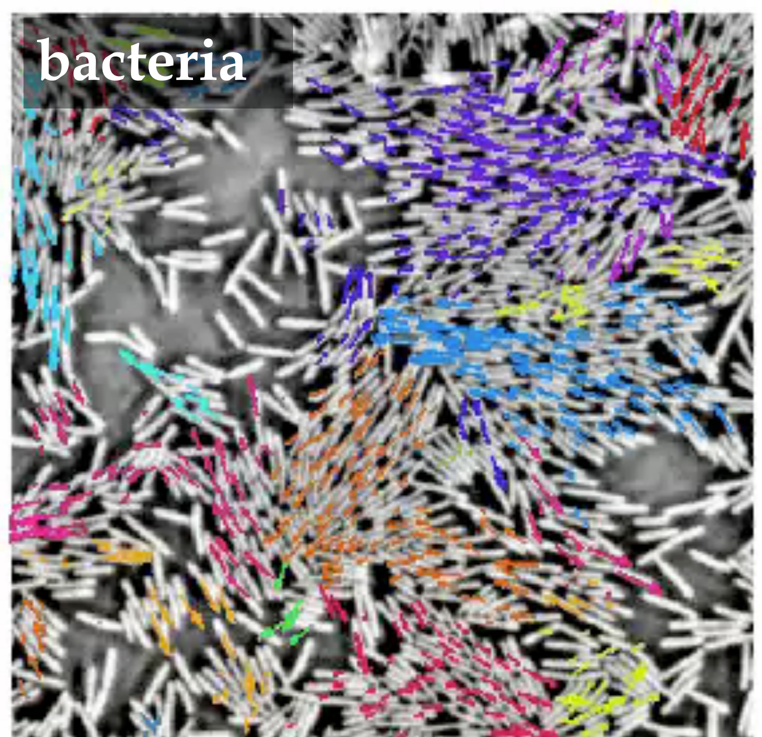
  Bialek et al. PNAS 2012; Cavagna et al. PRE 2014
  Bialek et al. PNAS 2014

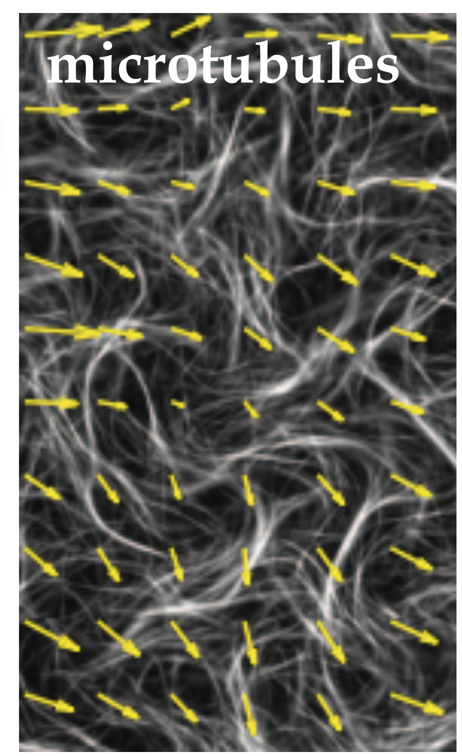


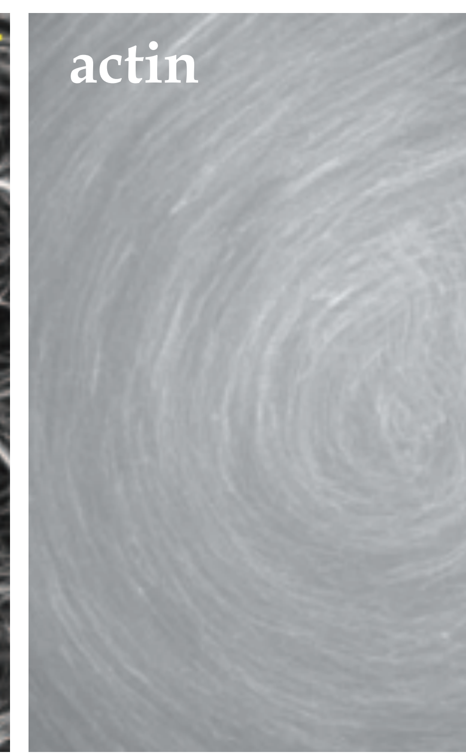
Collective motion and active matter











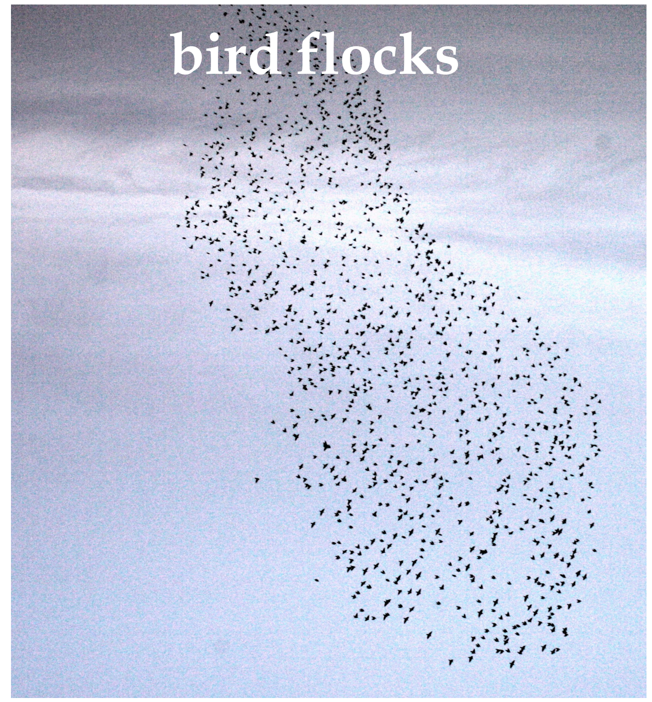
Supelveda et al., PLoS CP 2013

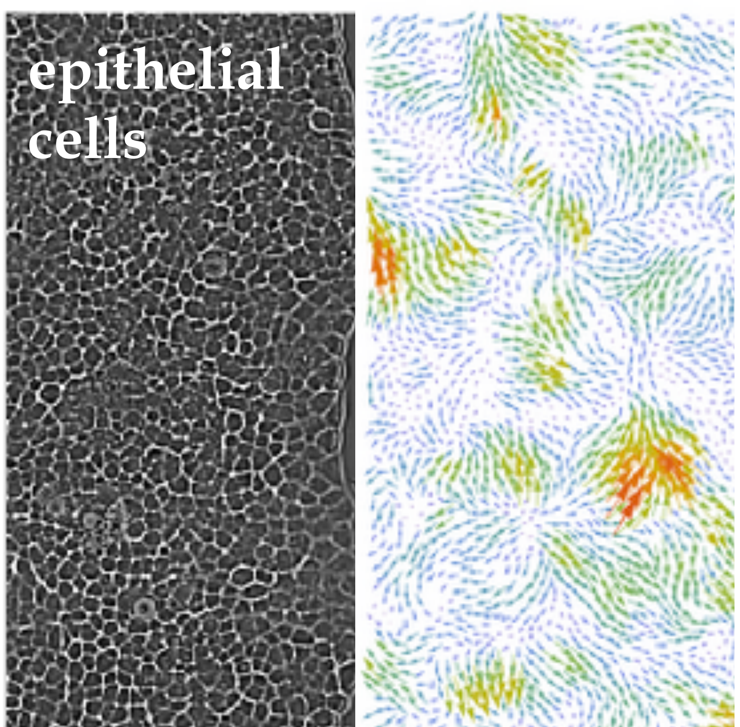
Zhang Be'er Florin & Swinney, PNAS 2010

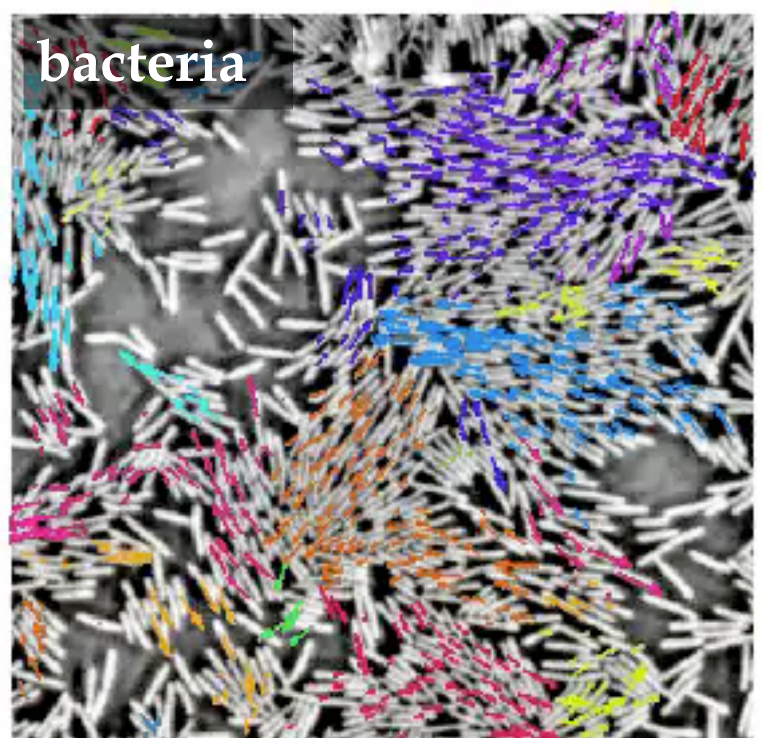
Sanchez et al., Nature 2012

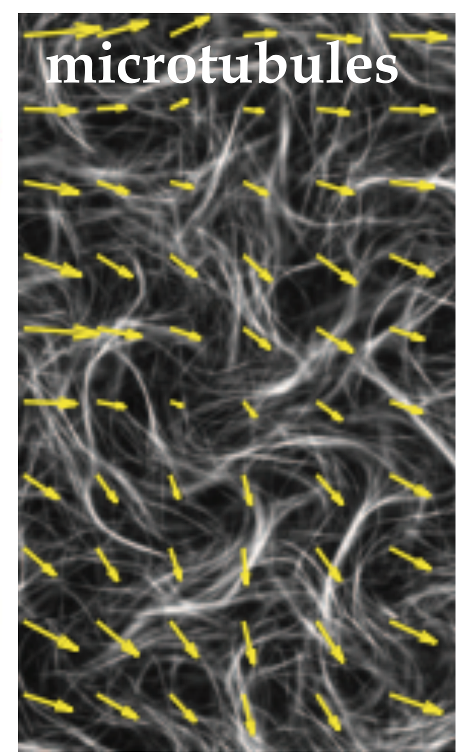
Schaller et al., Nature 2010

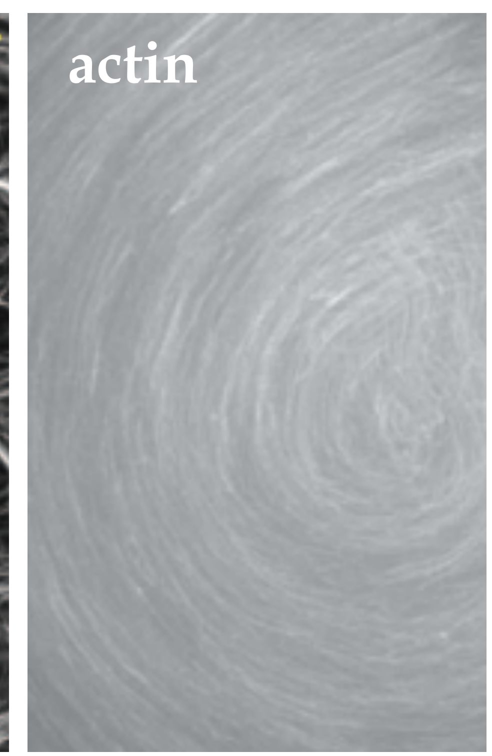
Collective motion and active matter











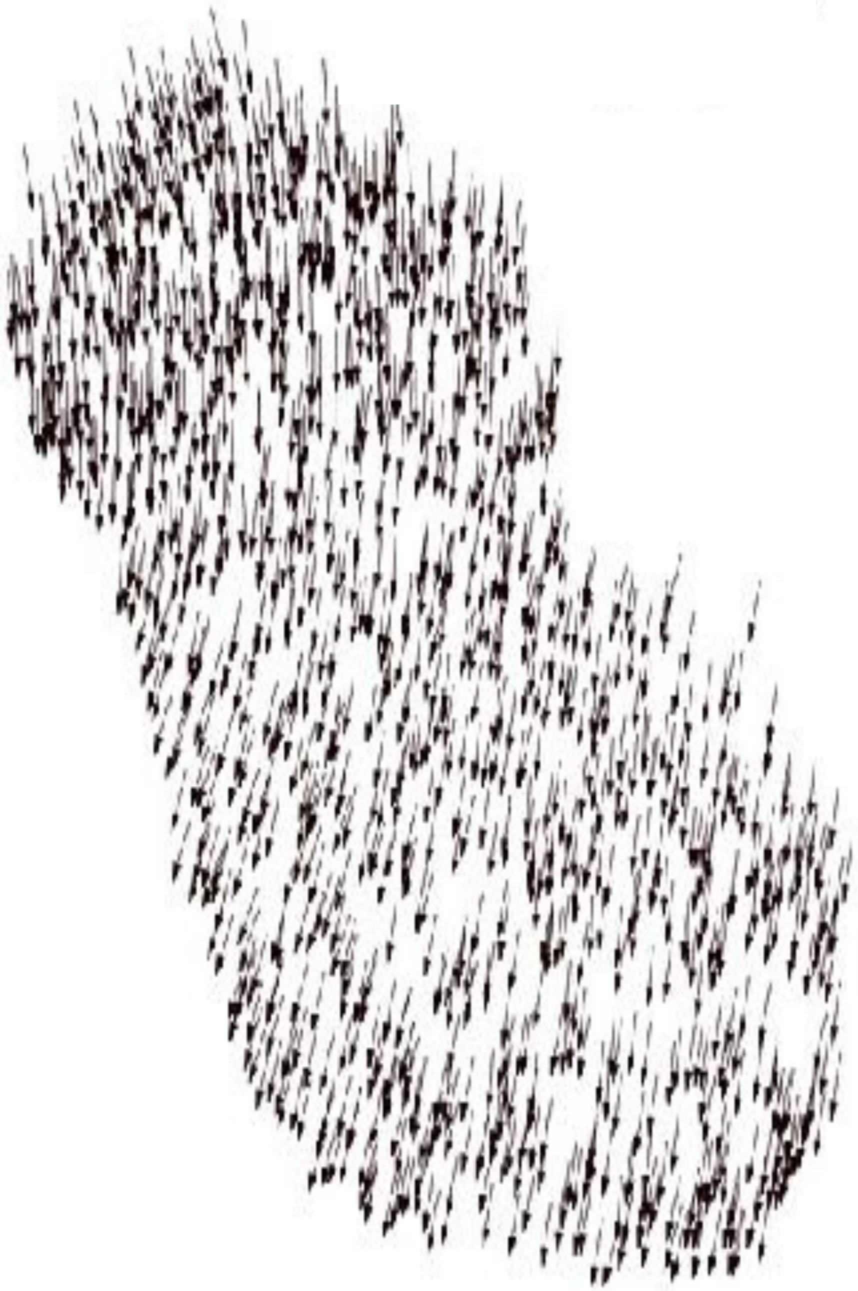
Supelveda et al., PLoS CP 2013

Zhang Be'er Florin & Swinney, PNAS 2010

Sanchez et al., Nature 2012

Schaller et al., Nature 2010

flocks of birds



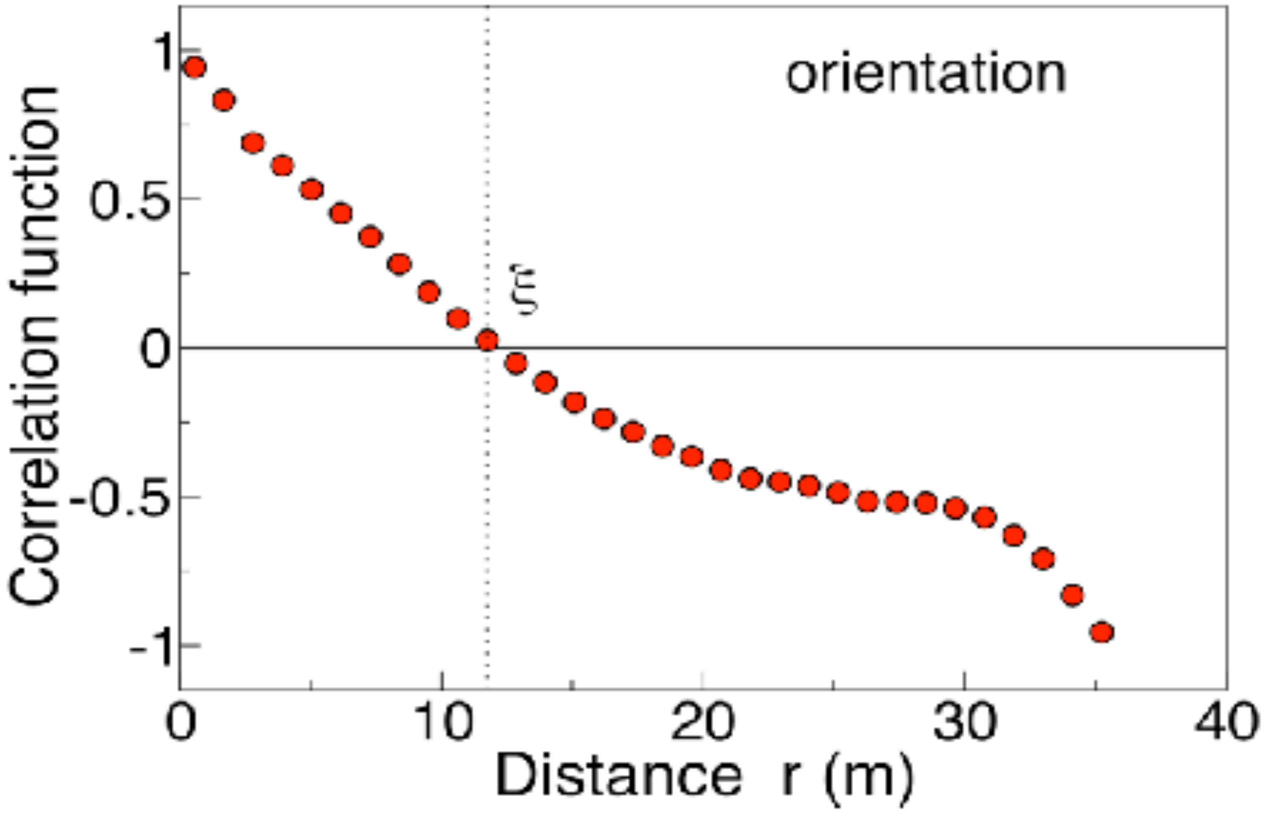
strong polarization

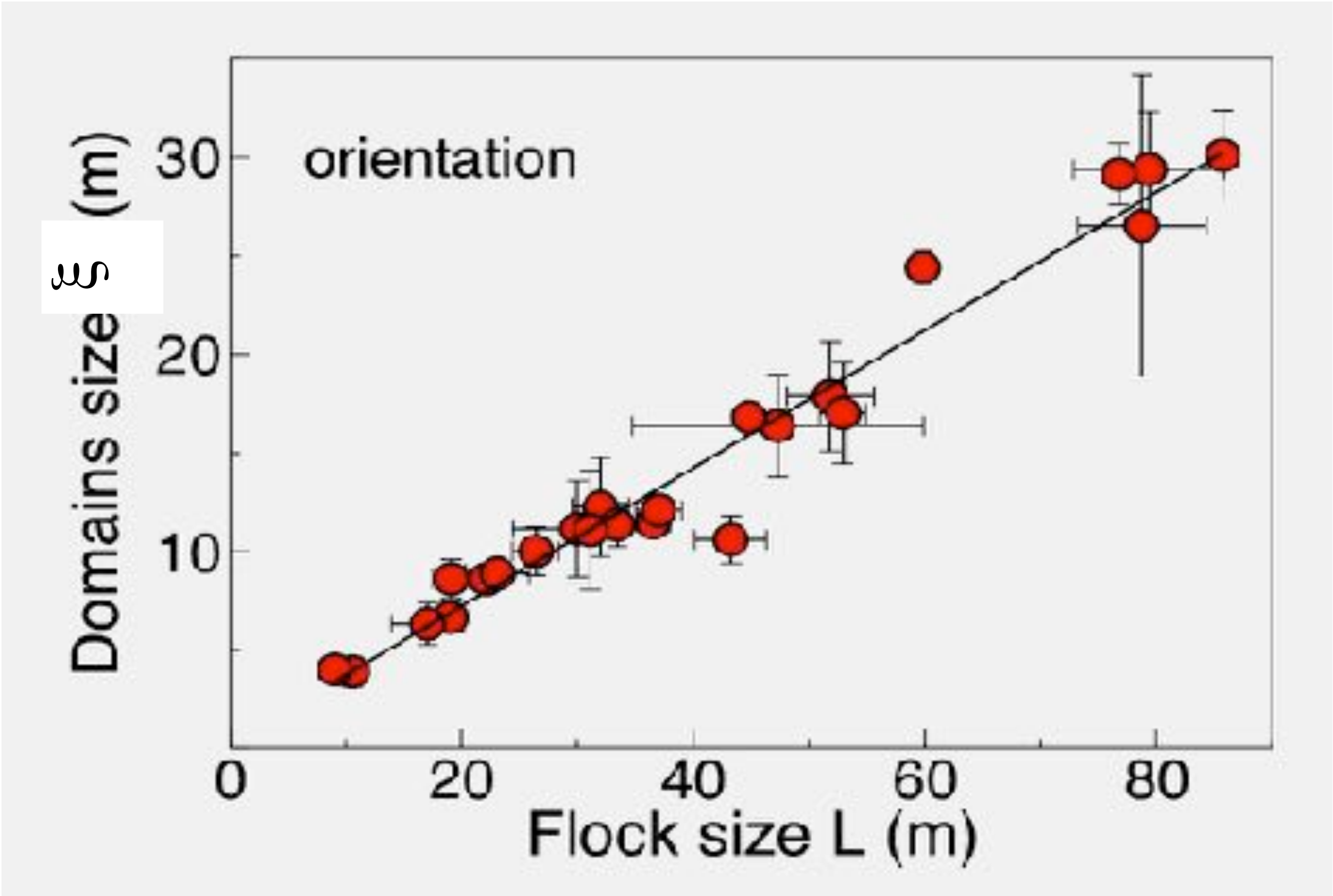
fluctuations around main orientation

$$\phi = \left| \frac{1}{N} \sum_{i=1}^{N} \frac{\vec{v}_i}{|\vec{v}_i|} \right| \sim 0.95$$

domains

scale free correlations





self-organised order,
not from centralized command

maximum entropy model for birds

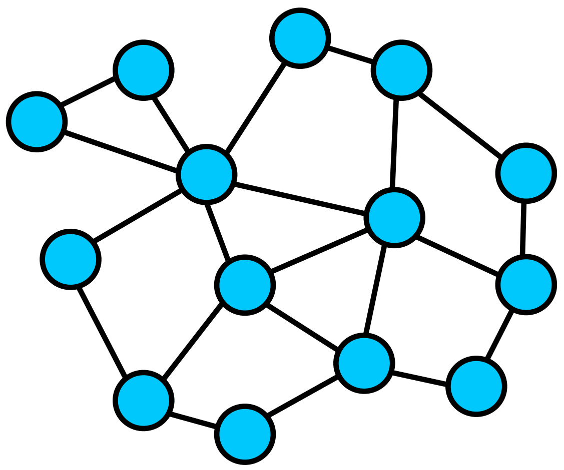
- velocity of bird $\vec{v}_i, \quad \vec{s}_i = \vec{v}_i / \|\vec{v}_i\|$

maximum entropy model for birds

- velocity of bird $\vec{v}_i, \quad \vec{s}_i = \vec{v}_i / \|\vec{v}_i\|$
- constrain correlation functions $C_{ij} = \langle \vec{s}_i \vec{s}_j \rangle$

$$P(\vec{s}_1, \ldots, \vec{s}_N) = \frac{1}{Z} \exp\left(\sum_{ij} J_{ij} \vec{s}_i \vec{s}_j \right) = \frac{1}{Z} \exp(-H)$$

