The Kavli Institute for Systems Neuroscience

Centre for the biology of memory

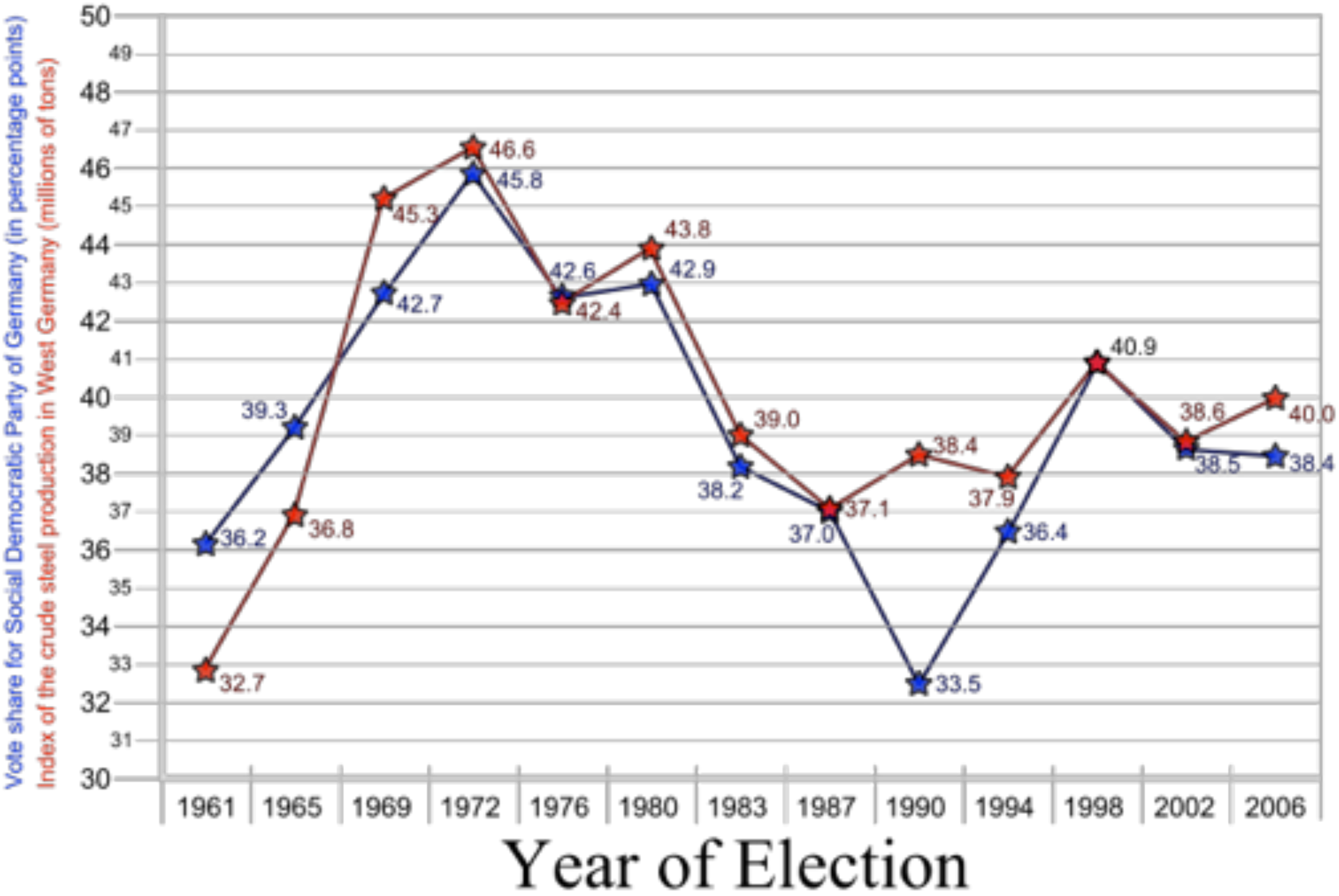
NORDITA
Nordic Institute
for Theoretical Physics