Heisenberg model on lattice

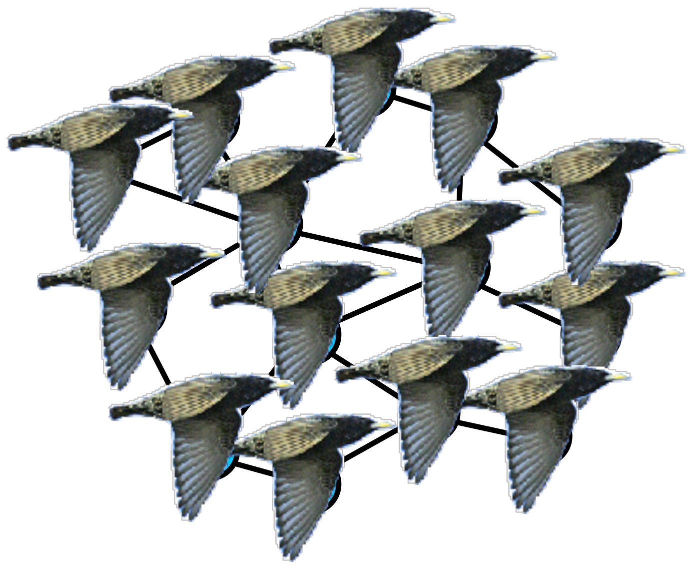


maximum entropy model for birds

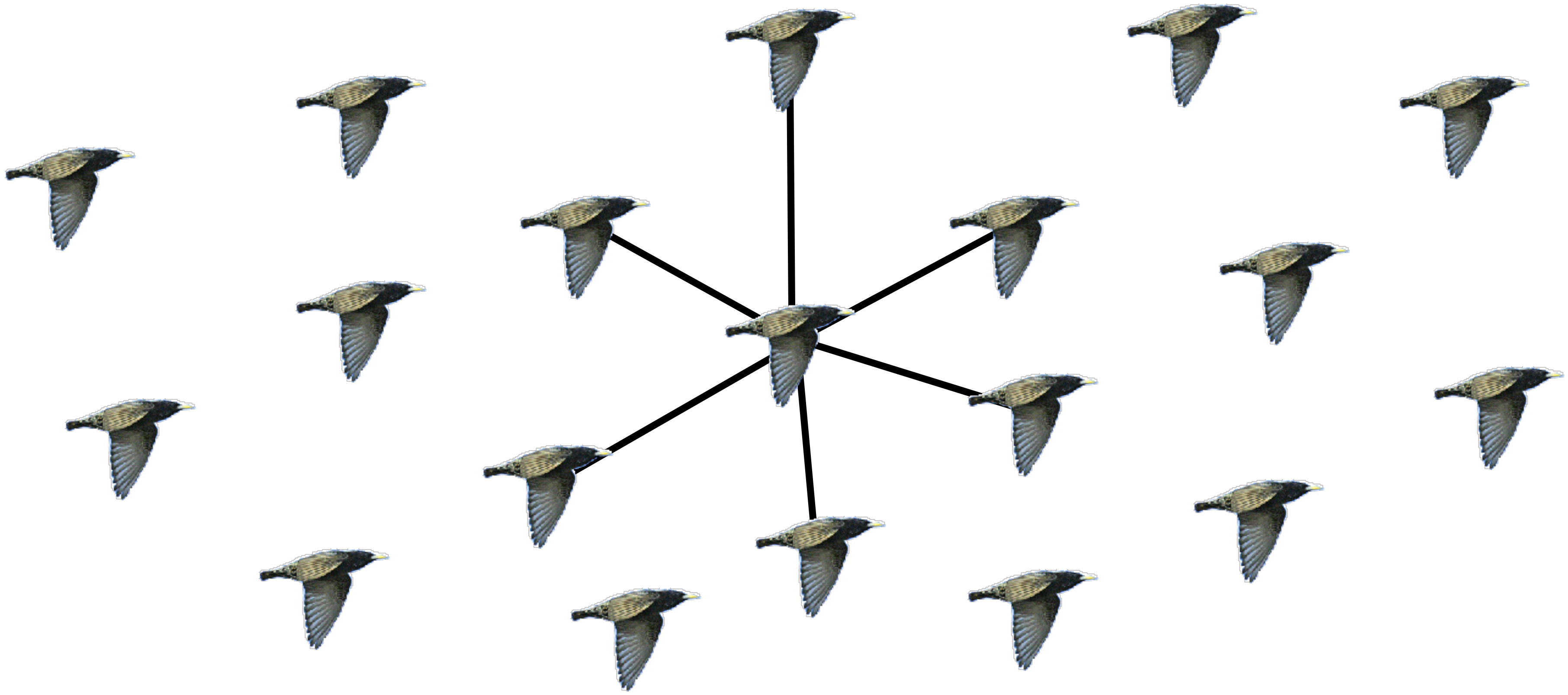
- velocity of bird $\vec{v}_i, \quad \vec{s}_i = \vec{v}_i / \|\vec{v}_i\|$
- constrain correlation functions $C_{ij} = \langle \vec{s}_i \vec{s}_j \rangle$

$$P(\vec{s}_1, \ldots, \vec{s}_N) = \frac{1}{Z} \exp\left(\sum_{ij} J_{ij} \vec{s}_i \vec{s}_j \right) = \frac{1}{Z} \exp(-H)$$

Heisenberg model on lattice



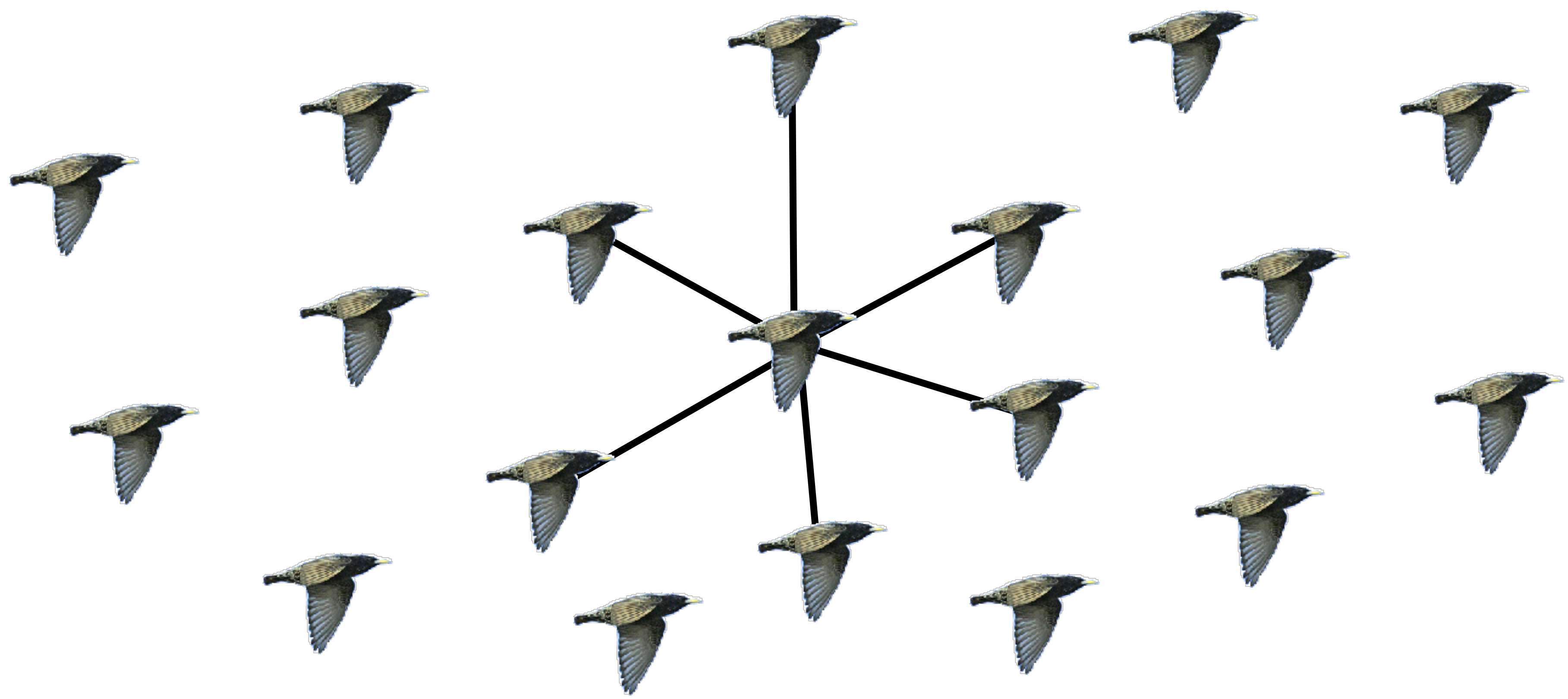
parametrisation



$$J_{ij} = \begin{cases} J & \text{if j is one i's } n_c \text{ first neighbors} \\ 0 & \text{otherwise} \end{cases}$$

(then symmetrized)

parametrisation



$$J_{ij} = \begin{cases} J & \text{if j is one i's } n_c \text{ first neighbors} \\ 0 & \text{otherwise} \end{cases}$$

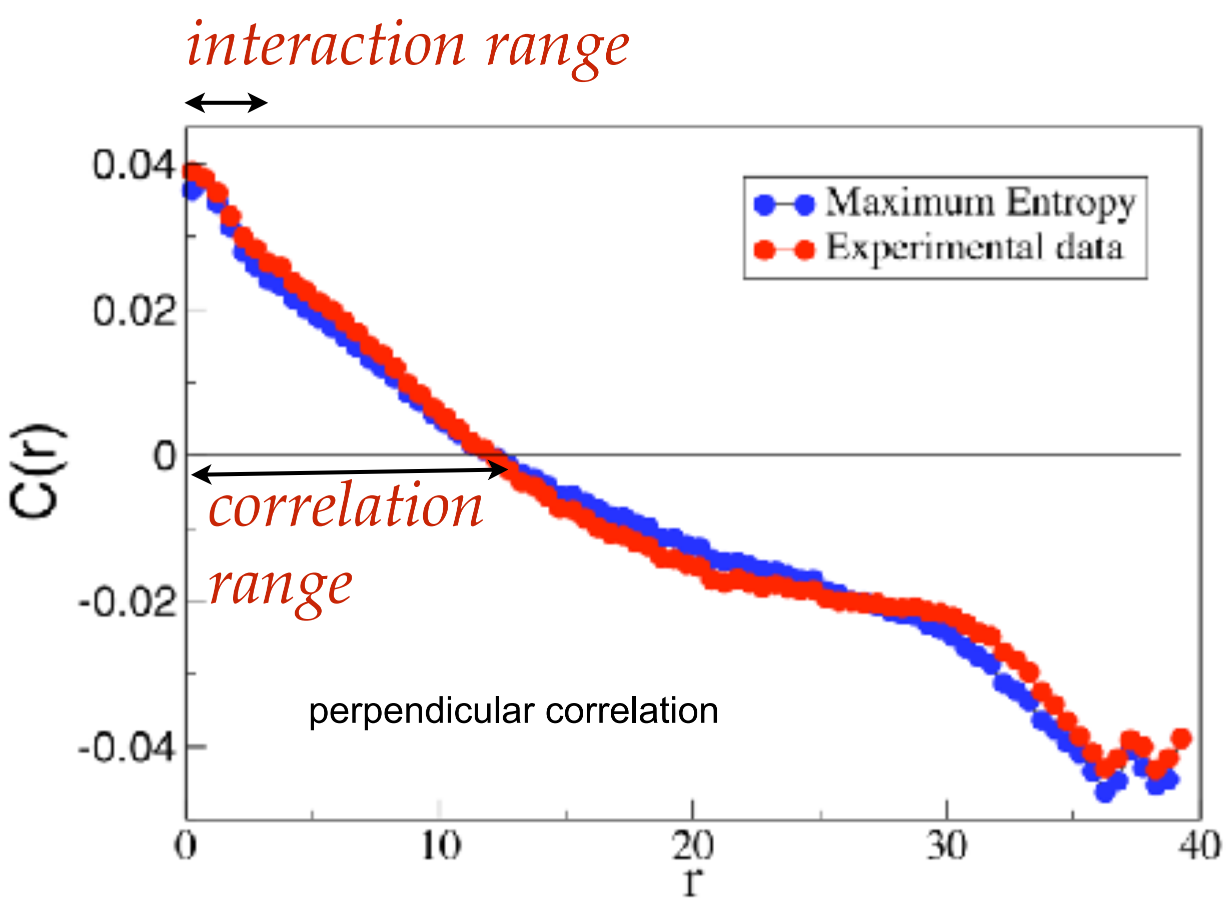
(then symmetrized)

Equivalent to maximum entropy with constraint on

$$C_{\text{int}} = \frac{1}{N}\sum_{i=1}^{N}\frac{1}{n_c}\sum_{j\in V(i)}\langle\vec{s}_i\vec{s}_j\rangle$$

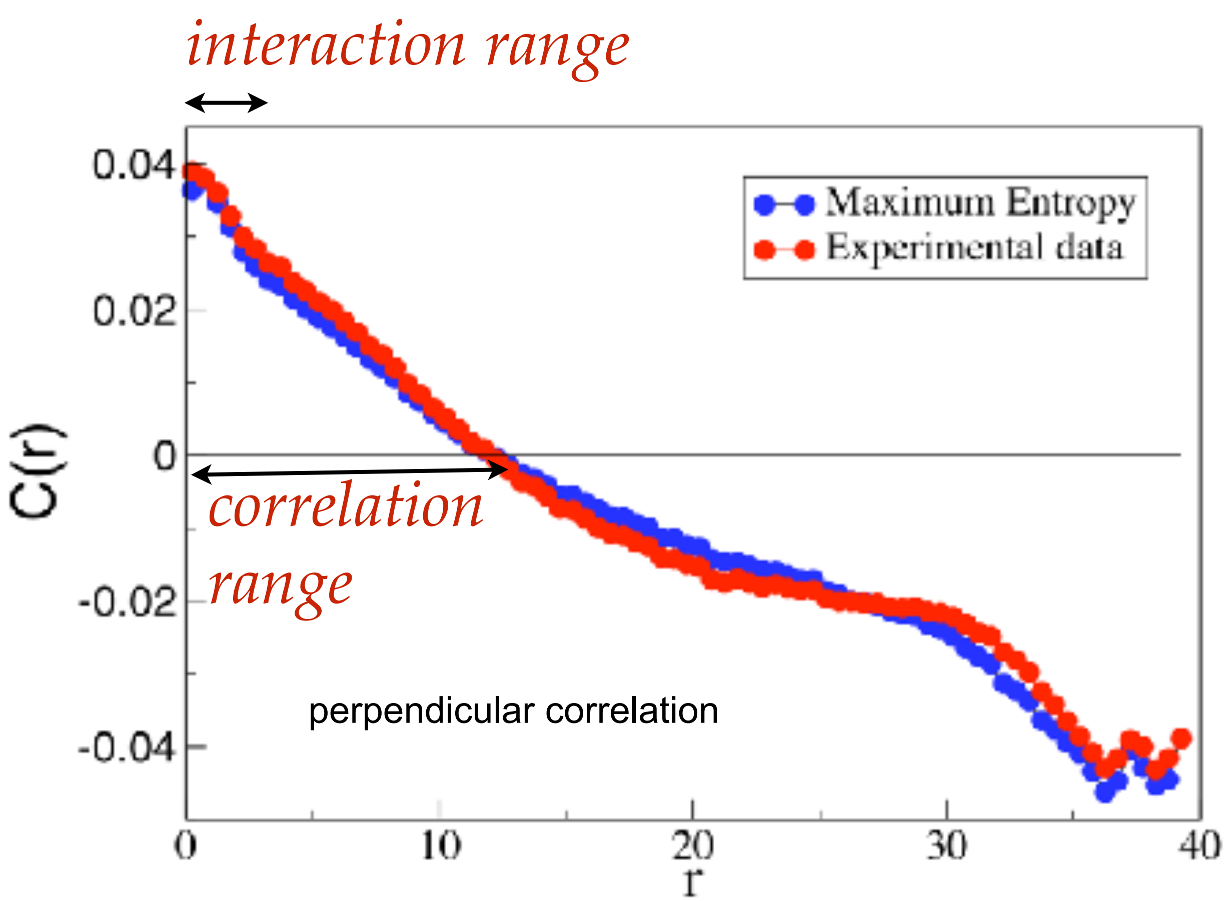
single snapshot – spatial averaging instead of ensemble averaging

predicting correlation functions

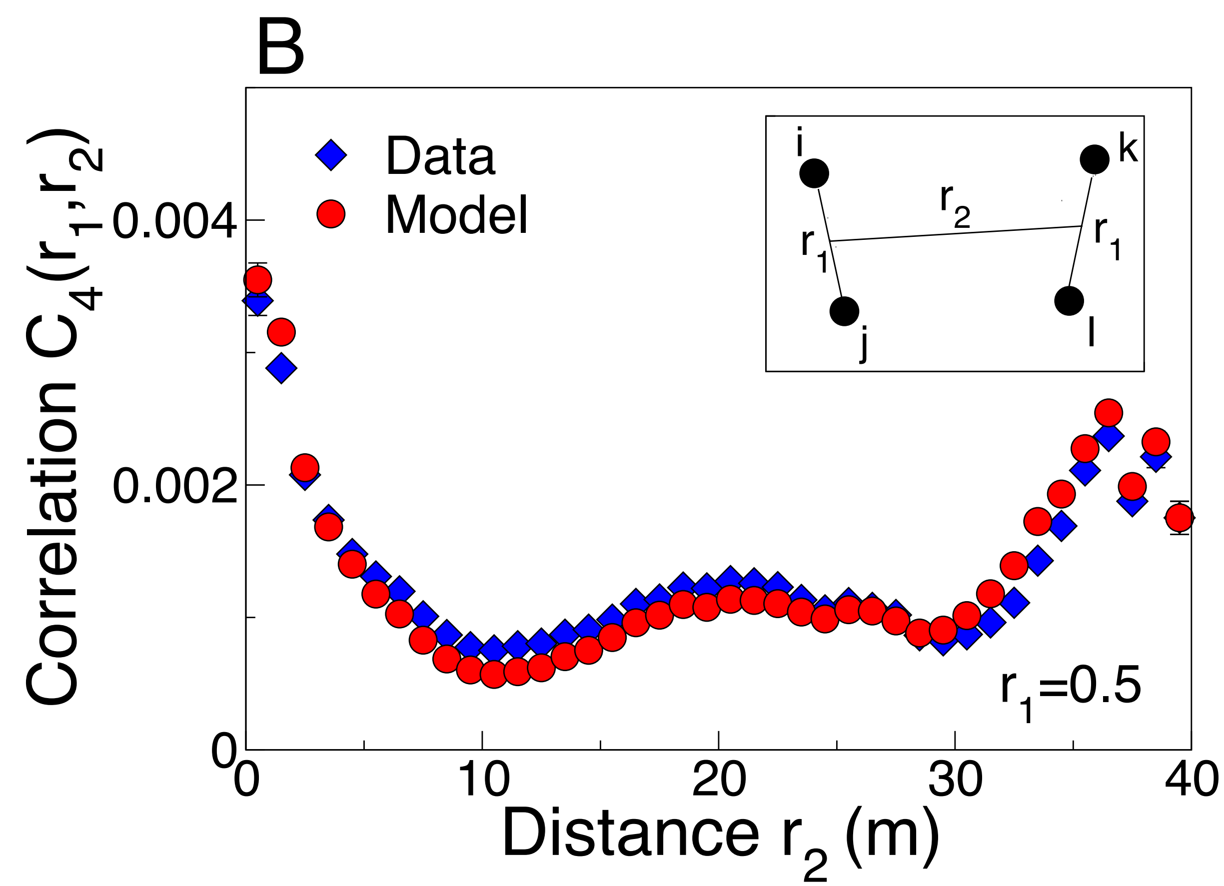


long-range order from local interactions

predicting correlation functions



4-bird correlation function

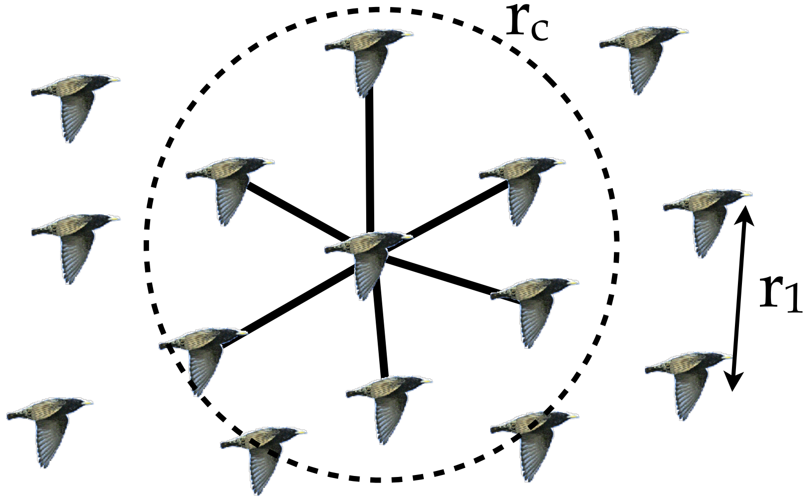


long-range order from local interactions

interaction range

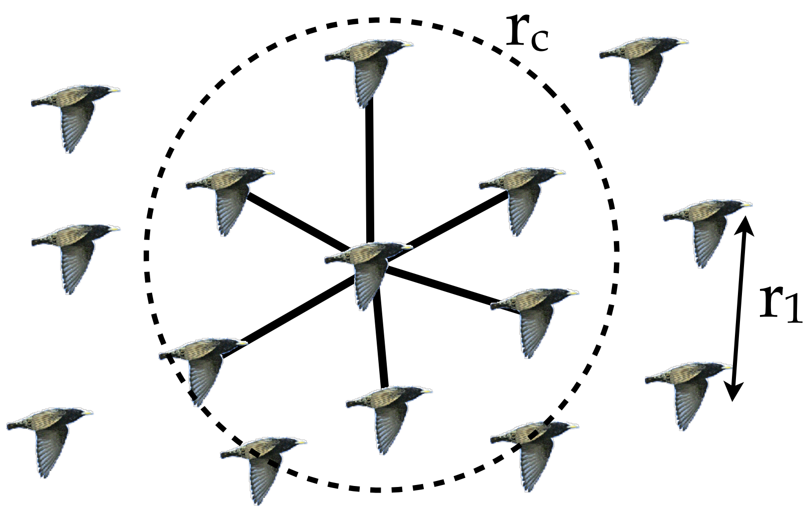
metric or **topological** ?

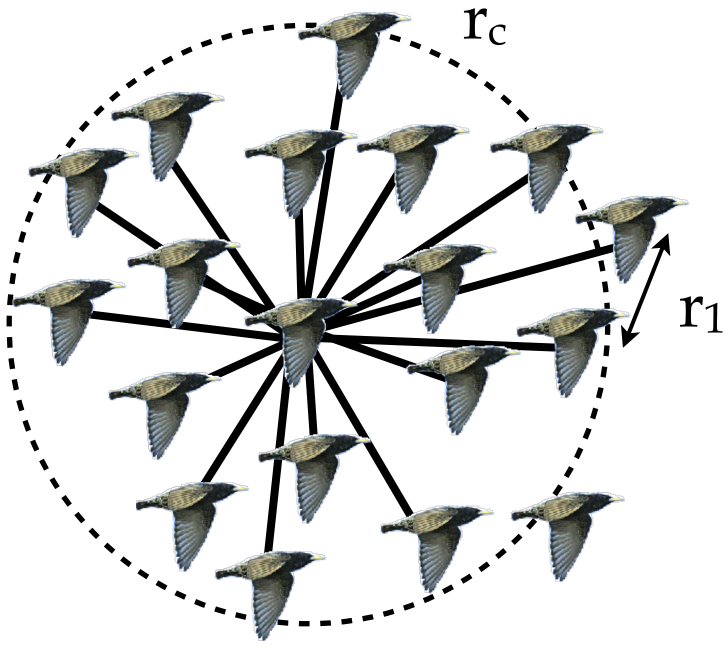
interaction range



metric or **topological** ?

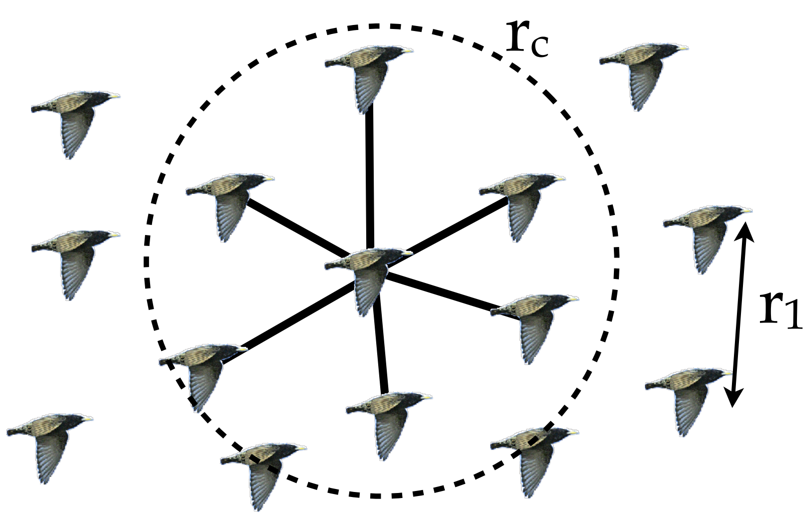
interaction range

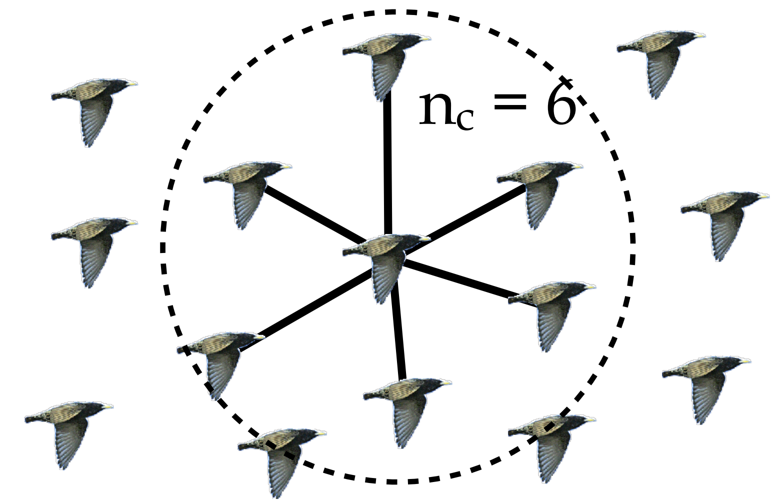




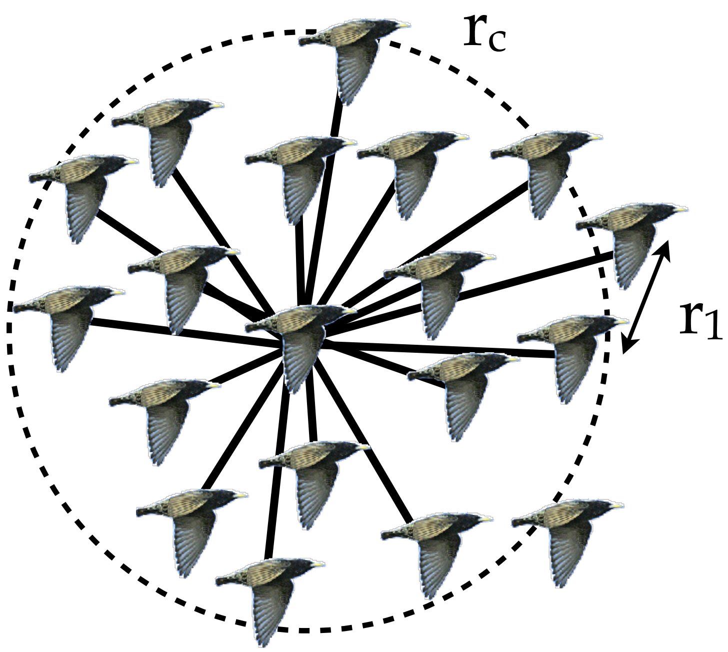
metric or **topological** ?

interaction range

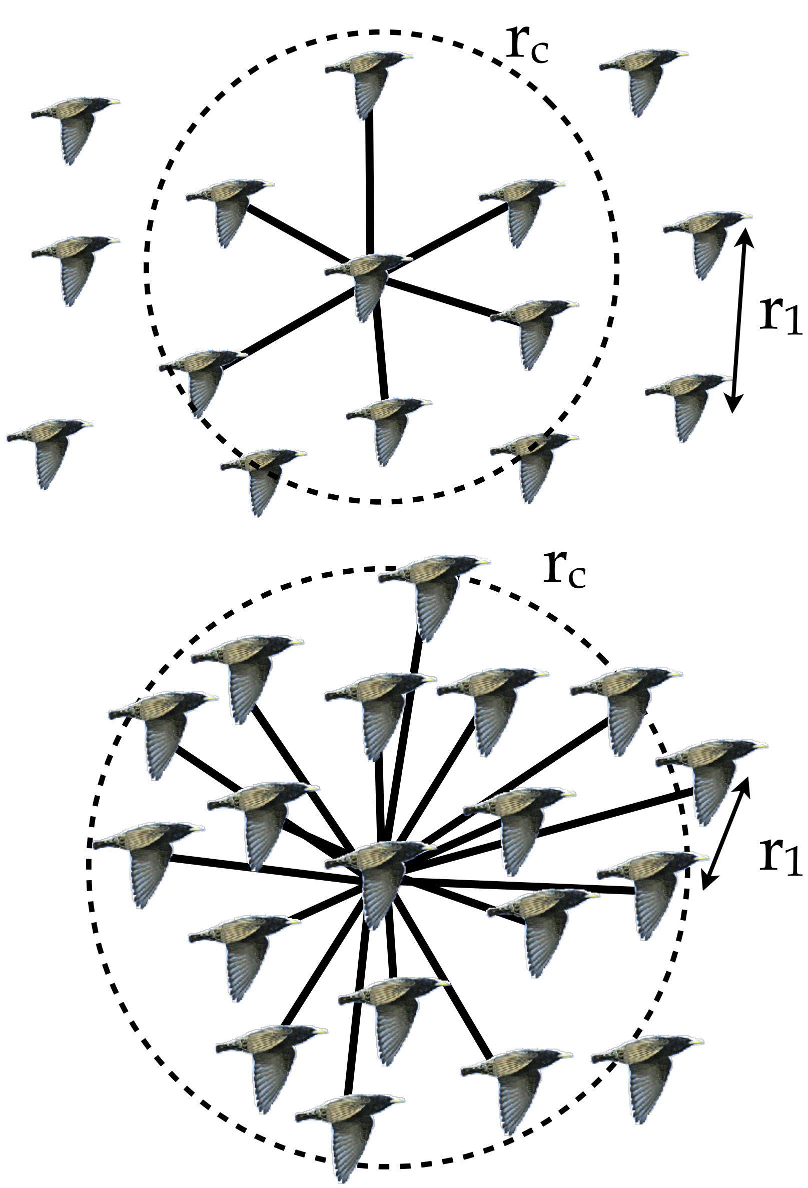




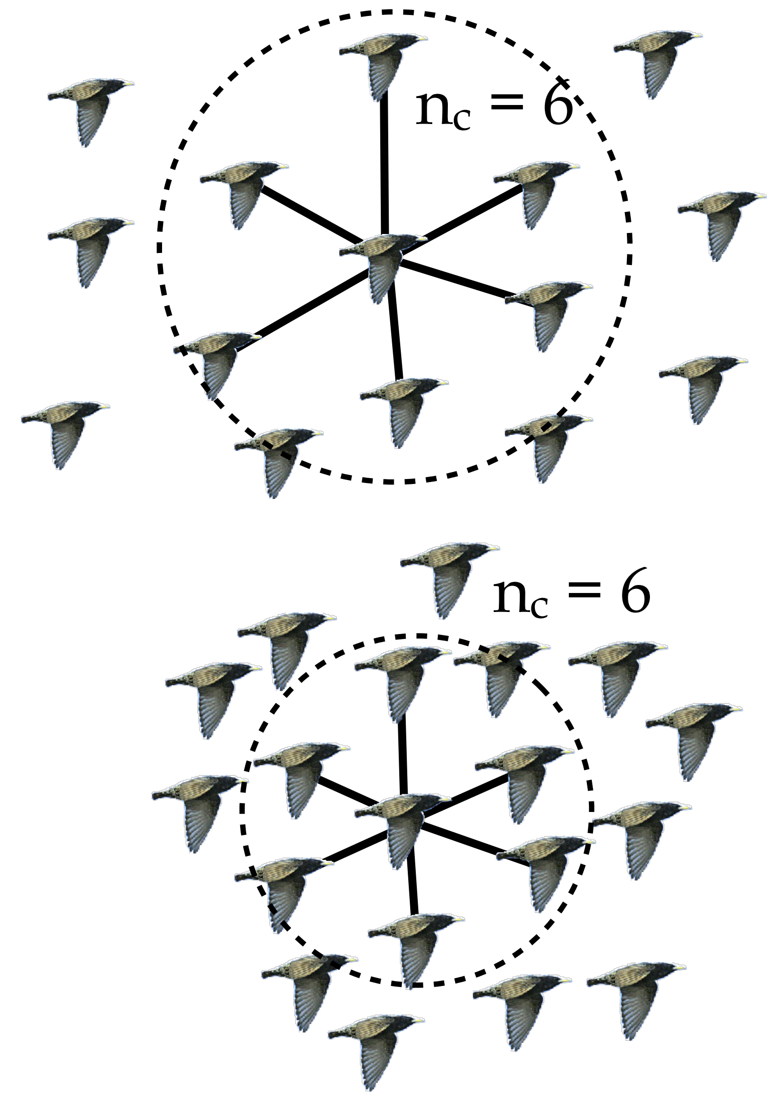
metric or **topological** ?



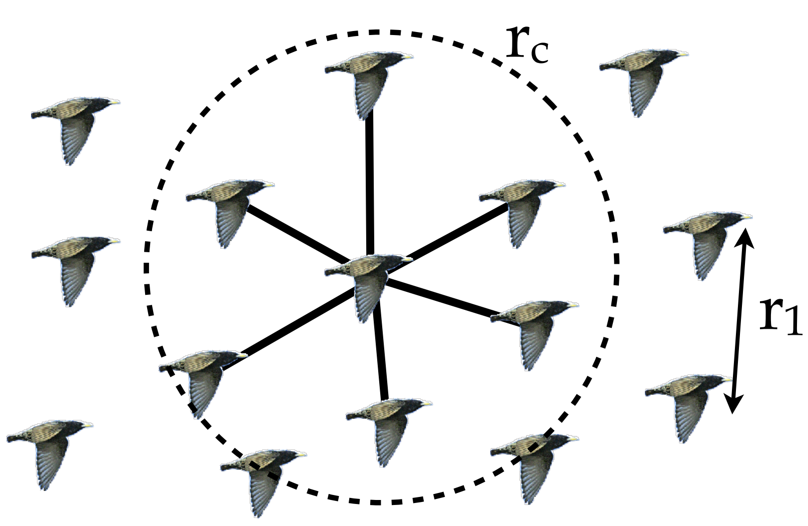
interaction range

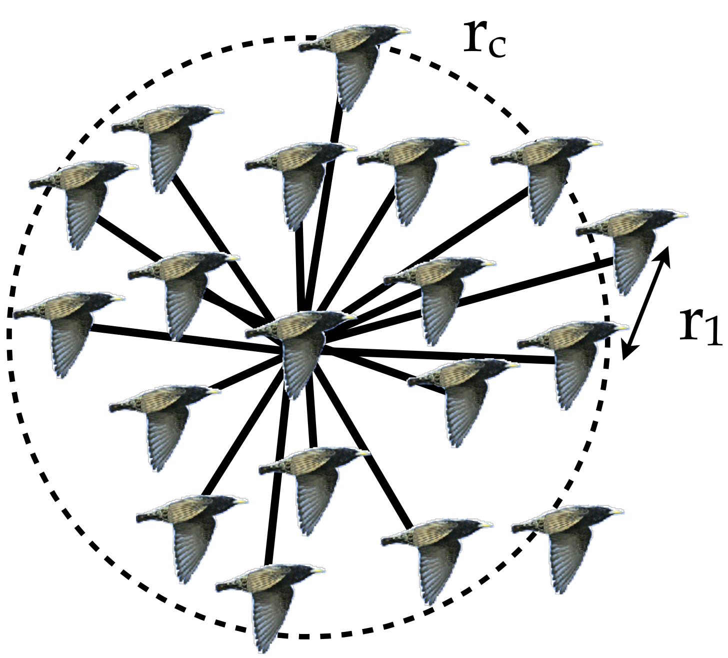


metric or **topological** ?

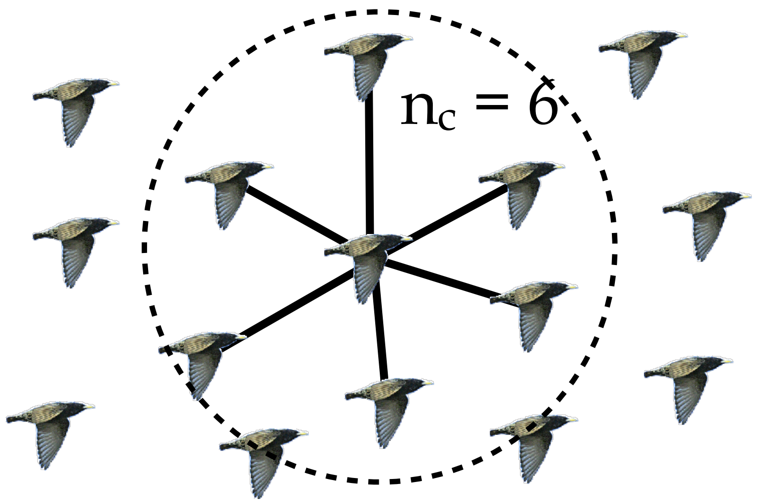


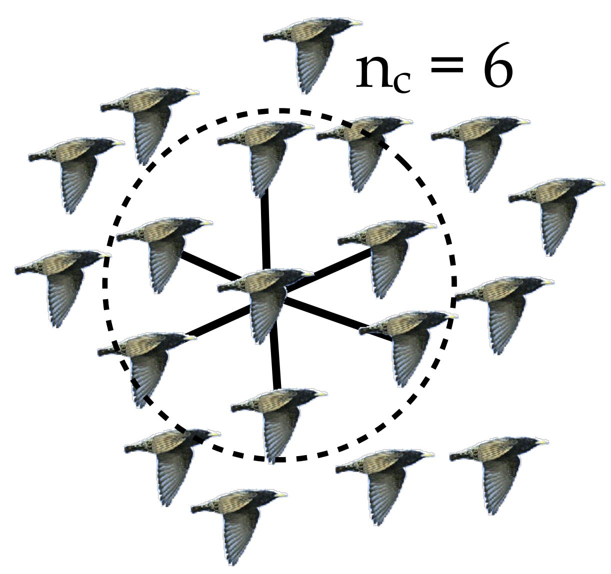
interaction range

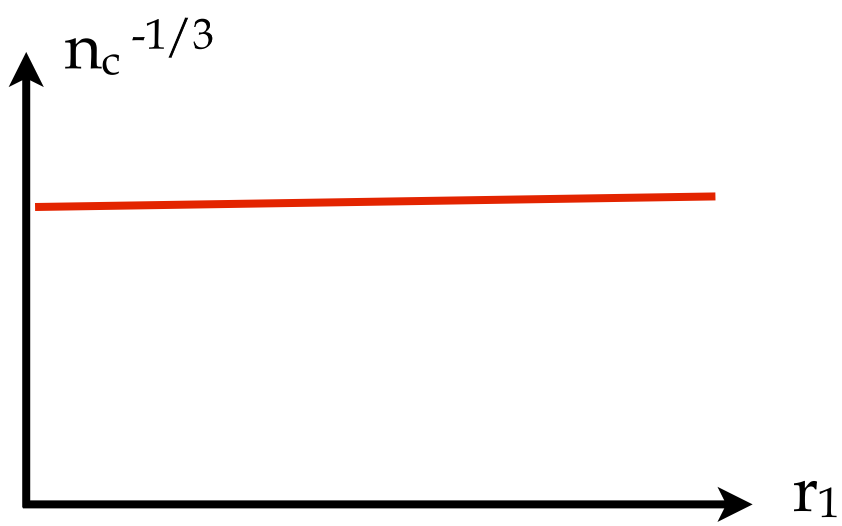




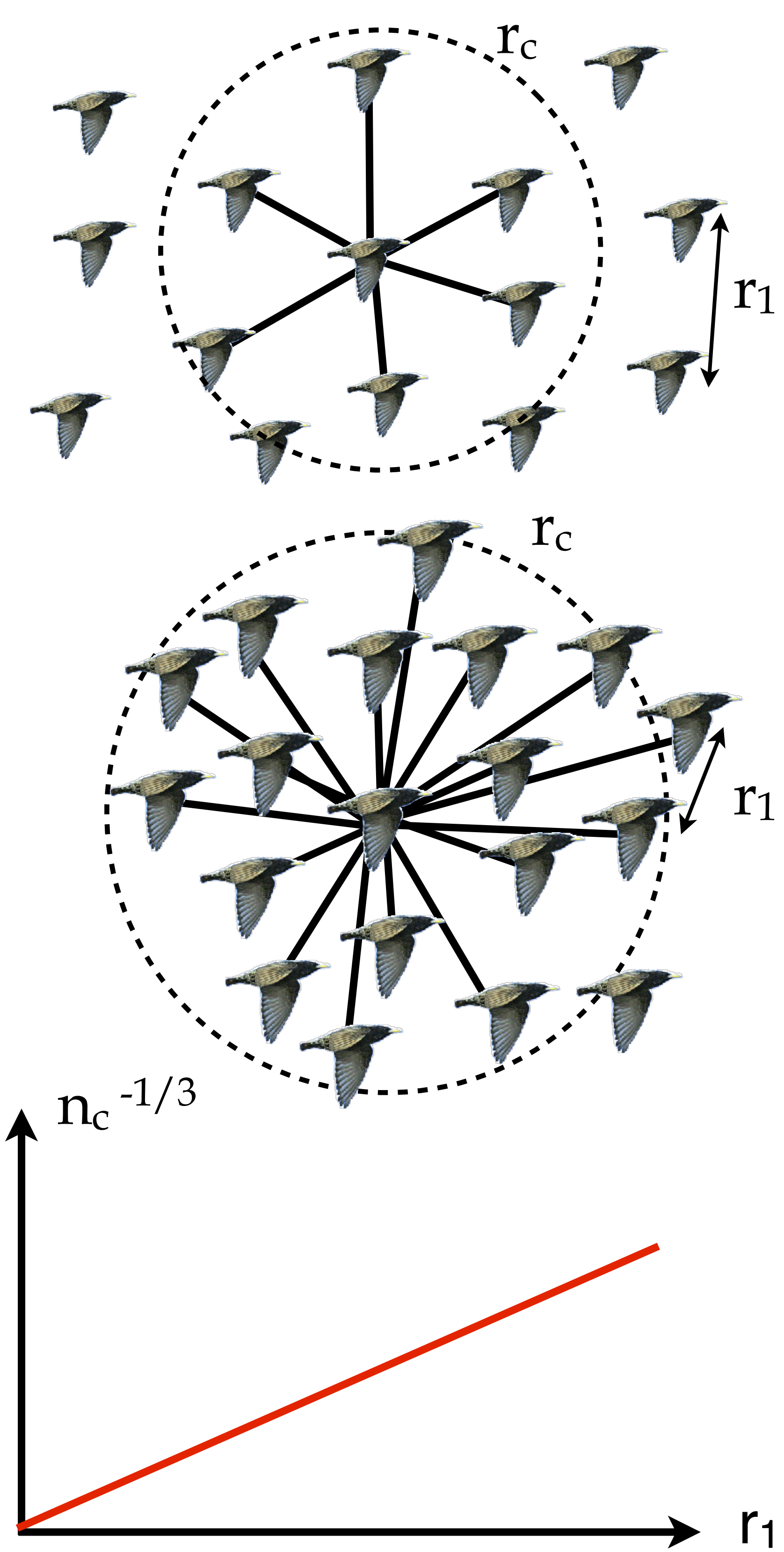
metric or **topological** ?





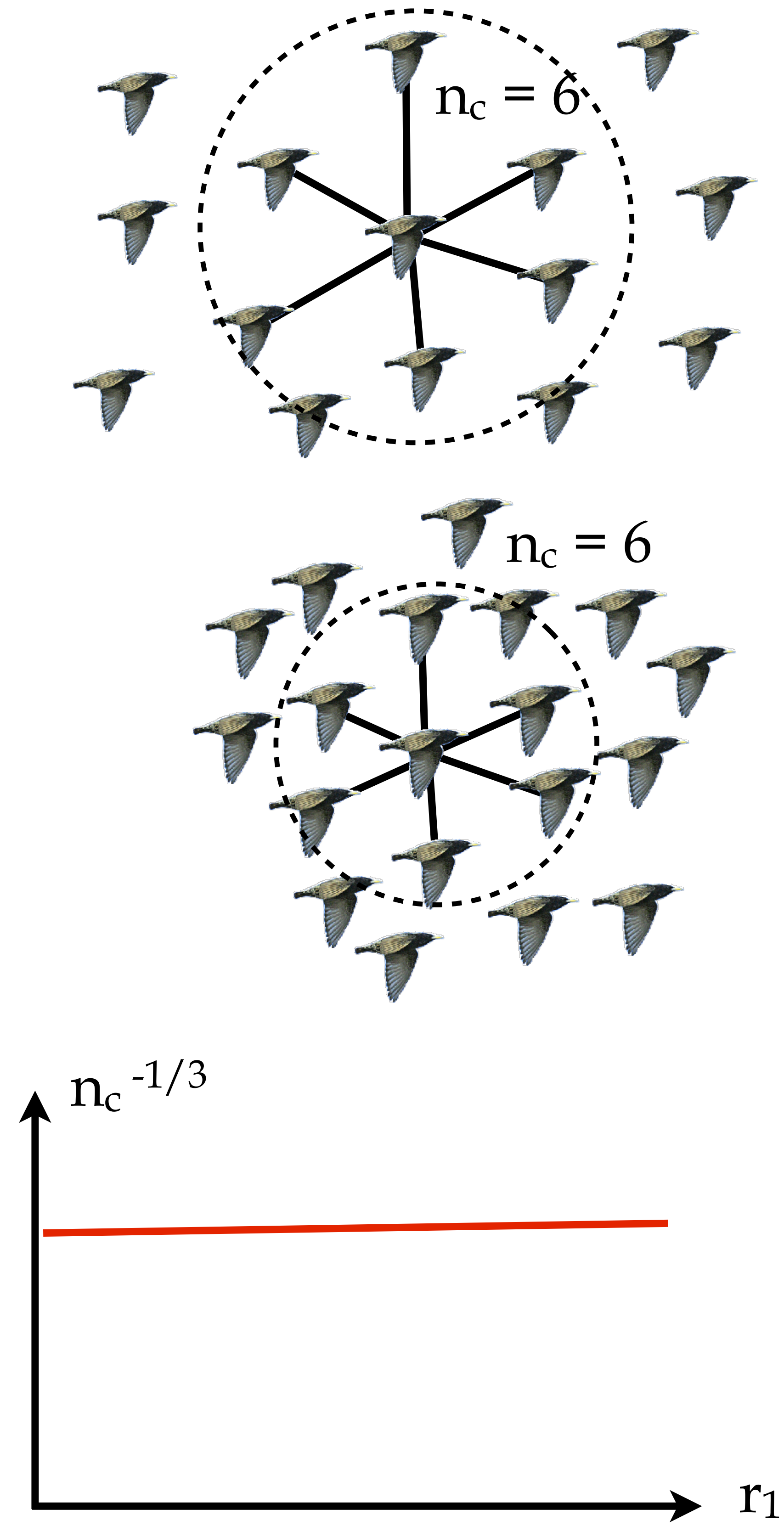


interaction range



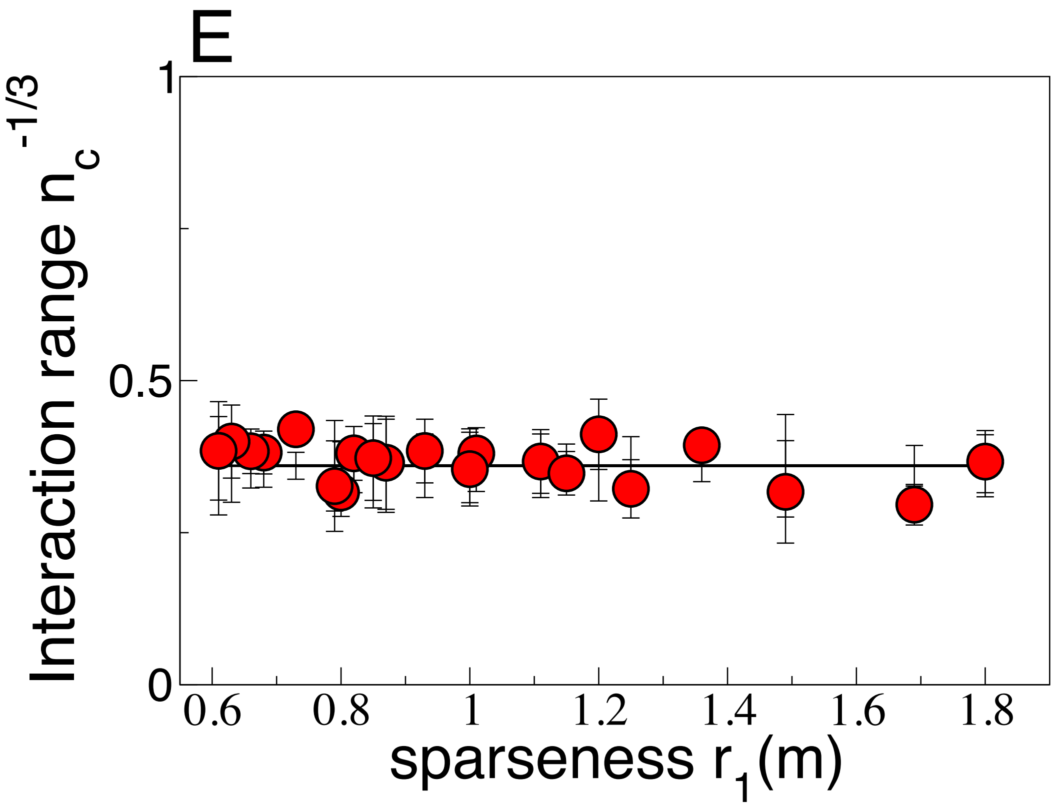
metric or **topological** ?