Mean Field Theory for Non-equilibrium Network Reconstruction

Yasser Roudi

Kavli Institute for Systems Neuroscience, Trondheim
NORDITA, Stockholm

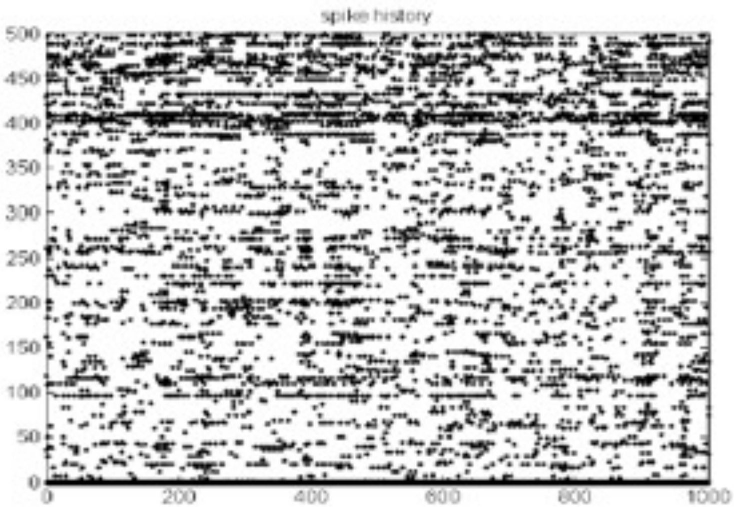
correlation is not connection

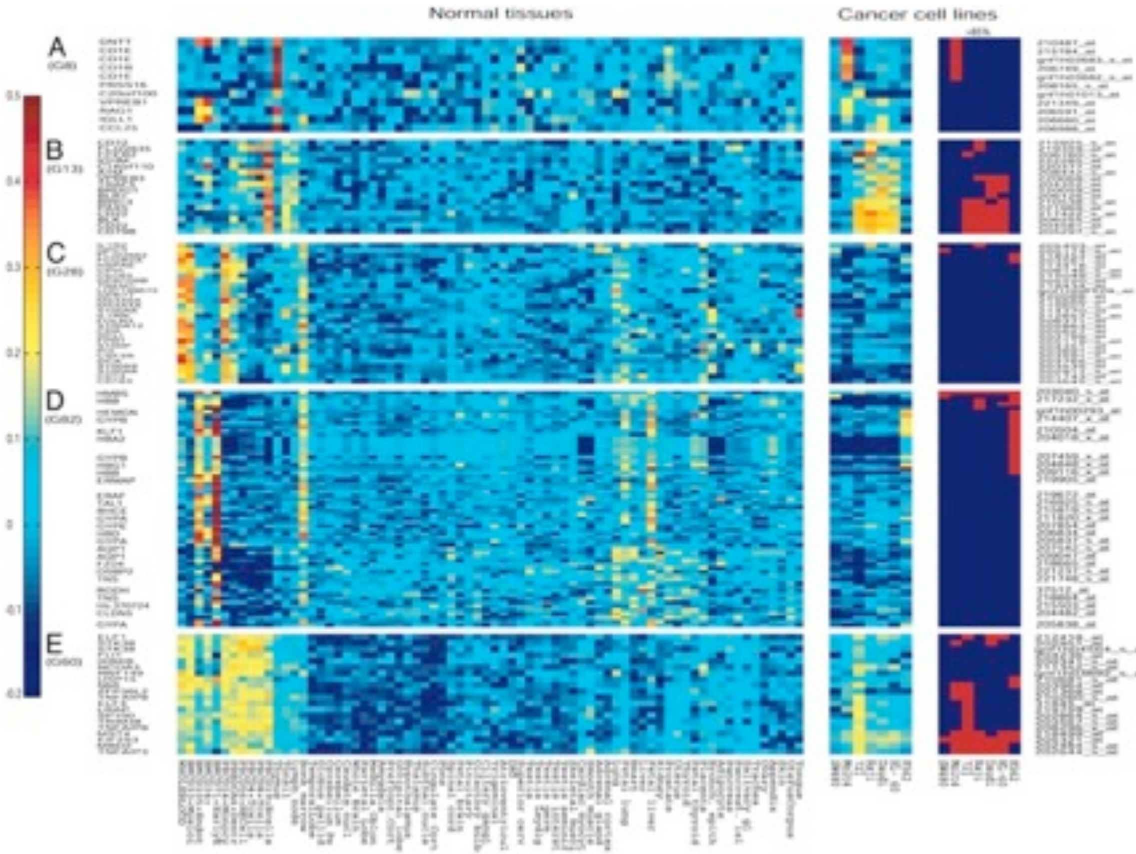


Mierscheid Law

J. M. Mierscheid (1983)

The vote share of the German Social Democratic Party (SPD) equals the index of the crude steel production in the Western federal states (source: Wikipedia)





- observing the covariation of the activities cannot directly tell us about the network connectivity.

can we use this type of data to infer connections?

outline

- A simple model, equilibrium inverse Ising problem, and its shortcomings.
- Fitting the kinetic Ising model.
- Mean-Field and TAP approximations for the kinetic model and quantifying their errors.
- On real data.

equilibrium inverse Ising problem

$$m_i = \langle s_i \rangle$$

$$C_{ij} = \langle s_i s_j \rangle - \langle s_i \rangle \langle s_j \rangle$$

find h_i and J_{ij} of