$$n_c \sim (r_c / r_1)^3$$



answer:

interaction is
topological not metric



Bialek et al PNAS 2012

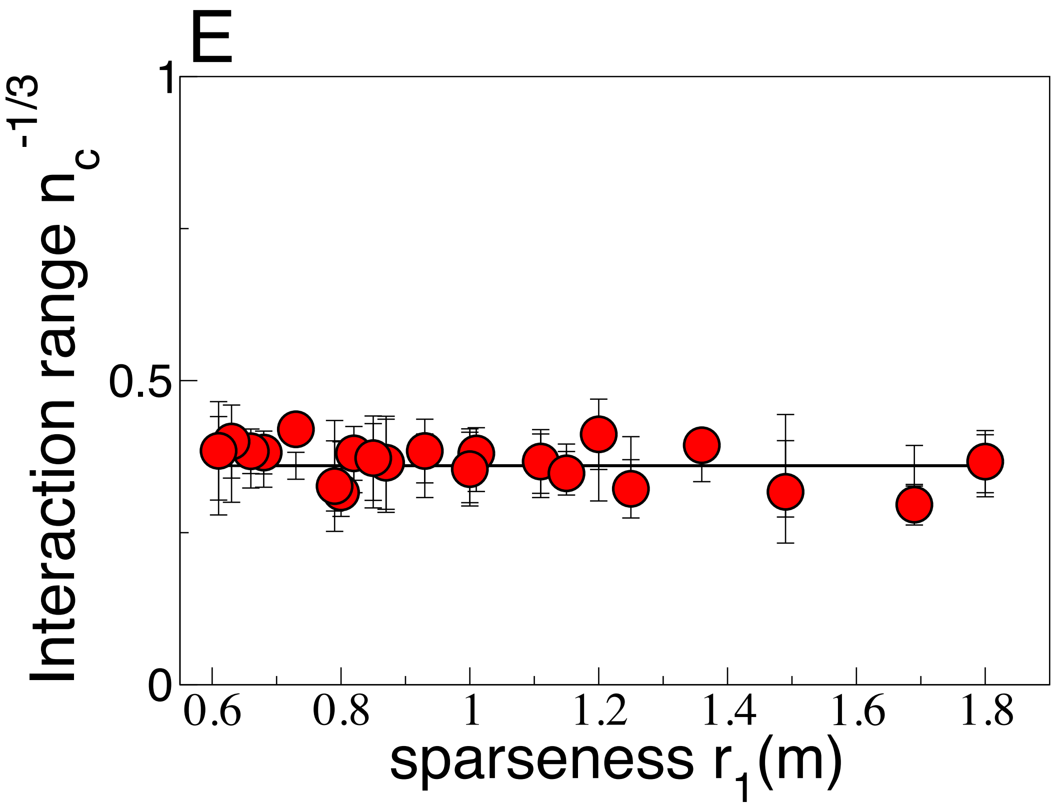
answer:

interaction is
topological not metric

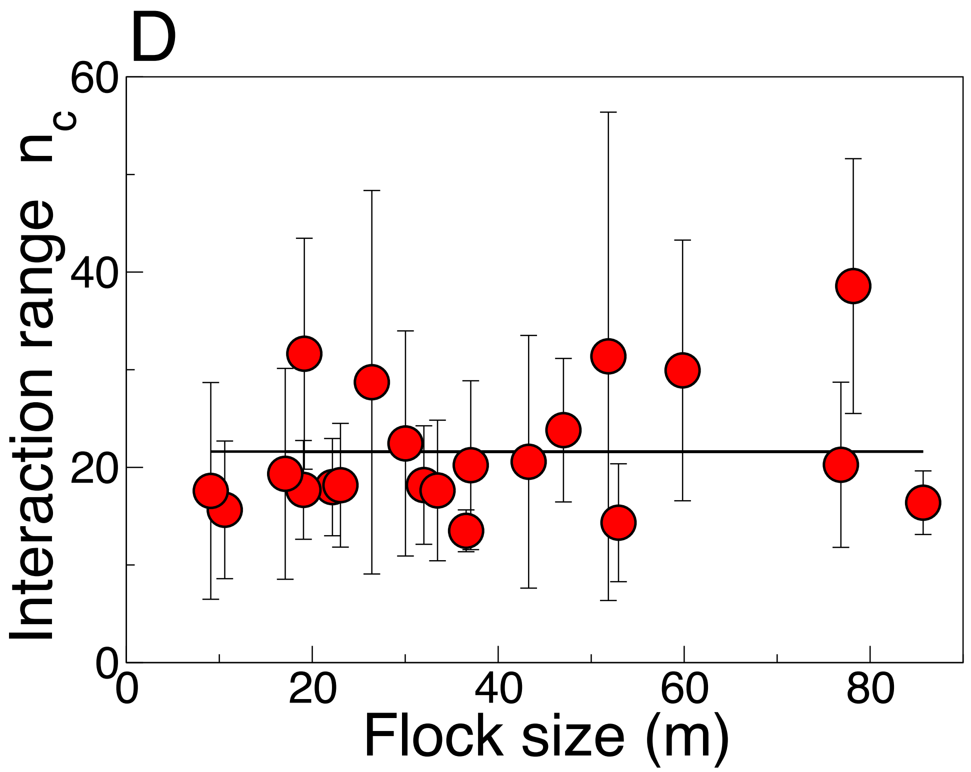
$n_c \sim 21$

does not depend on

flock density



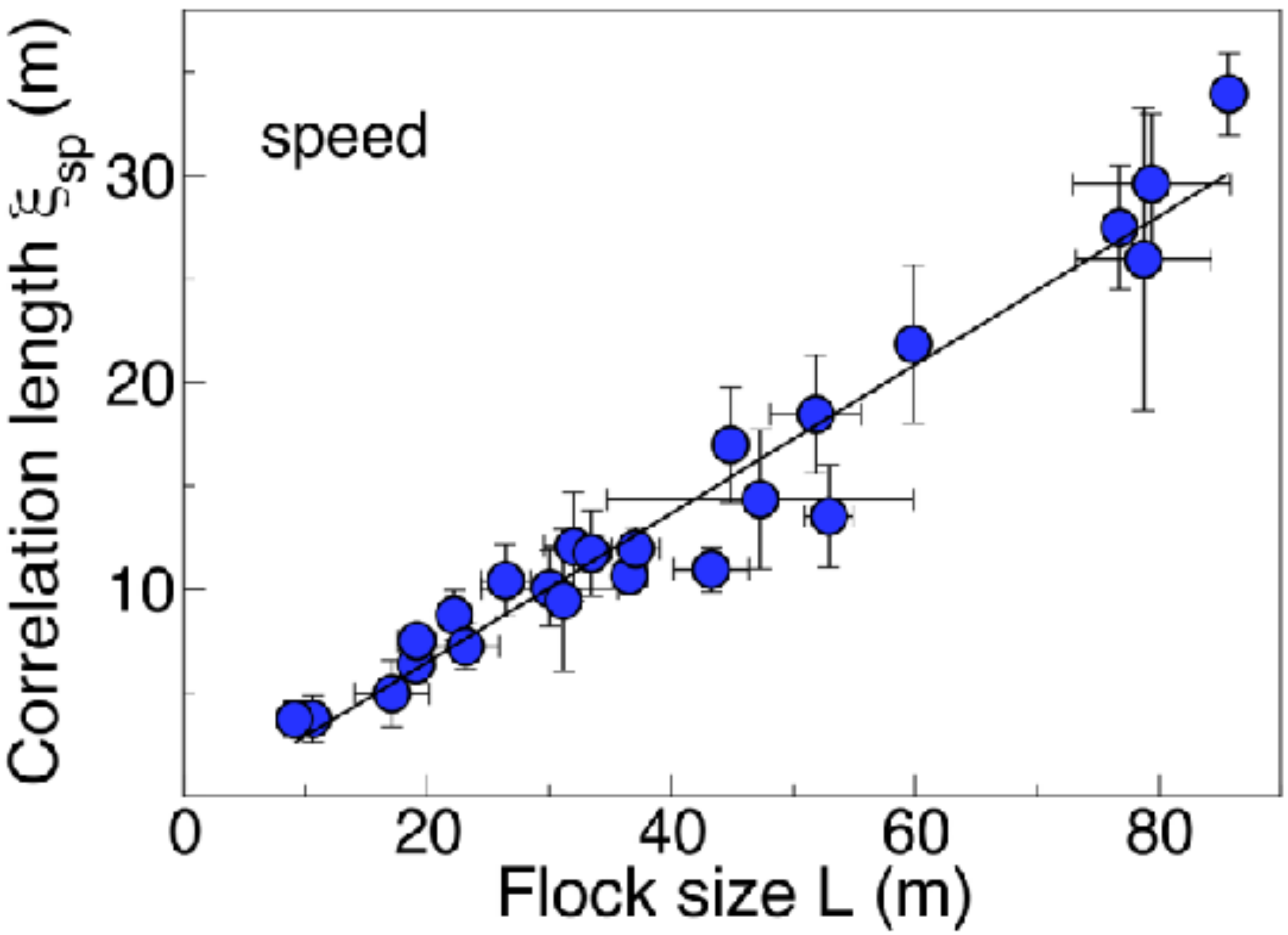
flock size



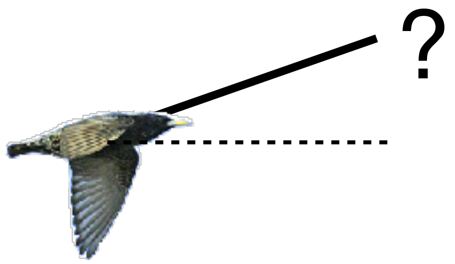
Bialek et al PNAS 2012

speed fluctuations are also scale free

- similar observations for fluctuations of modulus of speed



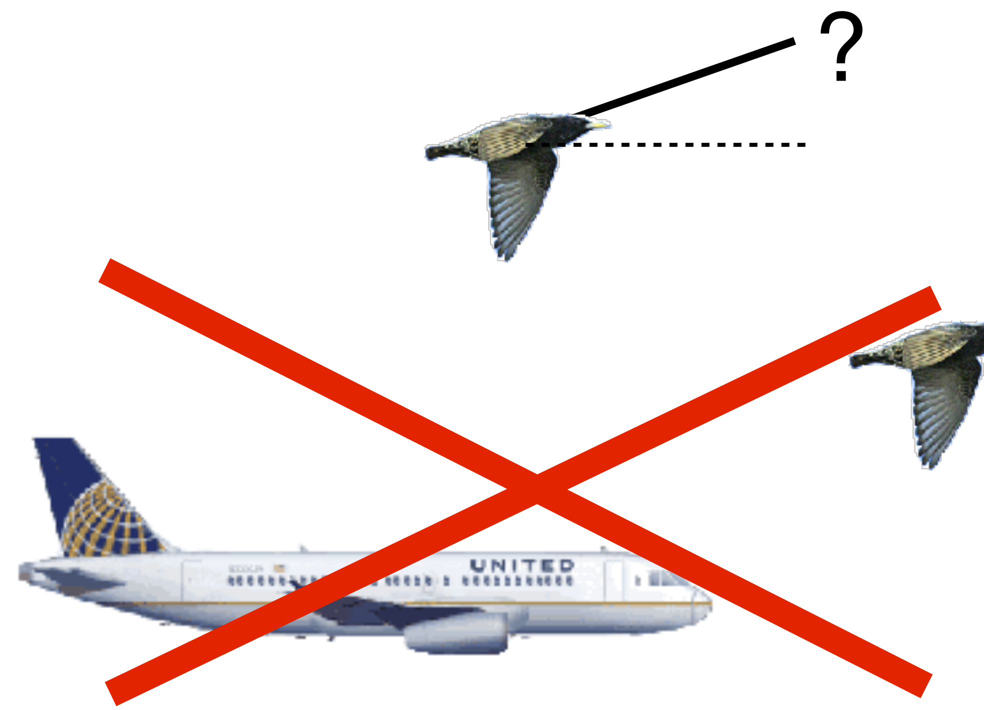
velocity control



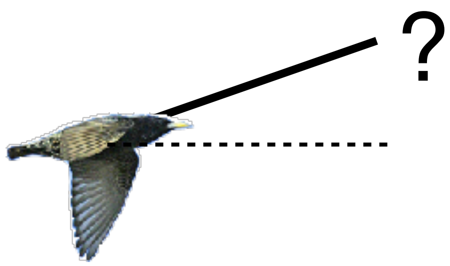
- orientation is arbitrary ; no preferred direction of flight
- but velocity v_i is not; has physical bounds

velocity control

- orientation is arbitrary ; no preferred direction of flight
- but velocity v_i is not; has physical bounds



velocity control



- orientation is arbitrary ; no preferred direction of flight

- but velocity v_i is not; has physical bounds

- Maximum entropy with constraint first two moments of speeds:

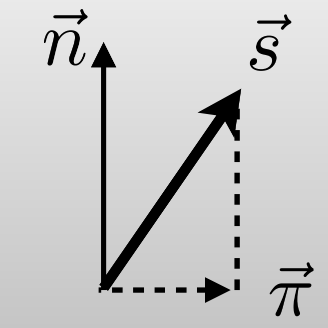
$$V = \frac{1}{N}\sum_i v_i \; ; \qquad V_2 = \frac{1}{N}\sum_i v_i^2$$

$$P(\vec{v}_1, \ldots, \vec{v}_N) = \frac{1}{Z}\exp\left[-\frac{J}{4}\sum_{ij} n_{ij}(\vec{v}_i - \vec{v}_j)^2 - \frac{g}{2}\sum_i (v_i - v_0)^2\right]$$

separation of orientation and speed

- in spin-wave approximation, Hamiltonian can be decomposed into independent *orientation* and *speed* parts: $P \propto \exp(-\mathcal{H}^{or}(\pi) - \mathcal{H}^{sp}(\epsilon))$

$$\vec{v}_i = v_0(1+\epsilon_i)\vec{s}_i$$



$$\mathcal{H}^{or}(\boldsymbol{\pi}) = \frac{Jv_0^2}{2}\sum_{ij} N_{ij}\vec{\pi}_i \cdot \vec{\pi}_j$$

"stiffness" due to speed control

$$\mathcal{H}^{sp}(\epsilon) = -\frac{Jv_0^2}{2}\sum_{ij}[N_{ij} + \frac{g}{J}\delta_{ij}]\epsilon_i\epsilon_j$$

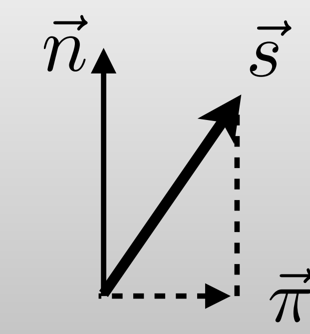
$$N_{ij} = -n_{ij} + \delta_{ij}\sum_k n_{ik}$$

- everything is still Gaussian
- system becomes critical at g = 0

separation of orientation and speed

- in spin-wave approximation, Hamiltonian can be decomposed into independent *orientation* and *speed* parts: $P \propto \exp(-\mathcal{H}^{or}(\pi) - \mathcal{H}^{sp}(\epsilon))$

$$\vec{v}_i = v_0(1+\epsilon_i)\vec{s}_i$$



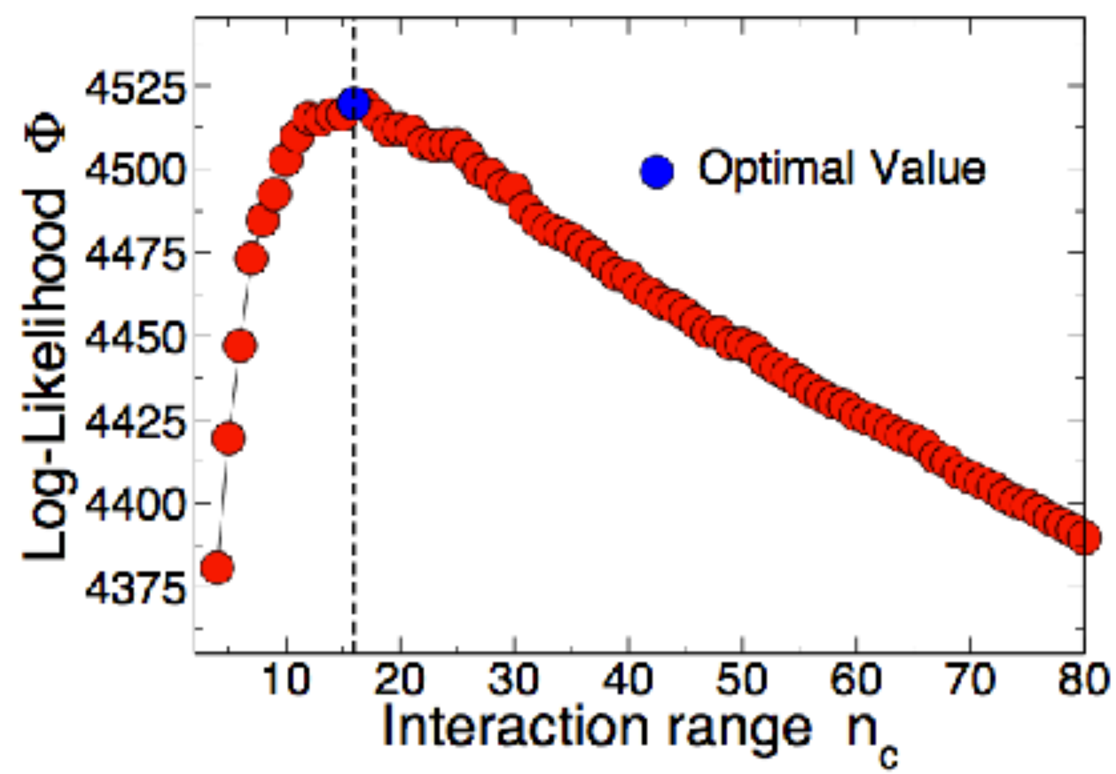
$$\mathcal{H}^{or}(\boldsymbol{\pi}) = \frac{Jv_0^2}{2}\sum_{ij} N_{ij}\vec{\pi}_i \cdot \vec{\pi}_j$$

"stiffness" due to speed control

$$\mathcal{H}^{sp}(\epsilon) = -\frac{Jv_0^2}{2}\sum_{ij}[N_{ij} + \frac{g}{J}\delta_{ij}]\epsilon_i\epsilon_j$$

$$N_{ij} = -n_{ij} + \delta_{ij}\sum_k n_{ik}$$

- everything is still Gaussian
- system becomes critical at g = 0
- find J, g and n_c



peer pressure *vs.* individual will

$$P(\vec{v}_1, \ldots, \vec{v}_N) = \frac{1}{Z} \exp\left[-\frac{J}{4} \sum_{ij} n_{ij} (\vec{v}_i - \vec{v}_j)^2 - \frac{g}{2} \sum_i (v_i - v_0)^2 \right]$$

coordination w/ neighbors

individual speed control

$$\frac{g}{J n_c} = 10^{-2}$$

peer pressure *vs.* individual will

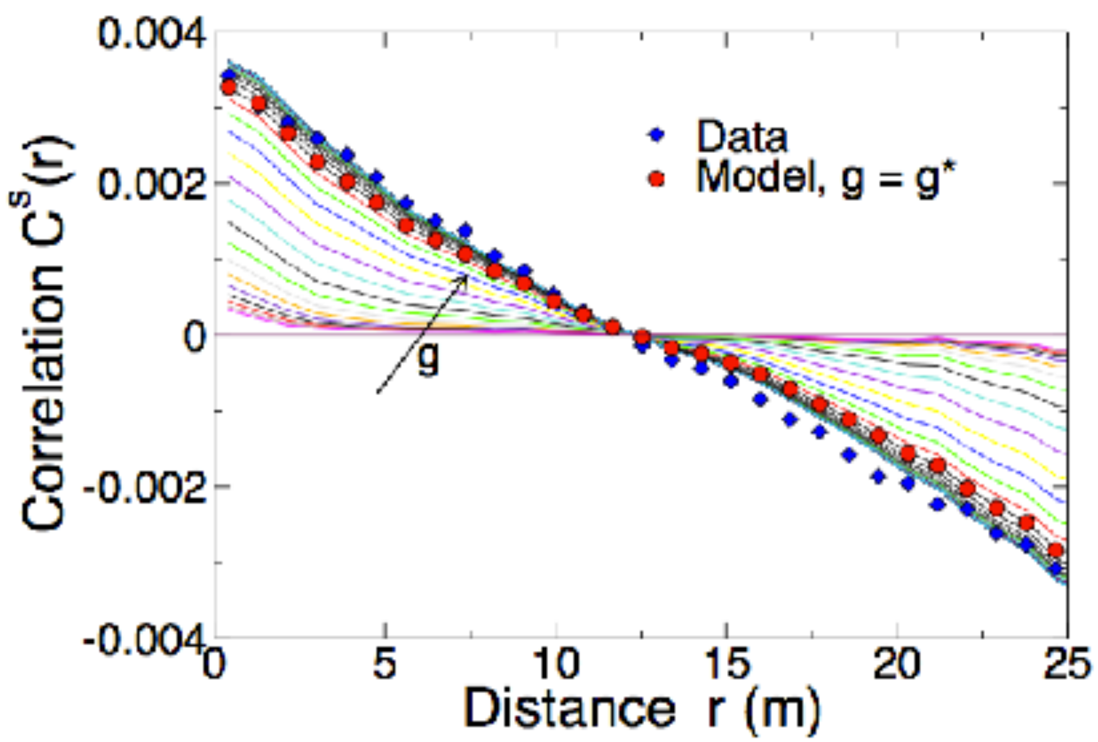
$$P(\vec{v}_1, \ldots, \vec{v}_N) = \frac{1}{Z} \exp \left[-\frac{J}{4} \sum_{ij} n_{ij} (\vec{v}_i - \vec{v}_j)^2 - \frac{g}{2} \sum_i (v_i - v_0)^2 \right]$$

coordination w/ neighbors

individual speed control

$$\frac{g}{J n_c} = 10^{-2}$$

- in continuous theory, $\xi \sim r_0 \sqrt{\frac{J n_c}{g}}$



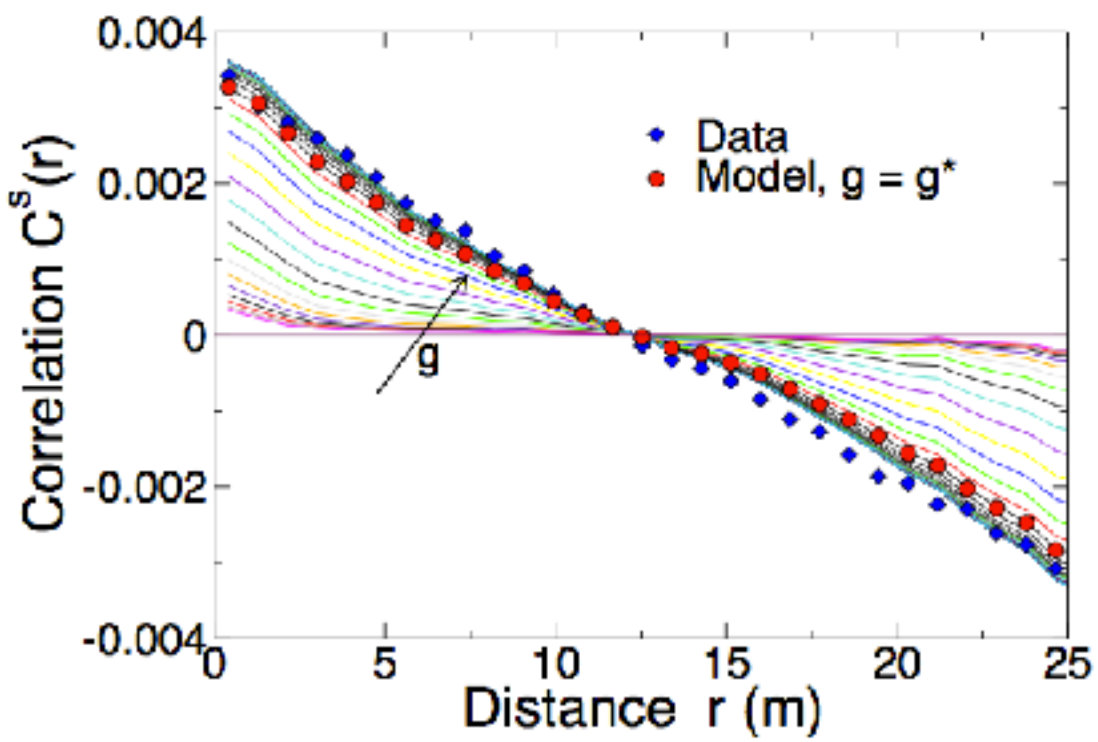
peer pressure *vs.* individual will

$$P(\vec{v}_1, \ldots, \vec{v}_N) = \frac{1}{Z} \exp\left[-\frac{J}{4}\sum_{ij} n_{ij}(\vec{v}_i - \vec{v}_j)^2 - \frac{g}{2}\sum_i (v_i - v_0)^2\right]$$

coordination w/ neighbors

individual speed control

$$\frac{g}{Jn_c} = 10^{-2}$$



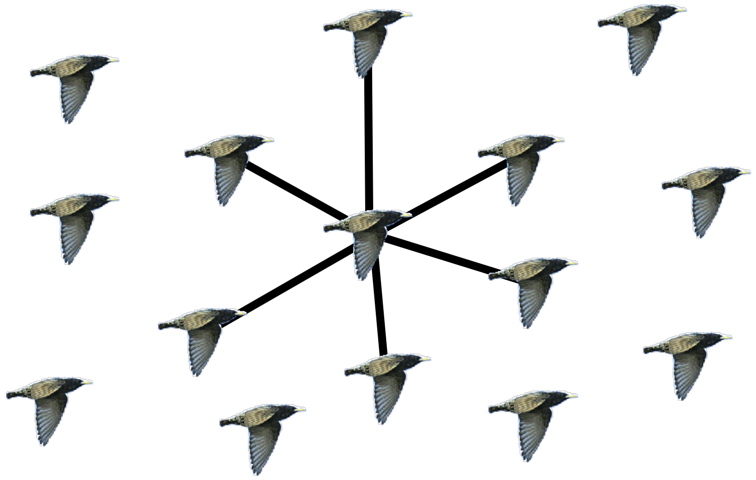
- in continuous theory, $\xi \sim r_0 \sqrt{\frac{Jn_c}{g}}$
- self-organisation (J) dominates individual speed control (g) to tightly regulate the speed of the flock

birds are pushovers, yet $\frac{\delta v}{v} \approx 0.07$

- possible function? enhanced response and information transfer upon predator attack, environmental cues

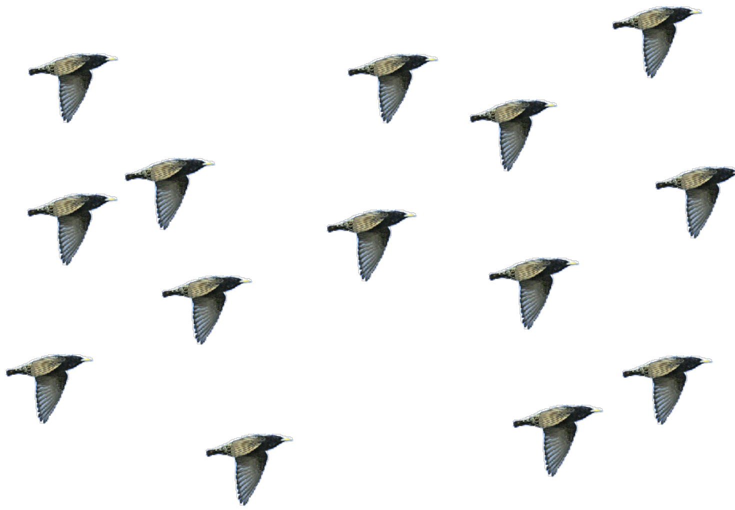
equilibrium vs. dynamics

- we’ve implicitly assumed equilibrium
- but birds exchange neighbours fast
  — out of equilibrium dynamics



equilibrium vs. dynamics

- we've implicitly assumed equilibrium
- but birds exchange neighbours fast
  – out of equilibrium dynamics

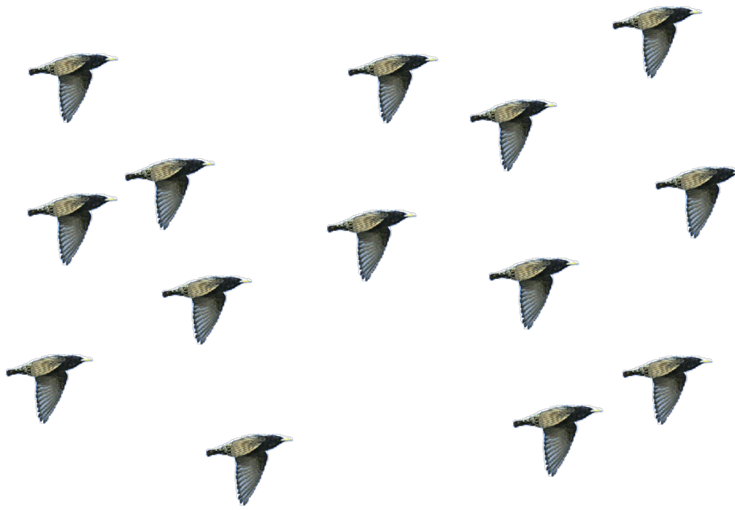


equilibrium vs. dynamics

- we've implicitly assumed equilibrium

- but birds exchange neighbours fast
  — out of equilibrium dynamics

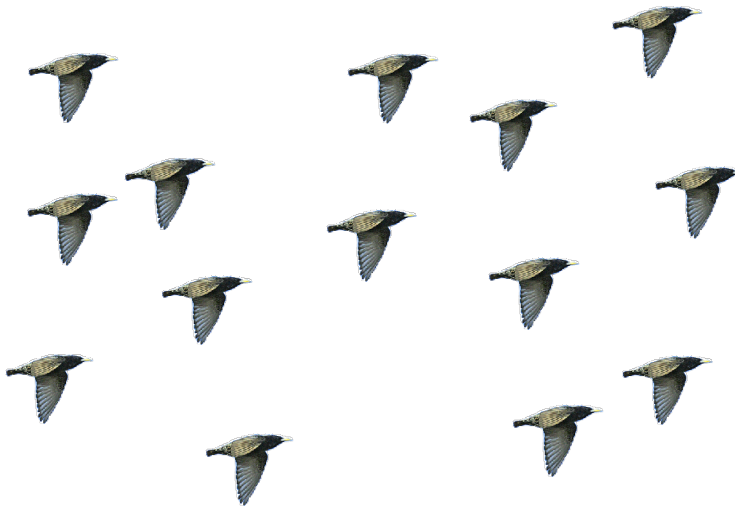
- *effective* number of interaction partners could be larger than the *instantaneous* one.



equilibrium vs. dynamics

- we've implicitly assumed equilibrium

- but birds exchange neighbours fast
  — out of equilibrium dynamics



- *effective* number of interaction partners could be larger than the *instantaneous* one.

- **theory**: it changes everything
  - existence of order in 2D (Mermin-Wagner theorem does not apply)
  - critical exponents *Tu Toner 1995, 1998, …*

dynamical inference

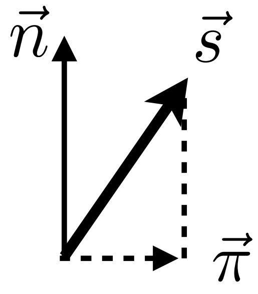
- Maximum entropy principle with constraints on $\langle \vec{s}_i(t) \cdot \vec{s}_j(t) \rangle$ *and*

$$\langle \vec{s}_i(t) \cdot \vec{s}_j(t + \delta t) \rangle$$

dynamical inference

- Maximum entropy principle with constraints on $\langle \vec{s}_i(t) \cdot \vec{s}_j(t) \rangle$ *and*

$$\langle \vec{s}_i(t) \cdot \vec{s}_j(t + \delta t) \rangle$$



- in the spin-wave approximation ($\pi \ll 1$), equivalent to:

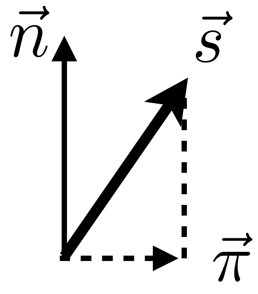
alignment *noise*

$$\vec{s}_i(t + \delta t) \approx \sum_j M_{ij;t} \vec{s}_j(t) + \vec{\epsilon}_i(t),$$

dynamical inference

- Maximum entropy principle with constraints on $\langle \vec{s}_i(t) \cdot \vec{s}_j(t) \rangle$ *and* $\langle d\vec{s}_i(t)/dt \cdot \vec{s}_j(t) \rangle$

$$\langle \vec{s}_i(t) \cdot \vec{s}_j(t+\delta t) \rangle \qquad \delta t \to 0$$



- in the spin-wave approximation ($\pi \ll 1$), equivalent to:

alignment *noise*

$$\vec{s}_i(t+\delta t) \approx \sum_j M_{ij;t} \vec{s}_j(t) + \vec{\epsilon}_i(t),$$

alignment *noise*

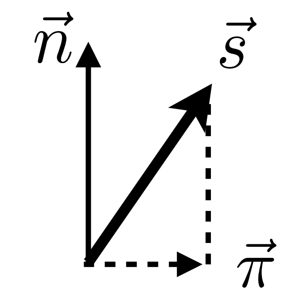
$$\frac{d\vec{s}_i}{dt} = \left(\sum_j J_{ij} \vec{s}_j + \vec{\xi}_i \right)_\perp$$

$$\langle \vec{\xi}_i(t) \xi_j(t') \rangle = 2dT\delta(t-t')$$

dynamical inference

- Maximum entropy principle with constraints on $\langle \vec{s}_i(t) \cdot \vec{s}_j(t) \rangle$ *and* $\langle d\vec{s}_i(t)/dt \cdot \vec{s}_j(t) \rangle$

$$\langle \vec{s}_i(t) \cdot \vec{s}_j(t+\delta t) \rangle \qquad \delta t \to 0$$



- in the spin-wave approximation ($\pi \ll 1$), equivalent to:

alignment *noise*

$$\vec{s}_i(t+\delta t) \approx \sum_j M_{ij;t} \vec{s}_j(t) + \vec{\epsilon}_i(t),$$

$$\frac{d\vec{s}_i}{dt} = \left(\sum_j J_{ij} \vec{s}_j + \vec{\xi}_i \right)_\perp$$

alignment *noise*

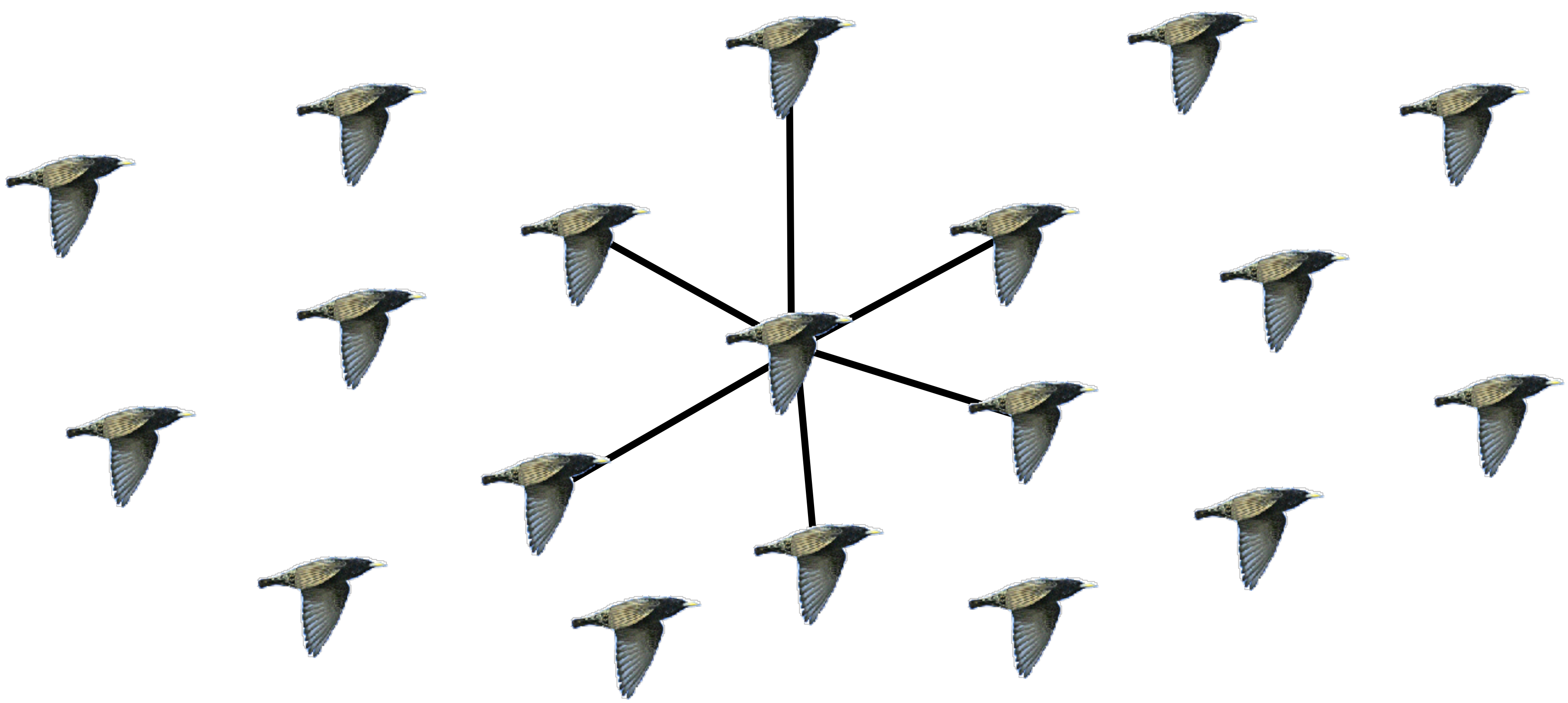
$$\langle \vec{\xi}_i(t) \xi_j(t') \rangle = 2dT\delta(t-t')$$

- Equilibrium distribution on a fixed network (J_{ij} constant and symmetric)

$$P(\vec{s}_1, \ldots, \vec{s}_N) = \frac{1}{Z} \exp\left(\frac{1}{T} \sum_{ij} J_{ij} \vec{s}_i \cdot \vec{s}_j \right)$$

Heisenberg model

parametrisation



$$J_{ij} = J \exp(-k_{ij}/n_c)$$

Cavagna Castello Dey Giardina Melillo Parisi Viale PRE 2015

k_{ij} is the rank of i's neighbour j, ordered by distance

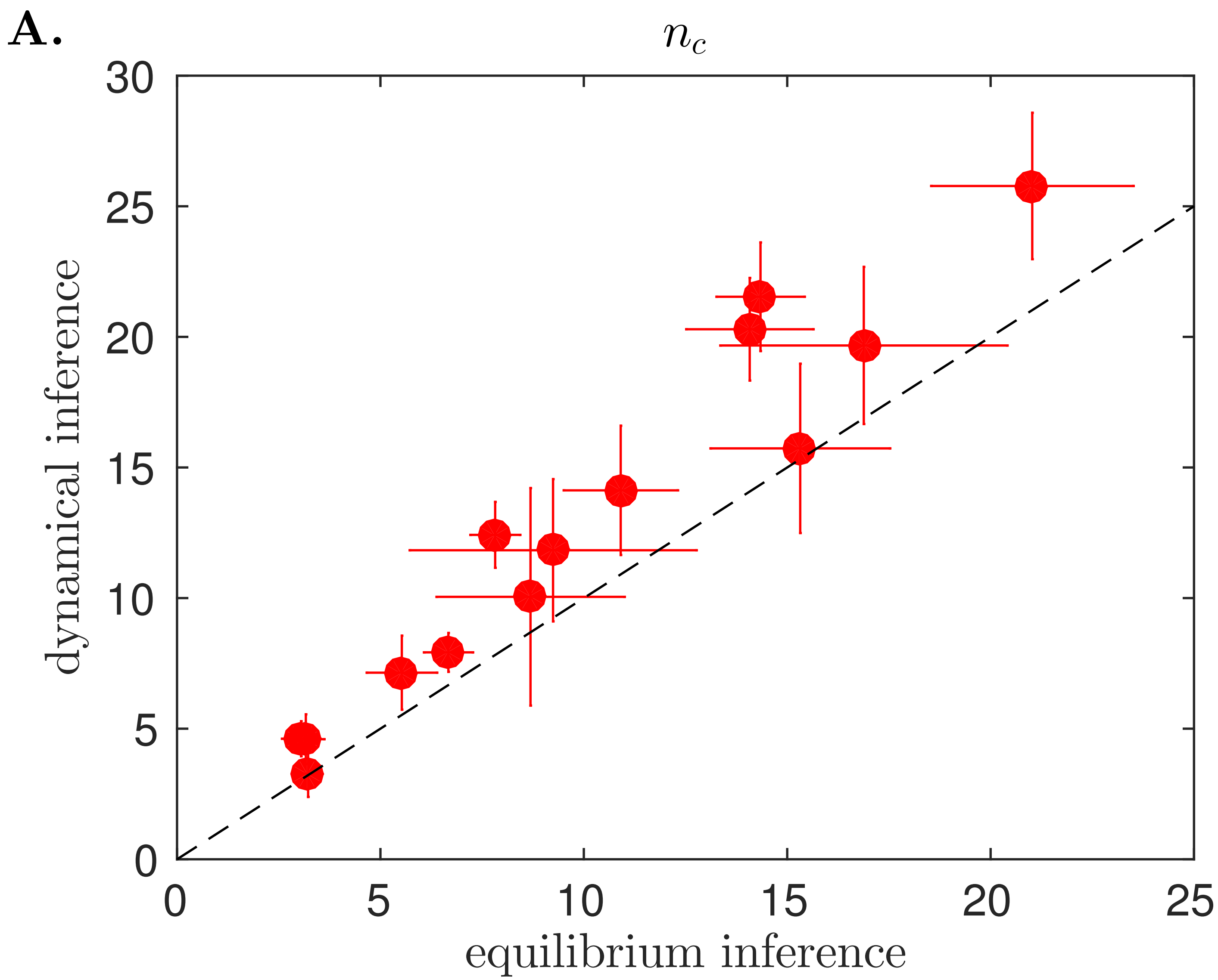
3 parameters: n_c, J and temperature T (controling noise)

maximum likelihood fit using new exact integration method

comparison with equilibrium inference

fit

$$\frac{d\vec{s}_i}{dt} = \left(\sum_j J_{ij} \vec{s}_j + \vec{\xi}_i \right)_\perp ,$$



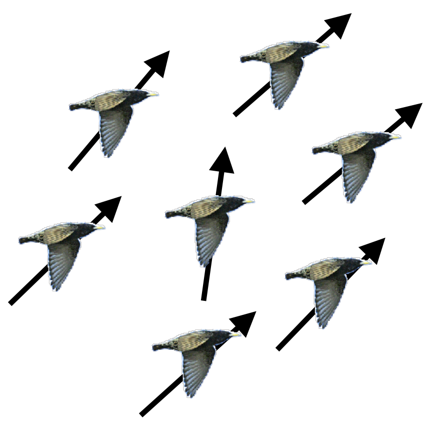
fit $\quad P(\vec{s}_1, \dots, \vec{s}_N) = \frac{1}{Z} \exp\left(\frac{1}{T} \sum_{ij} J_{ij} \vec{s}_i \cdot \vec{s}_j \right)$

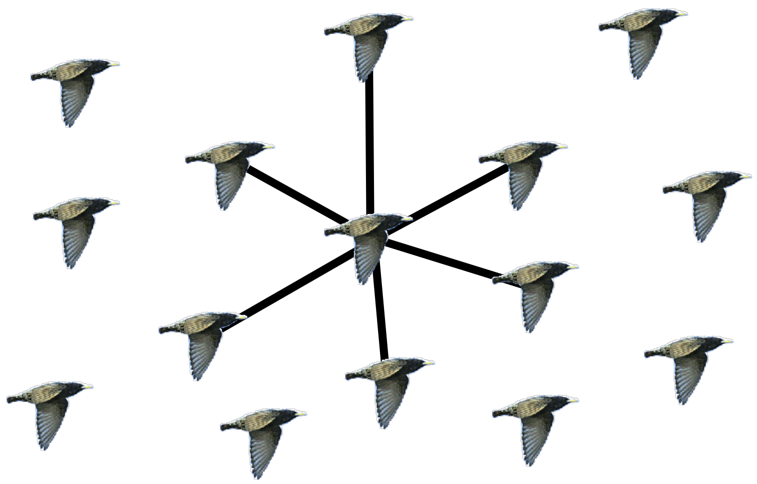
Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

a tale of two time scales

τ_{relax} how fast birds align with their local neighbourhood

τ_{network} how fast each bird renews its neighbours



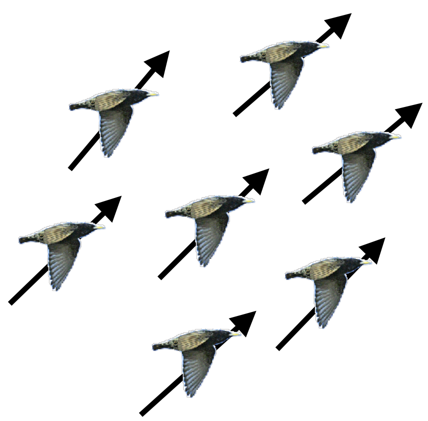


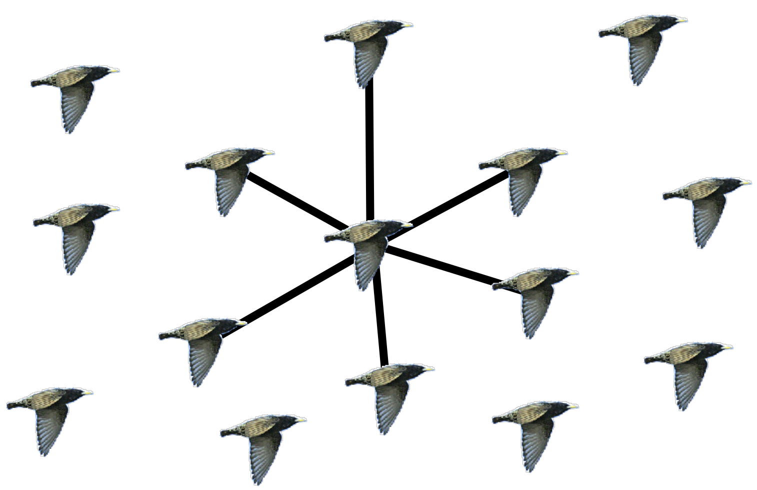
Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

a tale of two time scales

τ_{relax} how fast birds align with their local neighbourhood

τ_{network} how fast each bird renews its neighbours



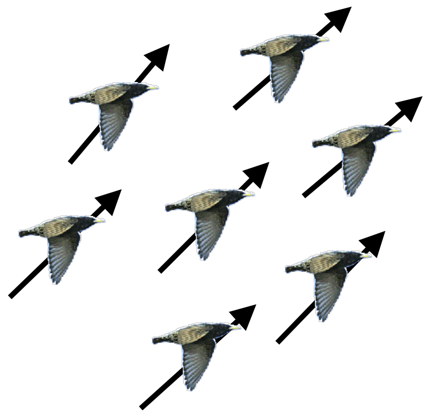


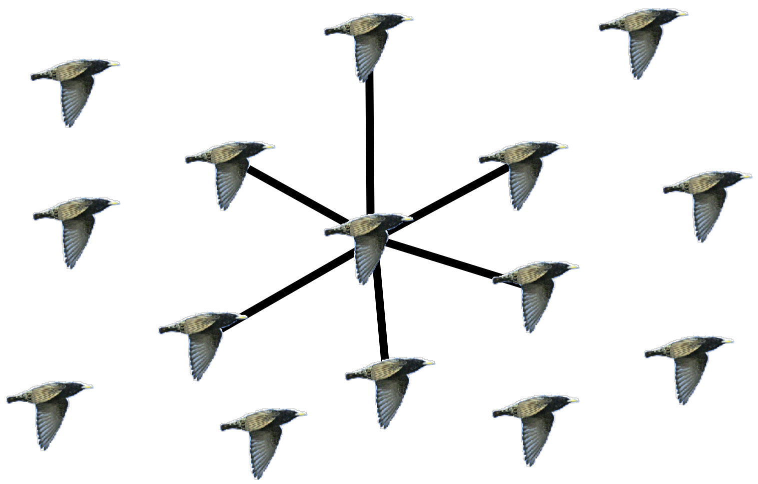
Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

a tale of two time scales

τ_{relax} how fast birds align with their local neighbourhood

τ_{network} how fast each bird renews its neighbours





$$\frac{d\vec{s}_i}{dt} = \left(\sum_j J_{ij} \vec{s}_j + \vec{\xi}_i \right)_\perp$$