$$\Pr(s_1, \ldots, s_N) = \frac{1}{Z} \exp\left[\sum_i h_i s_i + \sum_{i<j} J_{ij} s_i s_j\right]$$

Boltzmann Machine

- how to find h_i, J_{ij} for large N?

Exact method: Boltzmann learning

$$\delta J_{ij} = \eta \left[\langle S_i S_j \rangle_{data} - \langle S_i S_j \rangle_{current\, J,h} \right]$$

$$\delta h_i = \eta \left[\langle S_i \rangle_{data} - \langle S_i \rangle_{current\, J,h} \right]$$

Ackley, Hinton, Sejnowski 85

requires long Monte Carlo runs to compute model statistics

fast and reliable approximate methods exist

- independent-pairs

Roudi et al 09

- high absolute magnetization expansion

Roudi et al 09

$$m_i, m_j \to -1 \qquad J_{ij} = \frac{1}{4}\log\left[1 + \frac{C_{ij}}{(1+m_i)(1+m_j)}\right]$$

- nMFT

$$h_i = \tanh^{-1} m_i - \sum_j J_{ij} m_j \qquad C^{-1}_{ij} = \frac{\partial h_i}{\partial m_j} = \frac{\delta_{ij}}{1-m_i^2} - J_{ij}$$

- TAP

$$h_i = \tanh^{-1} m_i - \sum_j J_{ij} m_j + m_i \sum_j J_{ij}^2 (1 - m_j^2) \quad C^{-1}_{ij} = -J_{ij} - 2J_{ij}^2 m_i m_j$$