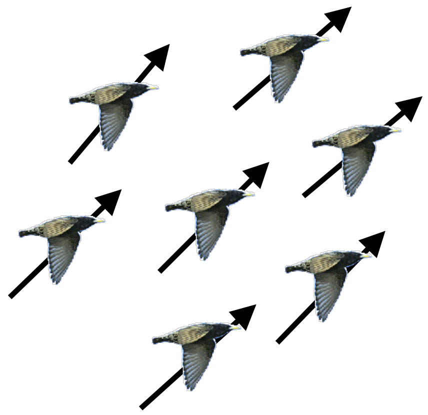
$\sim J\, n_c$

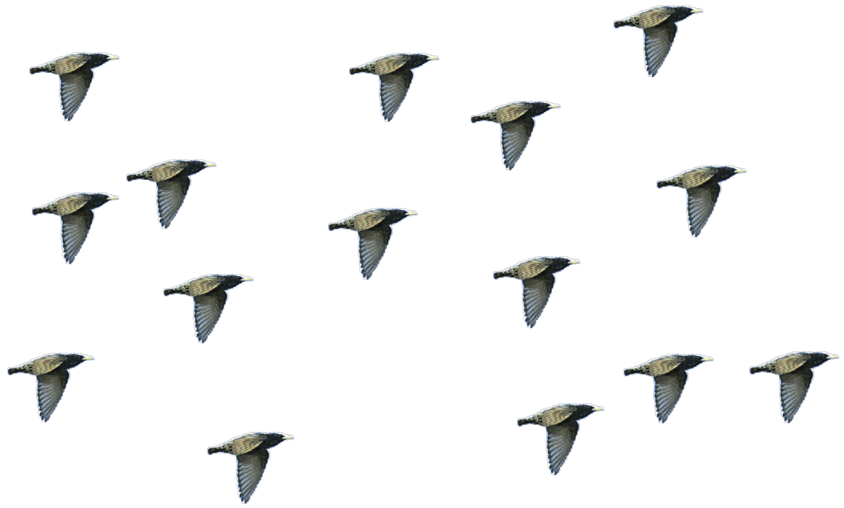
Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

a tale of two time scales

τ_{relax} how fast birds align with their local neighbourhood

τ_{network} how fast each bird renews its neighbours





$$\frac{d\vec{s}_i}{dt} = \left(\sum_j J_{ij}\vec{s}_j + \vec{\xi}_i \right)_\perp$$

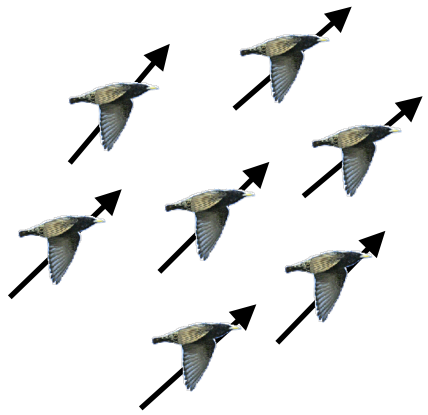
$\sim J\, n_c$

Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

a tale of two time scales

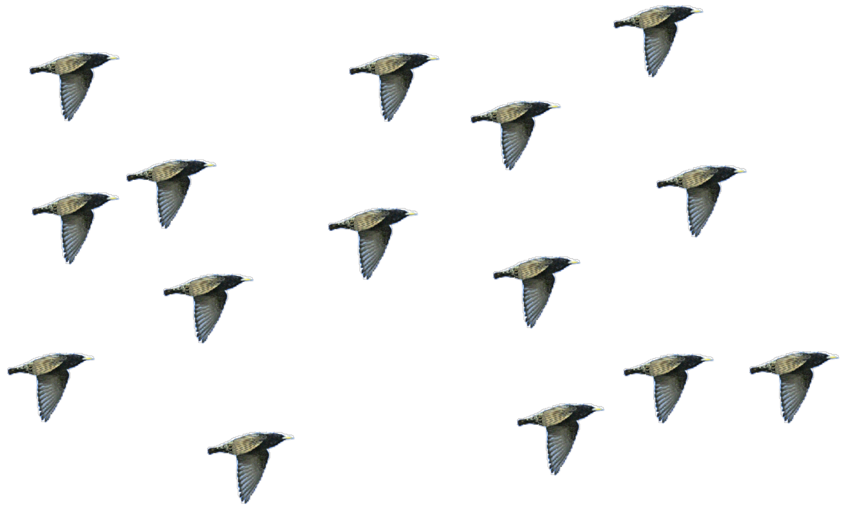
τ_{relax} how fast birds align with their local neighbourhood

τ_{network} how fast each bird renews its neighbours



$$\frac{d\vec{s}_i}{dt} = \left(\sum_j J_{ij} \vec{s}_j + \vec{\xi}_i \right)_\perp$$

$\sim J\, n_c$



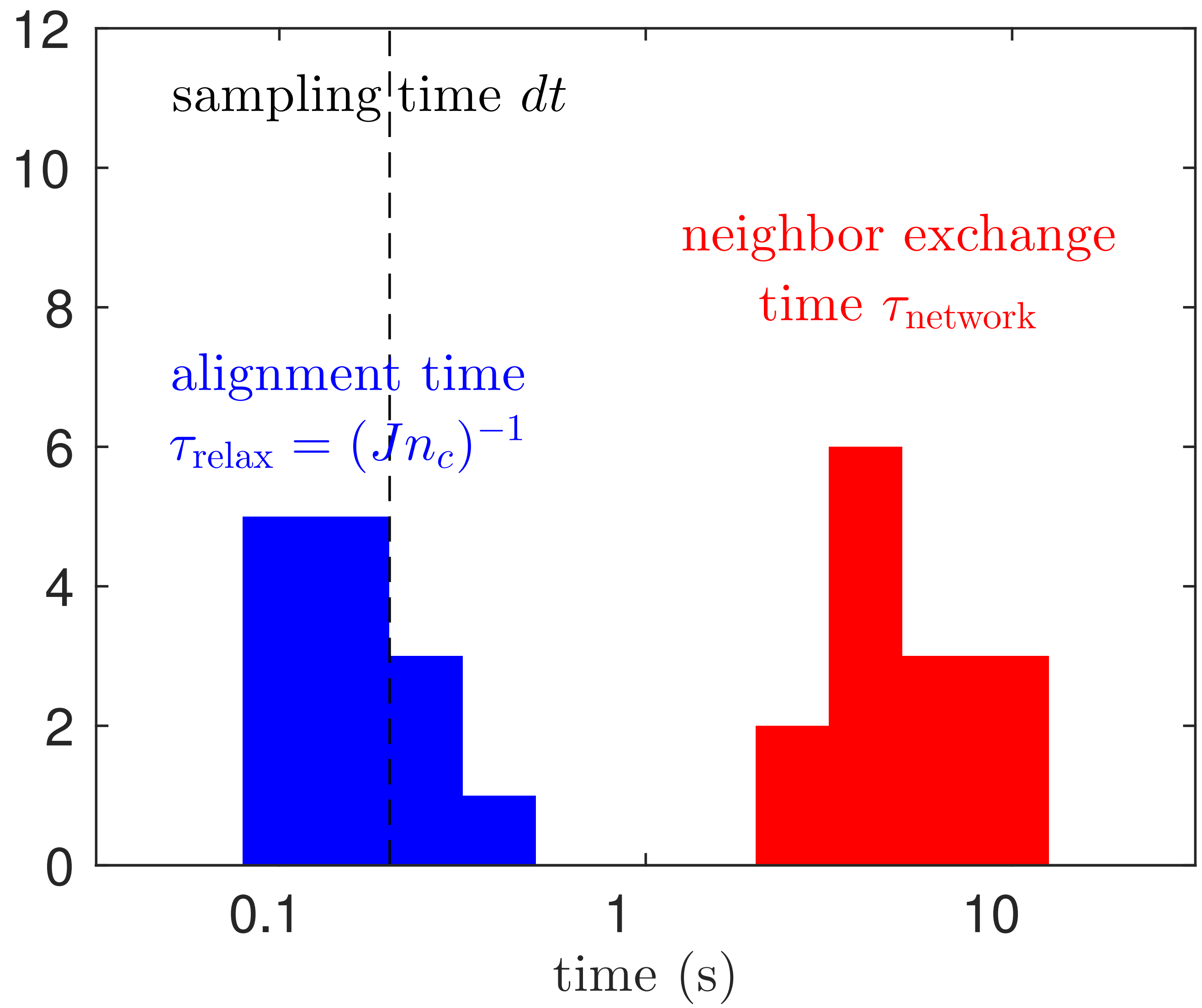
read off directly from data

Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

a tale of two time scales

τ_{relax} how fast birds align with their local neighbourhood

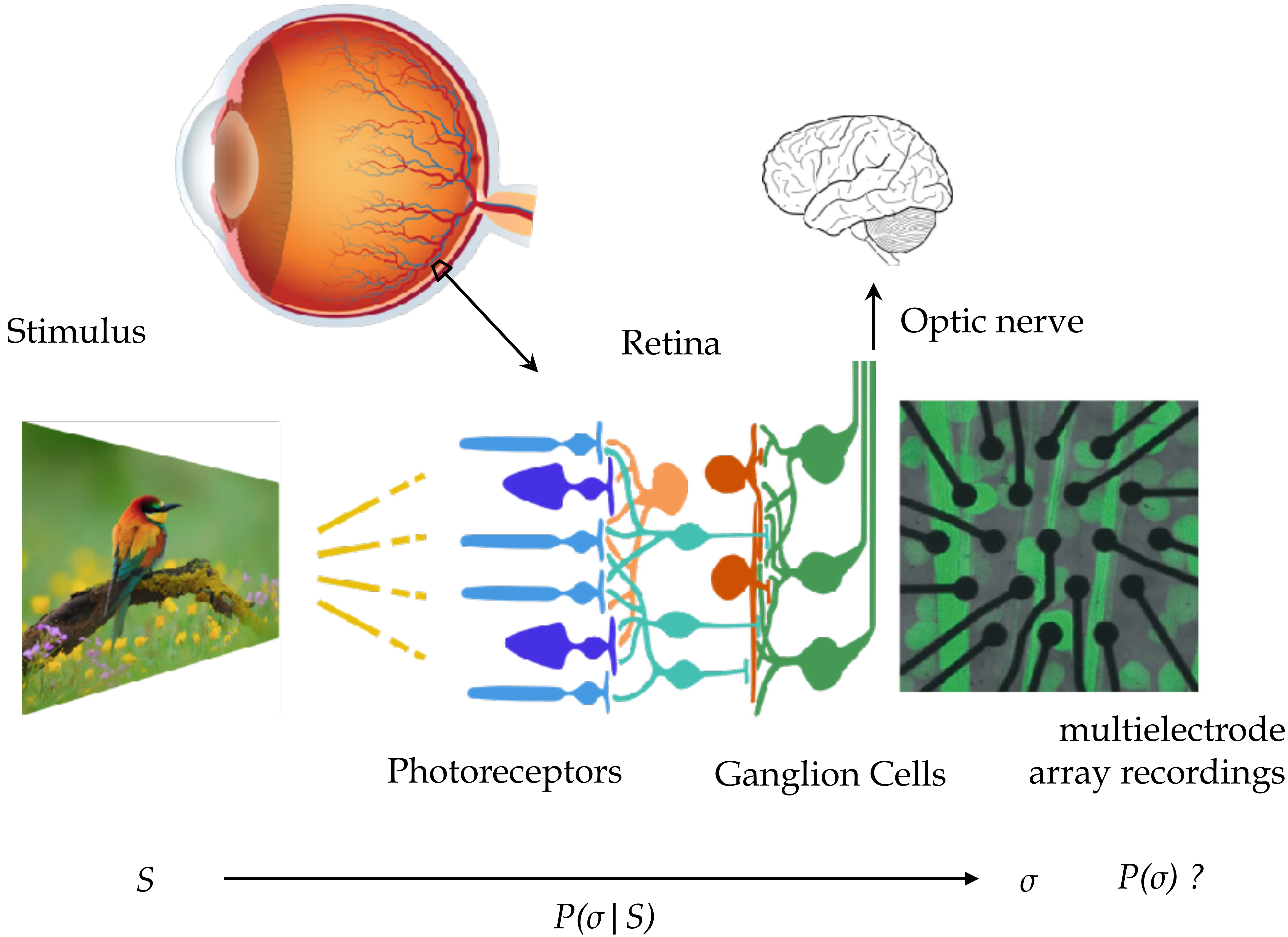
τ_{network} how fast each bird renews its neighbours



$\tau_{\text{relax}} \ll \tau_{\text{network}}$ **quasi equilibrium** — network evolves adiabatically

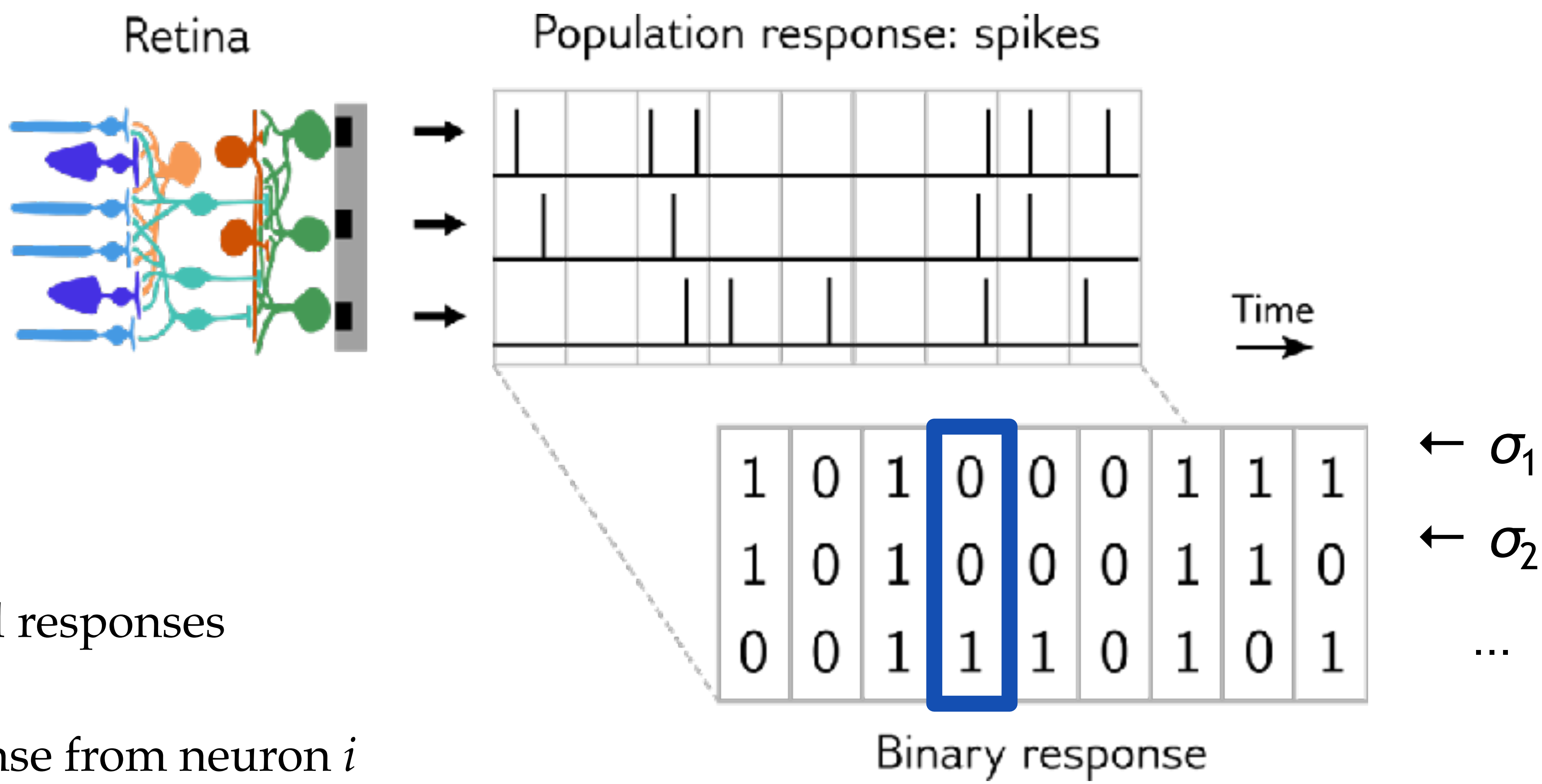
Mora Walczak Del Castello Ginelli Melillo Parisi Viale Cavagna Giardina, Nature Physics 2016

the retina



Stimulus
Retina
Optic nerve
Photoreceptors
Ganglion Cells
multielectrode
array recordings
S
$P(\sigma | S)$
σ
$P(\sigma)$?

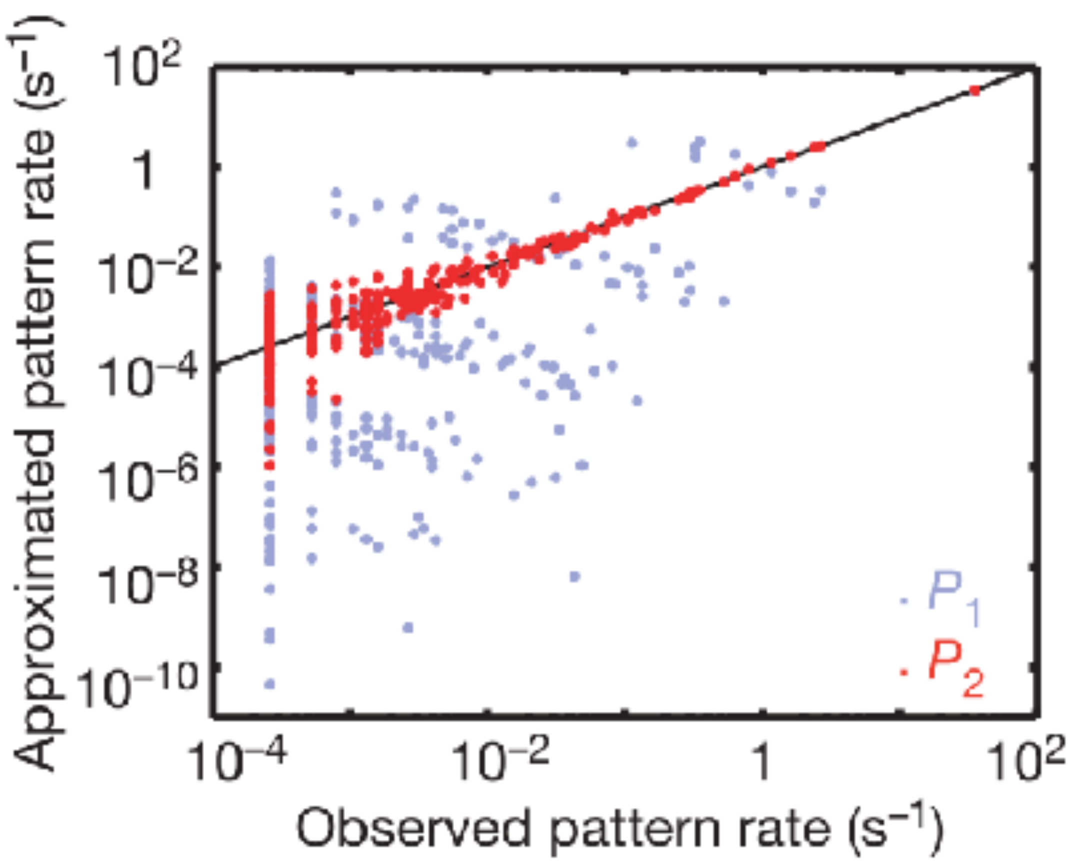
describing the response



- Binarized responses
- σ_i response from neuron i
- σ population response, single time bin
- $P(\sigma)$? 2^N states

neuron activities are correlated

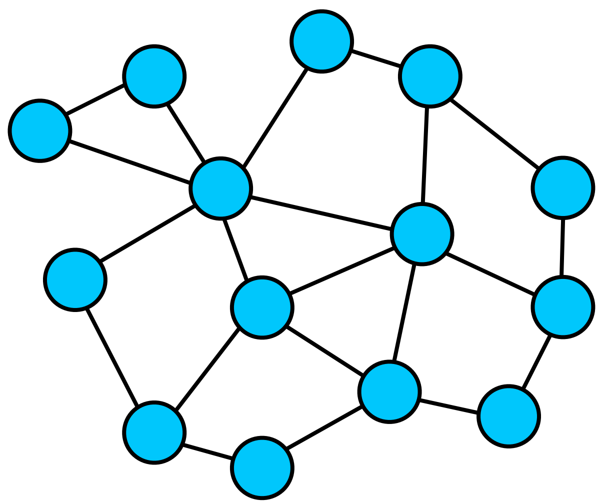
Schneidman et al, Nature 2005



independent $P_1(\boldsymbol{\sigma}) = \frac{1}{Z} e^{\sum_i h_i \sigma_i}$

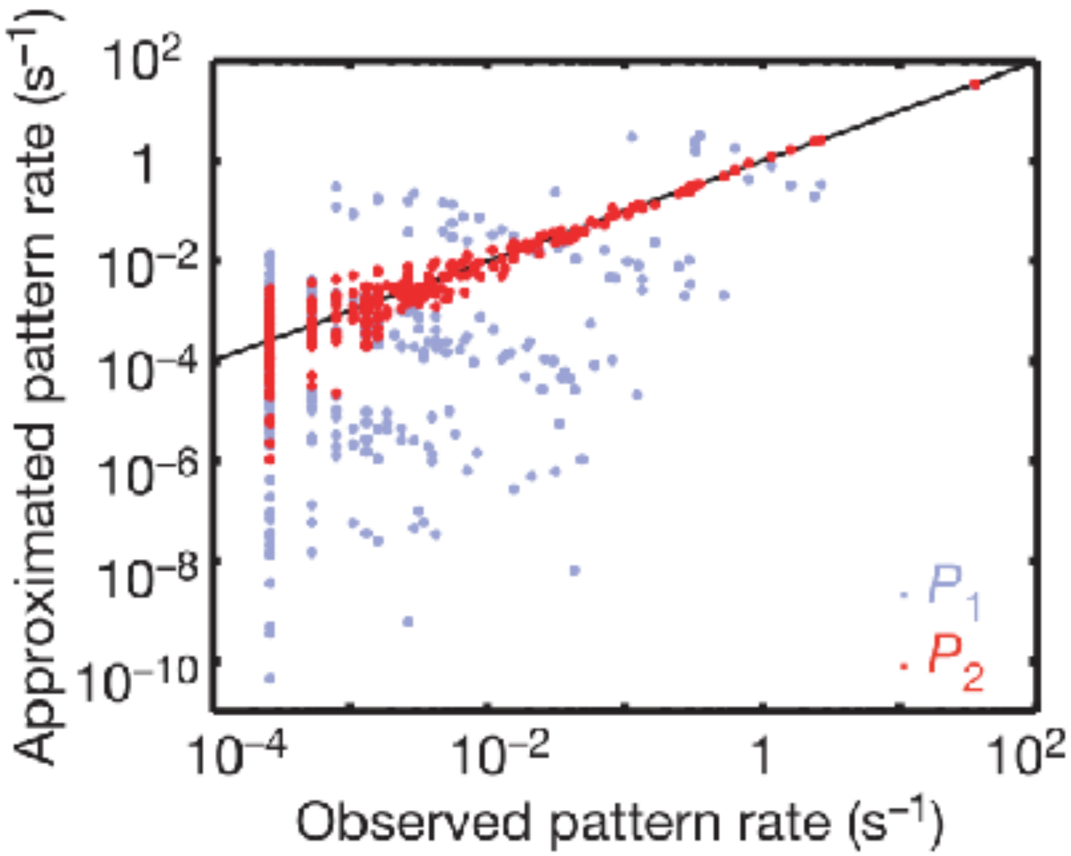
Ising model $P_2(\boldsymbol{\sigma}) = \frac{1}{Z} e^{\sum_i h_i \sigma_i + \sum_{ij} J_{ij} \sigma_i \sigma_j}$

Maximum Entropy constrained by $\langle \sigma_i \rangle$ $\langle \sigma_i \sigma_j \rangle$



neuron activities are correlated

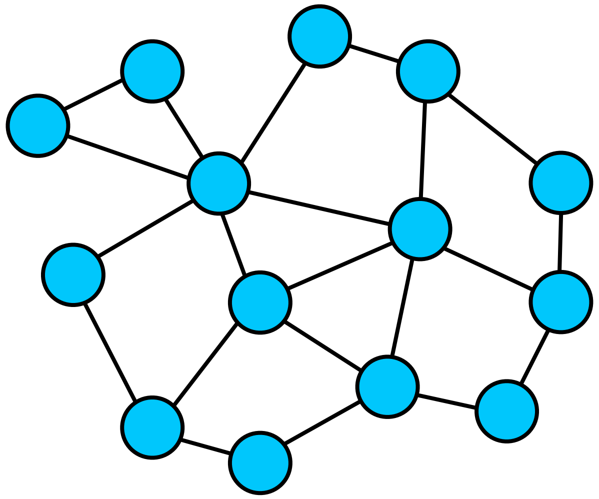
Schneidman et al, Nature 2005



independent $P_1(\boldsymbol{\sigma}) = \frac{1}{Z} e^{\sum_i h_i \sigma_i}$

Ising model $P_2(\boldsymbol{\sigma}) = \frac{1}{Z} e^{\sum_i h_i \sigma_i + \sum_{ij} J_{ij} \sigma_i \sigma_j}$

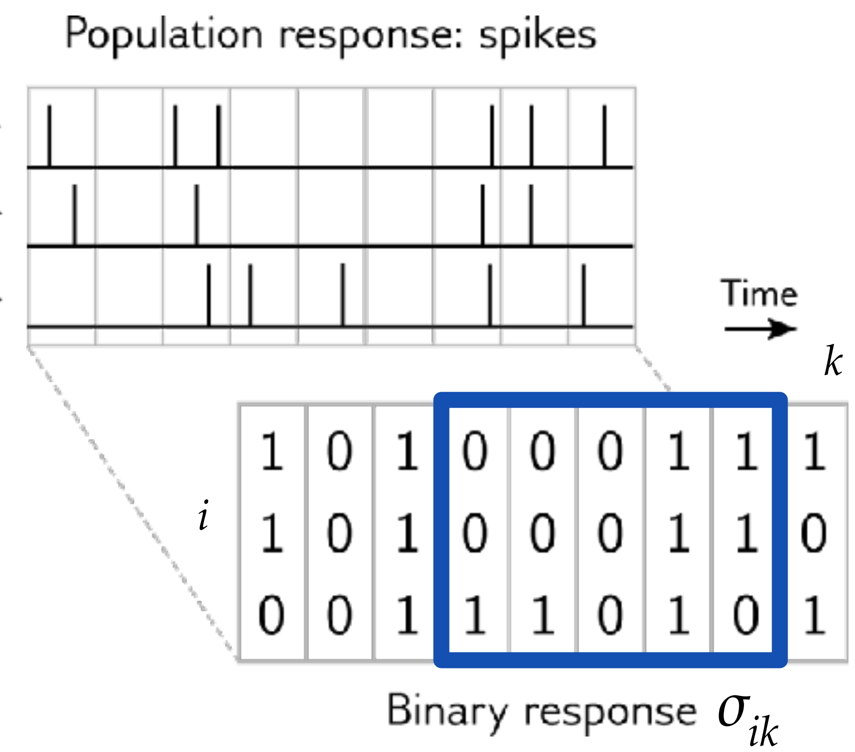
Maximum Entropy constrained by $\langle \sigma_i \rangle$ $\langle \sigma_i \sigma_j \rangle$



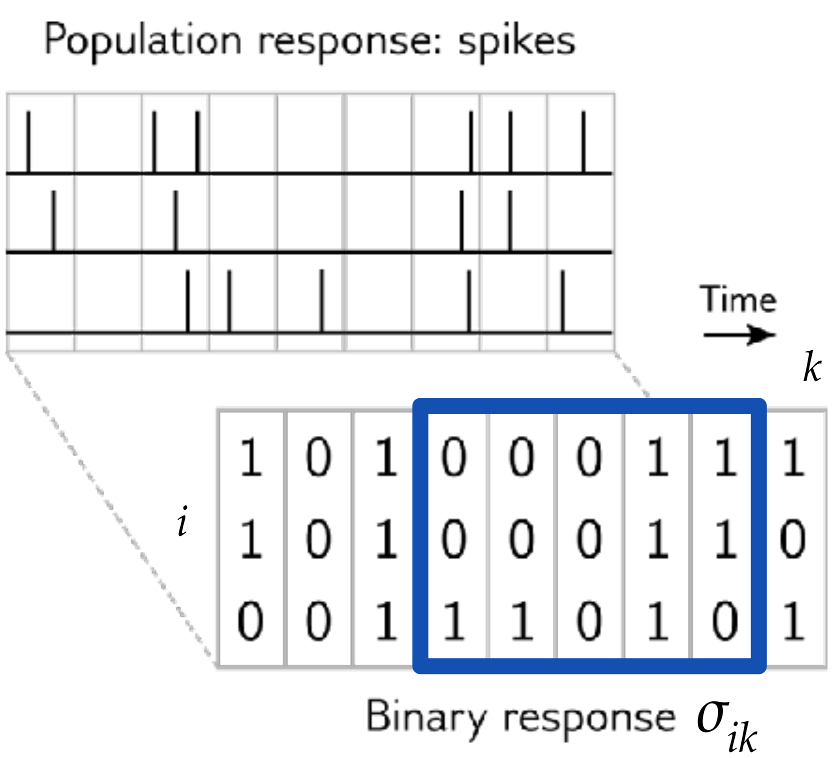
but Ising models

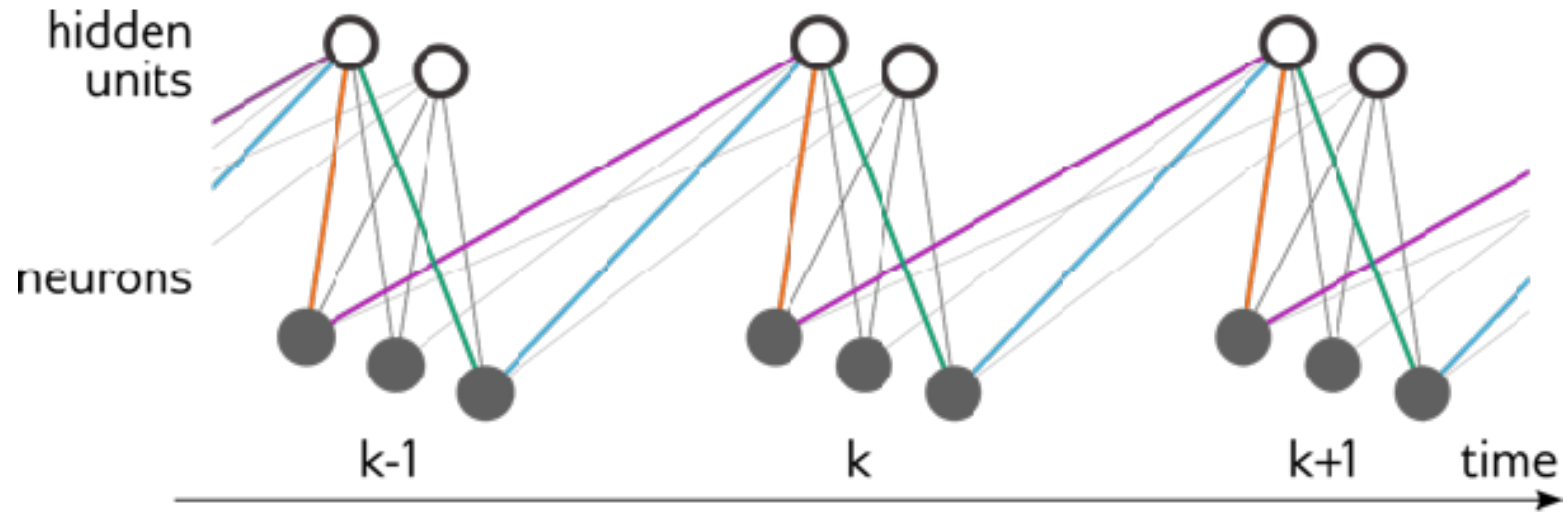
- are hard to fit
- don't describe higher-order correlations well
- ignore temporal correlations

Temporal Restricted Boltzmann Machine (TRBM)



Temporal Restricted Boltzmann Machine (TRBM)





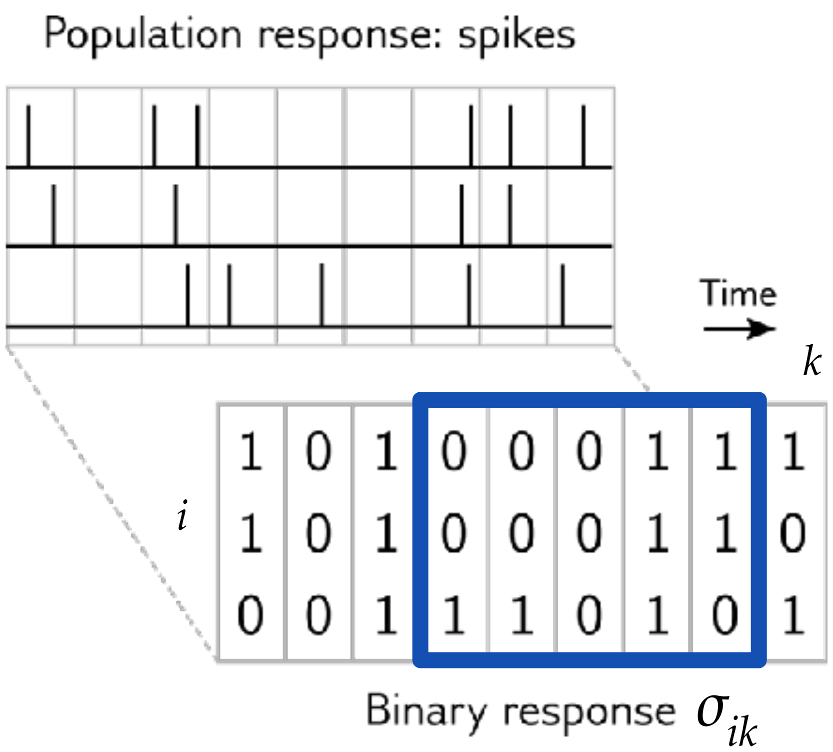
$$P[(\sigma_{it})] = \frac{1}{Z} \sum_{(h_{jt'})} \exp\left(\sum_{it} a_i \sigma_{it} + \sum_{jt'} b_j h_{jt'} + \sum_{ijtt'} W_{ji,t'-t} \sigma_{it} h_{jt'} \right)$$

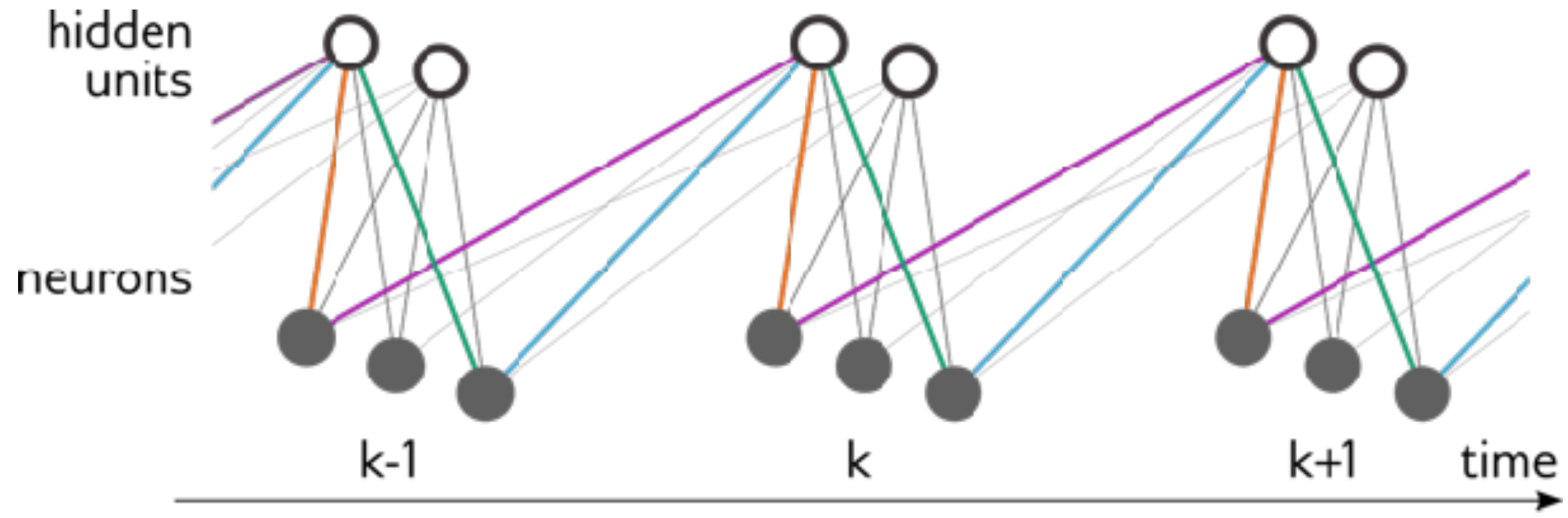
Neuron firing rate

Hidden unit firing rate

Coupling

Temporal Restricted Boltzmann Machine (TRBM)



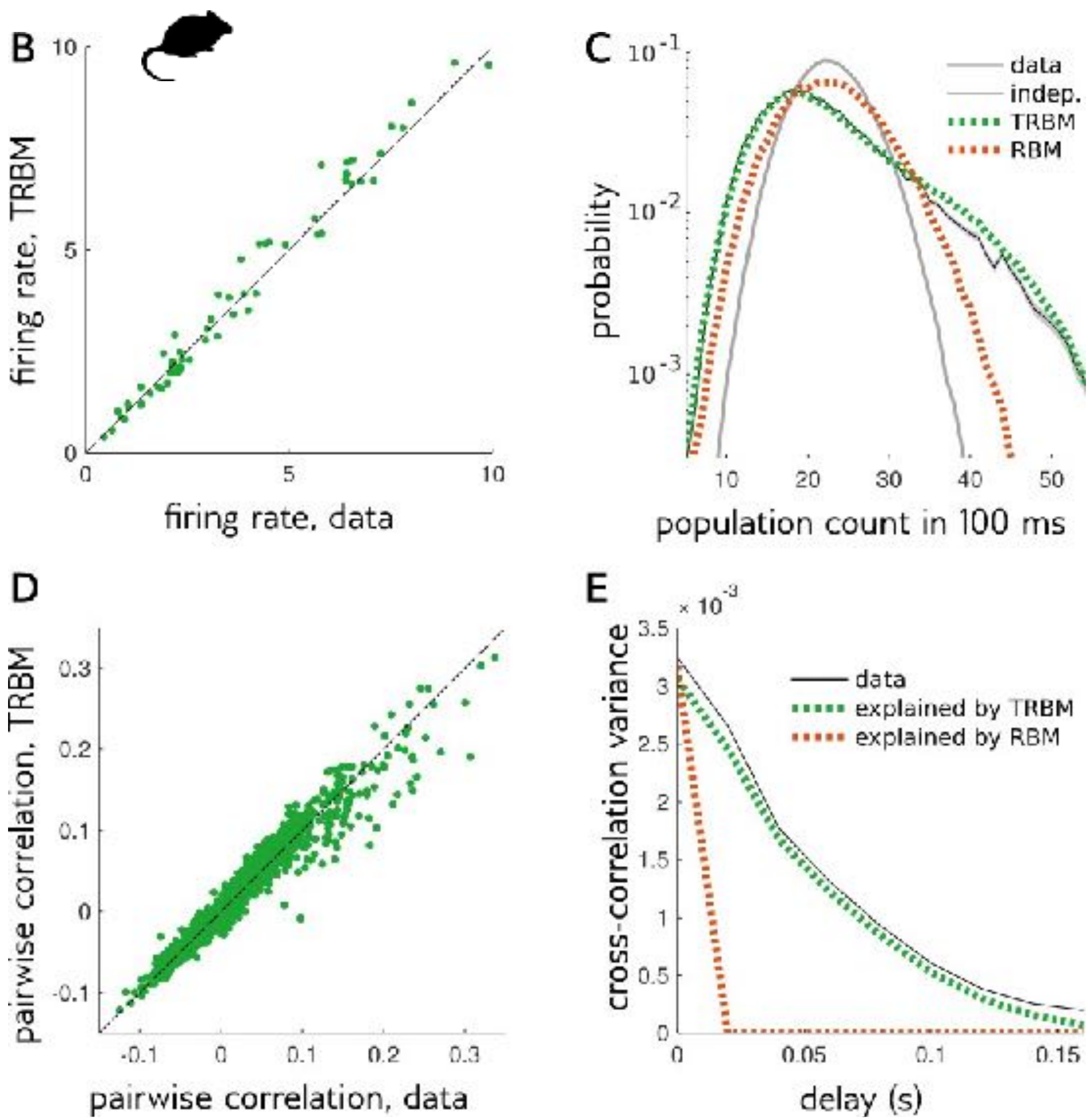


$$P[(\sigma_{it})] = \frac{1}{Z} \sum_{(h_{jt'})} \exp\left(\sum_{it} a_i \sigma_{it} + \sum_{jt'} b_j h_{jt'} + \sum_{ijtt'} W_{ji,t'-t} \sigma_{it} h_{jt'} \right)$$

Neuron firing rate — Hidden unit firing rate — Coupling

- spatial-**temporal, high-order** correlations
- easy to **sample** (block sampling)
- easy to **fit** (contrastive divergence)

performance on rat retina

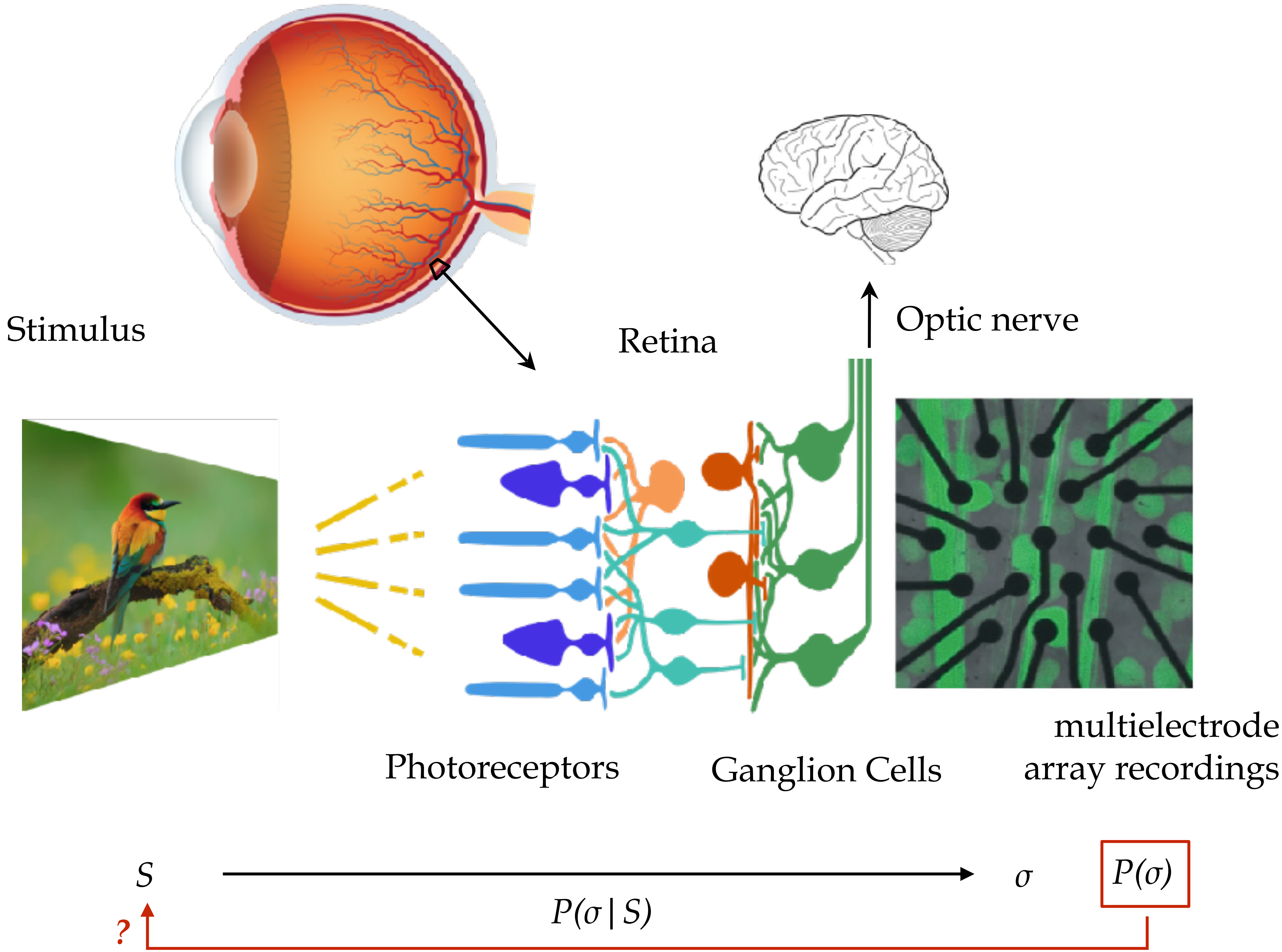


60 neurons, rat retina
10 hidden units per cell
stimulus: random bar

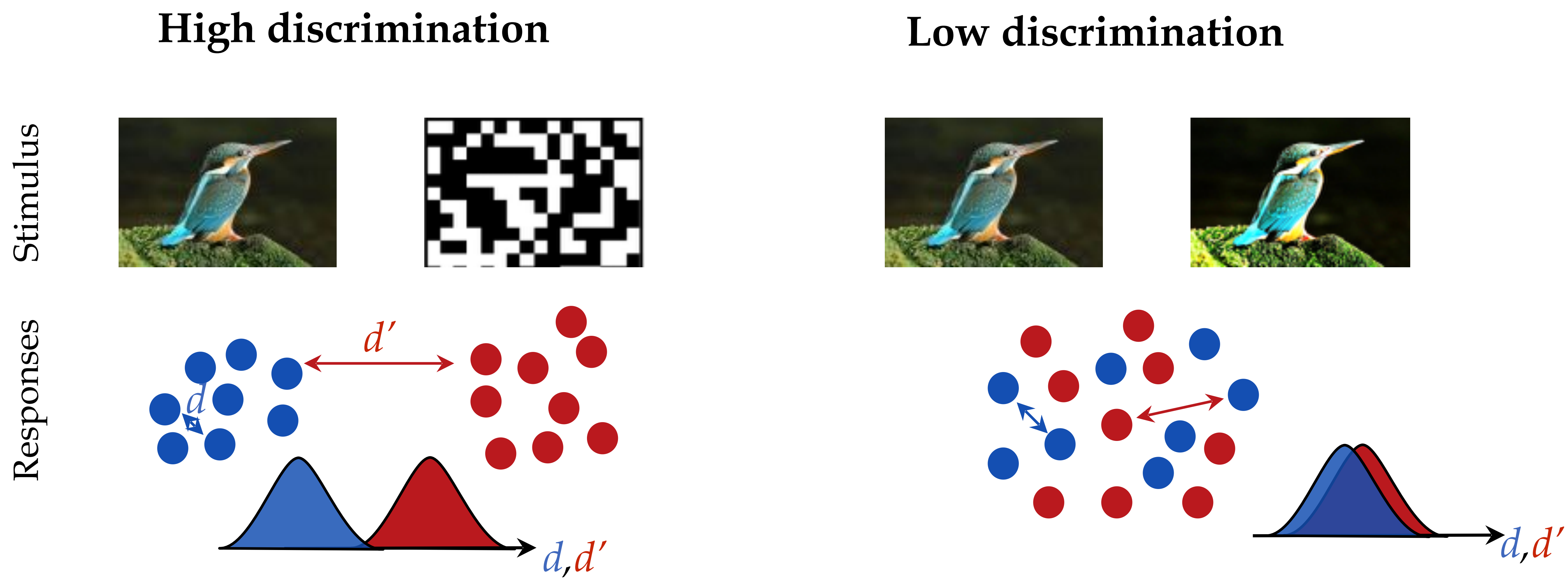
Population count:
number of spikes
in the population

Explained variance
of pairwise
correlations

back to stimulus

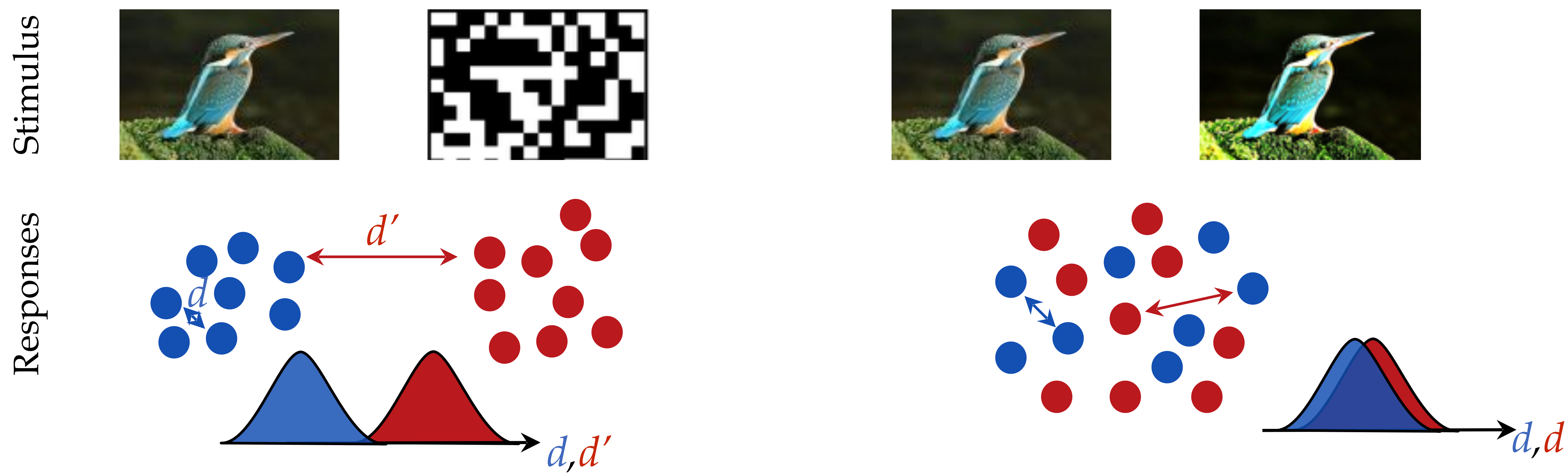


metric and discrimination



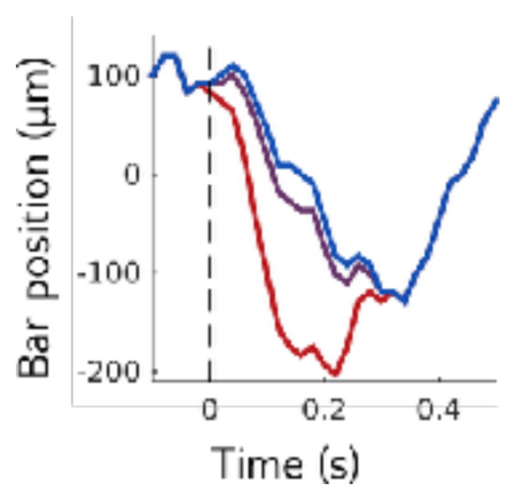
metric and discrimination

High discrimination **Low discrimination**



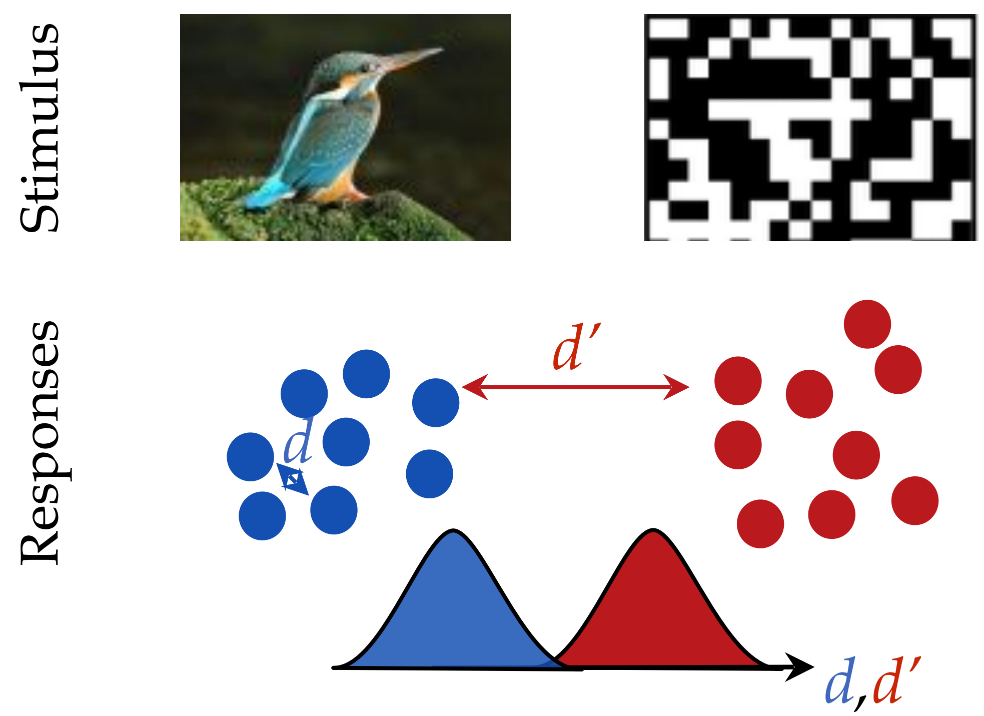
Perturbative approach

Stimulus: bar in motion, reference + perturbations

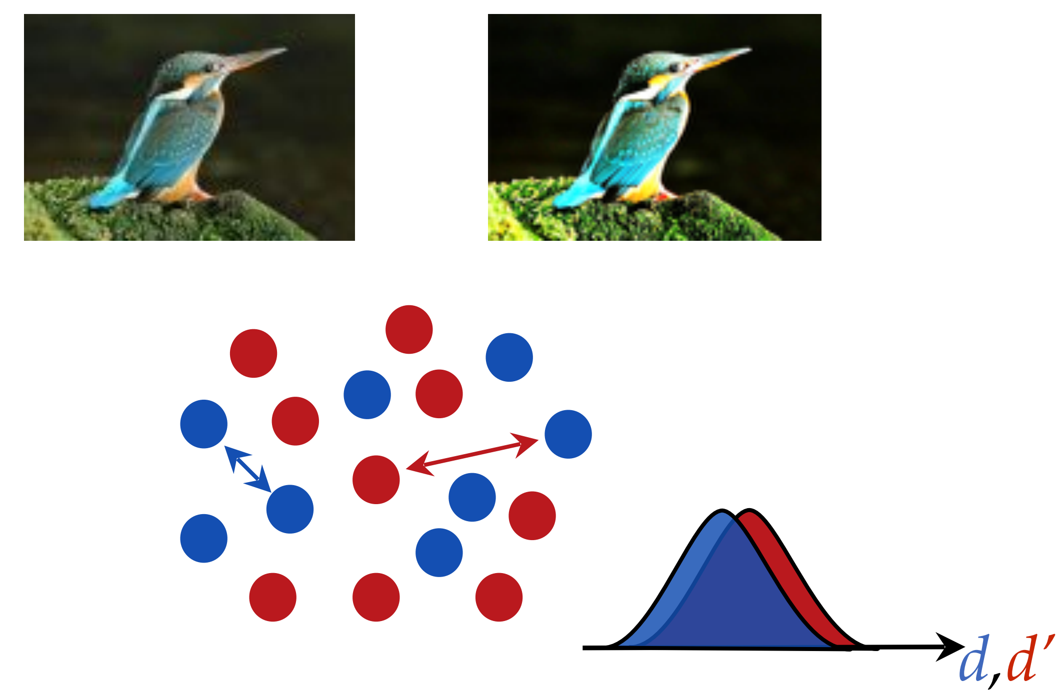


metric and discrimination

High discrimination

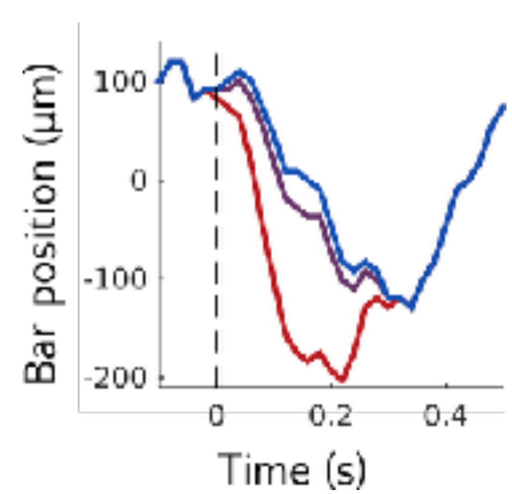


Low discrimination

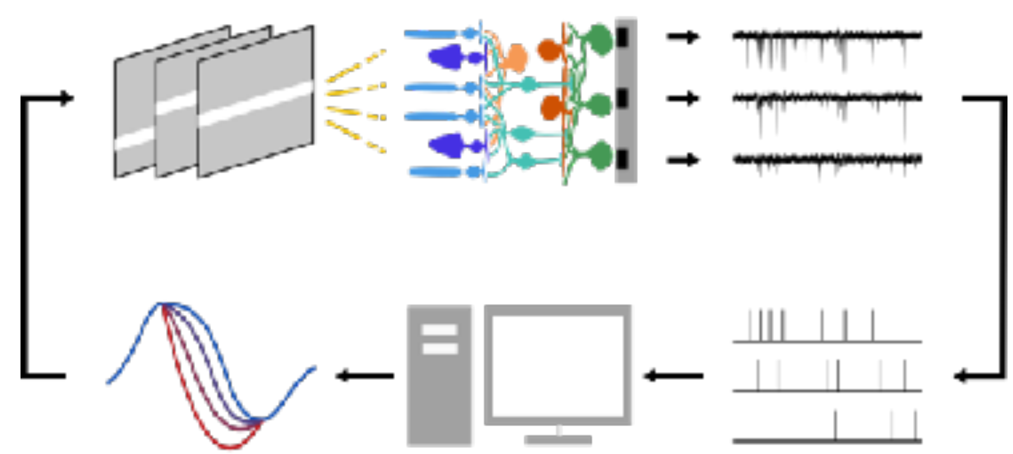


Perturbative approach

Stimulus: bar in motion, reference + perturbations



Online adaptation of perturbations



TRBM metric

- metric defined on hidden variables (modulated by how they impact cells)

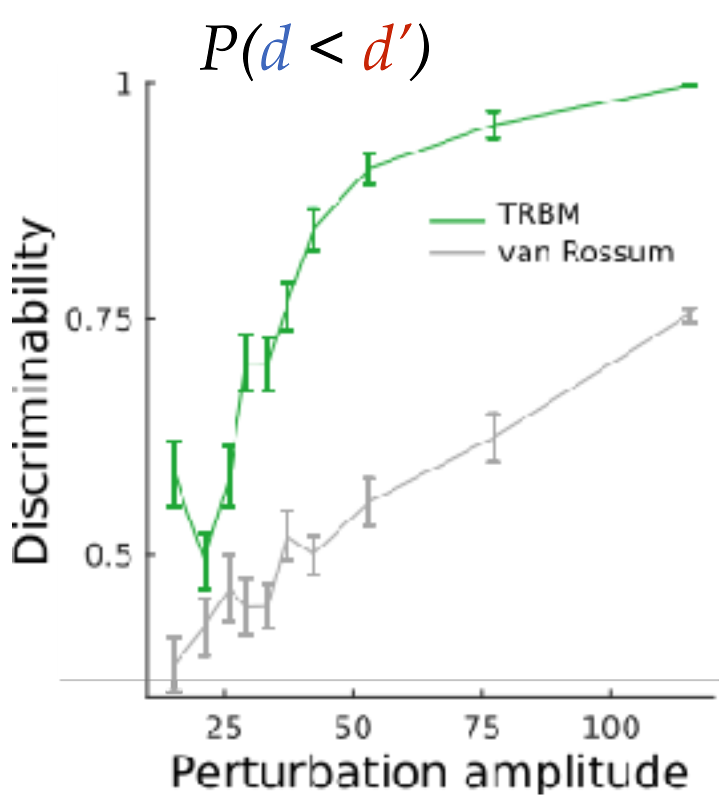
$$d(\sigma^1, \sigma^2)^2 = \mathrm{var}_\sigma\left[\ \left(\langle h|\sigma^1\rangle - \langle h|\sigma^2\rangle\right)^\mathsf{T} w\sigma\ \right]$$

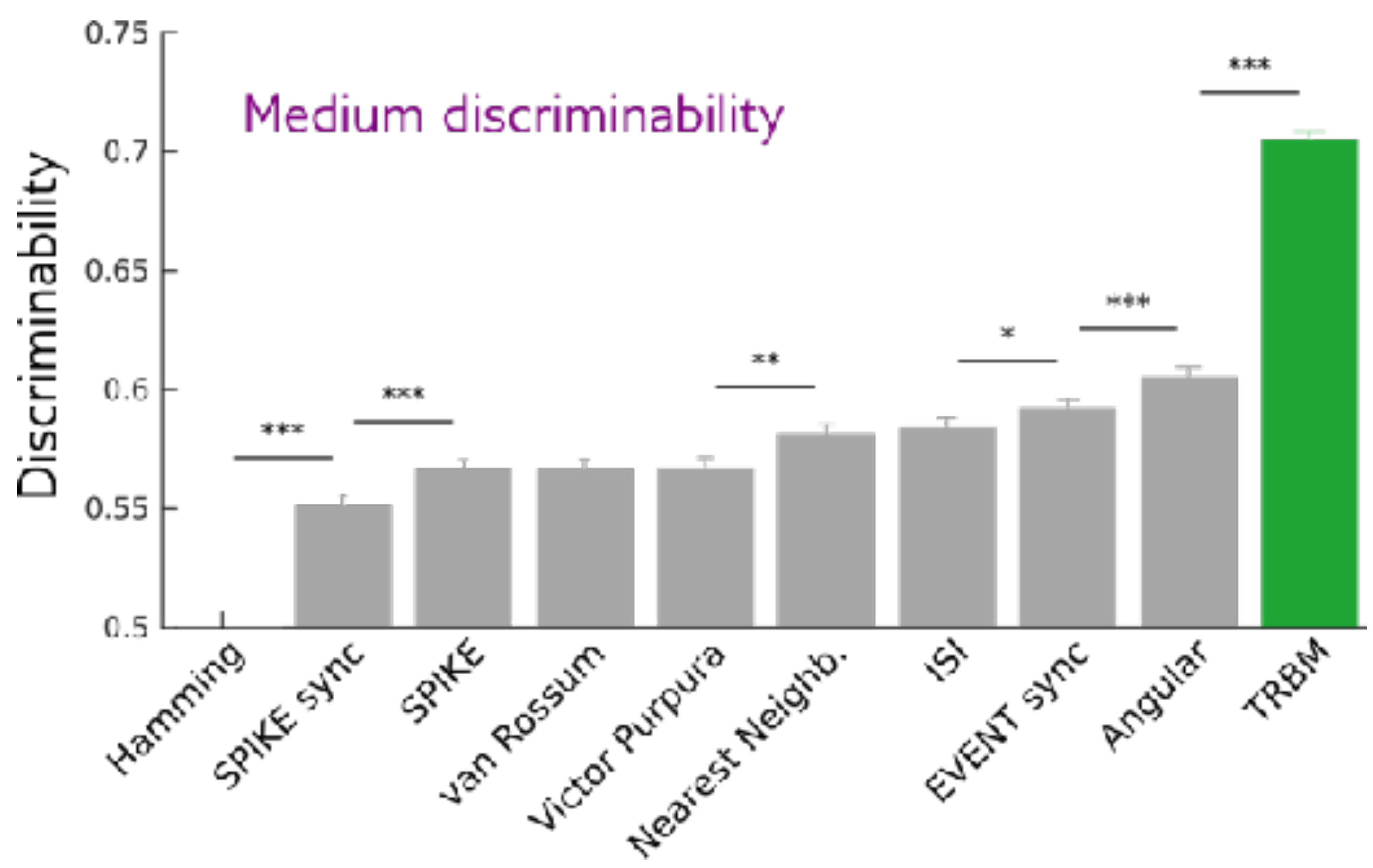
TRBM metric

- metric defined on hidden variables (modulated by how they impact cells)

$$d(\sigma^1,\sigma^2)^2 = \mathrm{var}_\sigma\left[\,\left(\langle h|\sigma^1\rangle - \langle h|\sigma^2\rangle\right)^\intercal w\sigma\,\right]$$

- outperforms all existing metrics



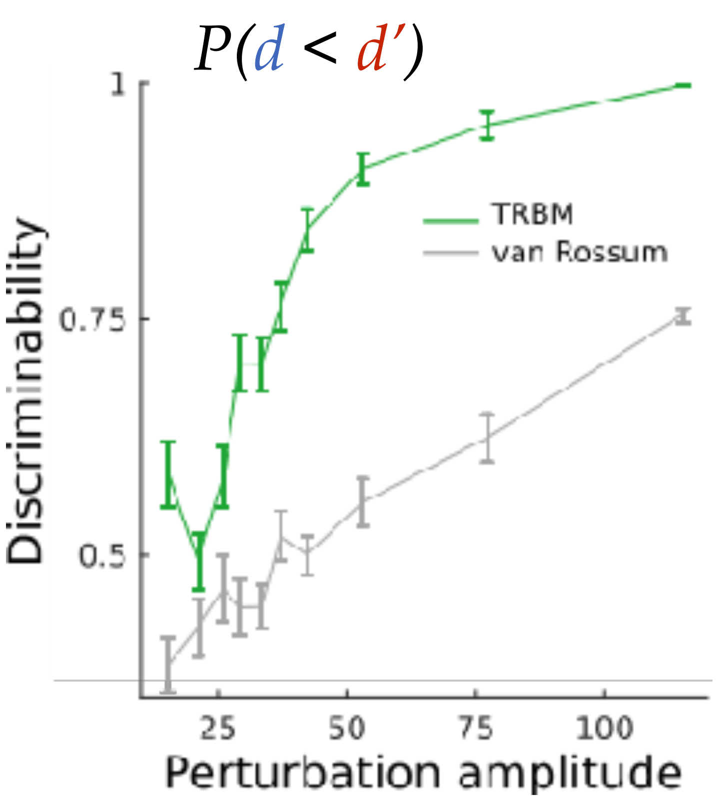


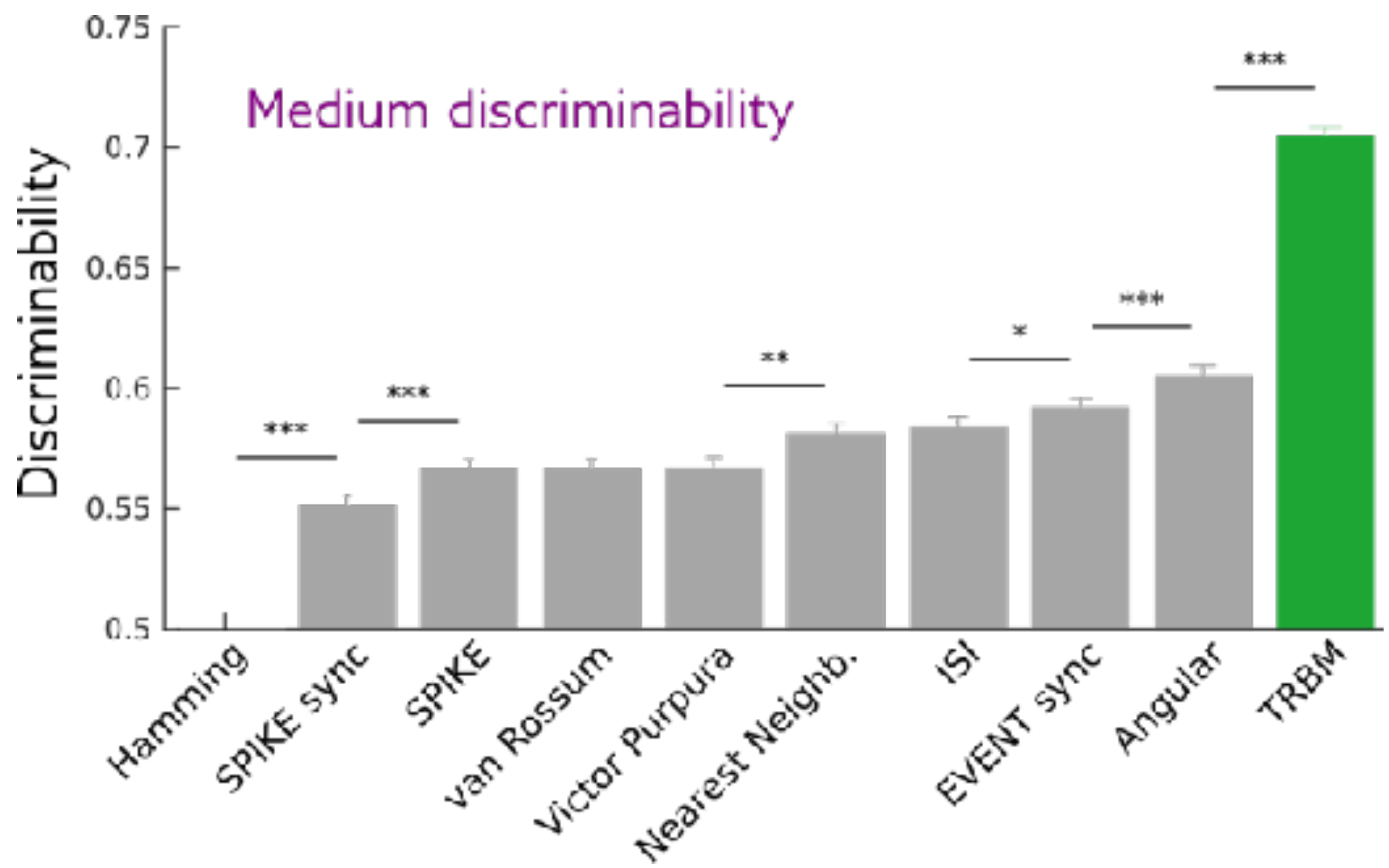
TRBM metric

- metric defined on hidden variables (modulated by how they impact cells)

$$d(\sigma^1, \sigma^2)^2 = \mathrm{var}_\sigma\left[\ \left(\langle h|\sigma^1\rangle - \langle h|\sigma^2\rangle\right)^\intercal w\sigma\ \right]$$

- outperforms all existing metrics





- unsupervised = no adjustable parameter

learning without supervision

- supervised learning

$$S \longrightarrow \sigma$$

$$P(\sigma \mid S)$$

learning without supervision

- supervised learning

learning without supervision

- supervised learning

S → σ

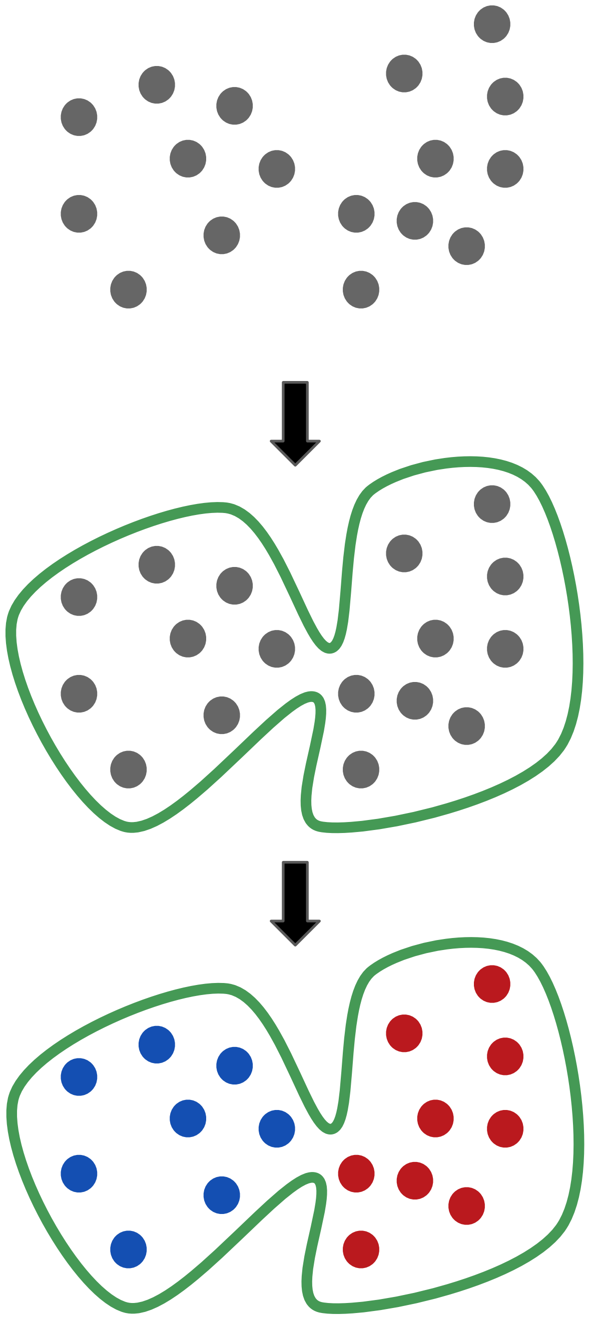
$P(\sigma \mid S)$

- unsupervised learning

Responses to
unknown stimuli
$P(\sigma)$

Model response
distribution

Discriminate responses to
different stimuli

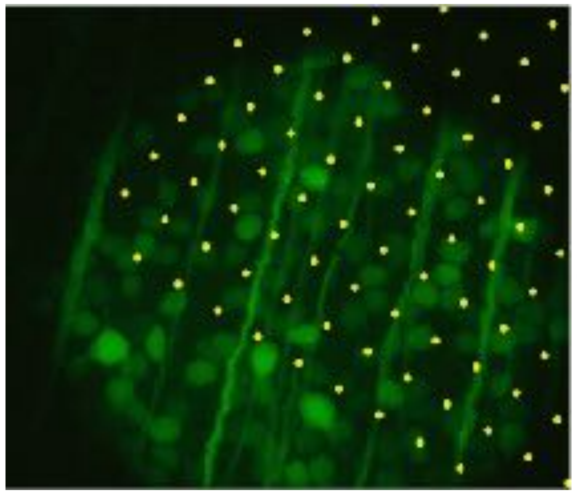


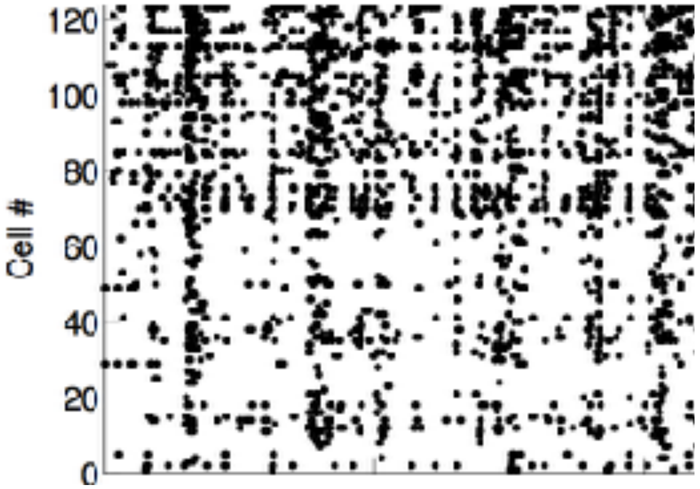
conclusions

- **statistical physics** to study **emergent behaviour** in biological systems

- in birds
  - **global** correlations from **local** interactions
  - interaction rule is **topological**, not metric
  - **critical** fluctuations of velocity
  - **local equilibrium**

- in neurons
  - **hidden-variable** spin model of correlated population activity
  - derived **metric** outperforms others despite being **unsupervised**





- application to other biological networks?