Kappen & Rodriguez 98, Tanaka 98

- Sessak-Monasson, BP, SusP

Sessak & Monasson 09   Mezard & Mora 09   Aurell, Olion & Roudi 10

binary representation of spike trains

- bin the spike train
- for each neuron i, if it

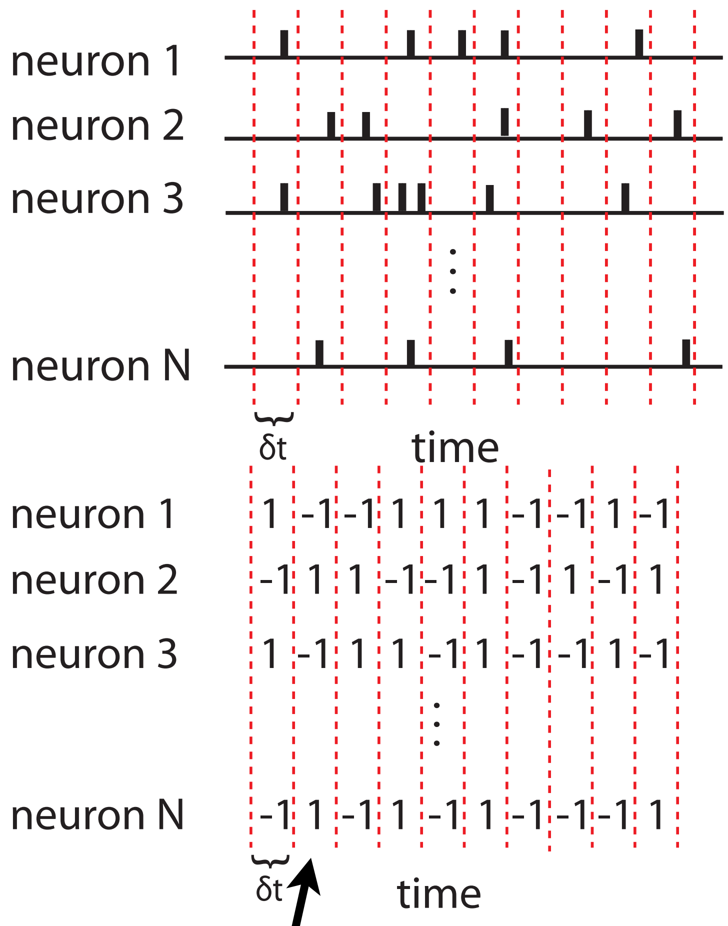
  spiked in bin t $\rightarrow s_i(t) = 1$

  did not spike in bin t $\rightarrow s_i(t) = -1$

- a binary representation of spike trains $S(t) = (s_1(t), s_2(t), \ldots, s_N(t))$
- compute experimental means and corr.

$$\langle s_i \rangle_{\mathrm{data}} = \frac{1}{T} \sum_t s_i(t)$$

$$\langle s_i s_j \rangle_{\mathrm{data}} = \frac{1}{T} \sum_t s_i(t) s_j(t)$$



$$S(t=2) = (1, -1, \ldots, -1)$$

fit the Ising distribution (find hs and Js)

$$\Pr_{\rm pair}(\mathbf{S}) = \frac{1}{Z_{\rm pair}} \exp\left[\sum_i h_i s_i + \sum_{i<j} J_{ij} s_i s_j\right]$$

such that

$$\langle s_i \rangle_{\rm pair} = \langle s_i \rangle_{\rm data}$$
$$\langle s_i s_j \rangle_{\rm pair} = \langle s_i s_j \rangle_{\rm data}$$

functional couplings

this yields the simplest probability model for the spike trains that

the maximum entropy distribution given means and correlations.

Schneidman et al Nature 05, Shlens et al J. Neurosci. 06

- how good are these approximations compared to the exact learning for neural data?

simplified model of circuitry in a small (~0.5 mm) region of neocortex

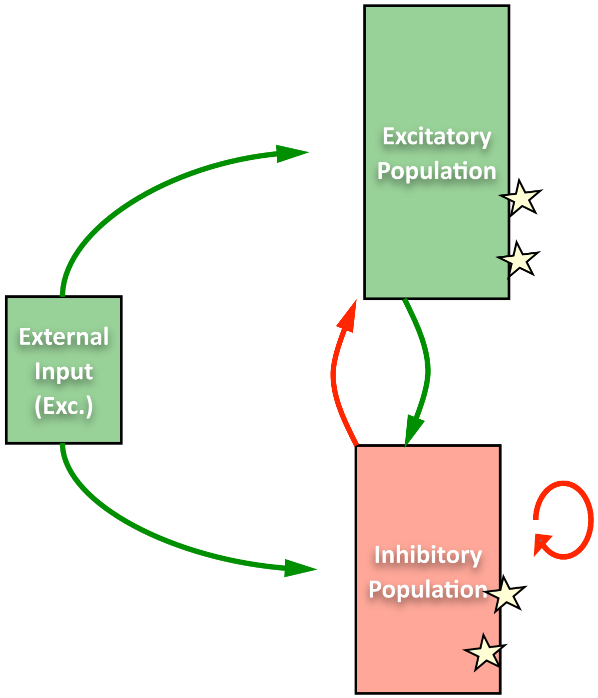
2 populations in network:
Excitatory, Inhibitory

Excitatory external drive (“rest of brain”)

realistic modeling: Hodgkin-Huxley-like neurons, conductance-based synapses

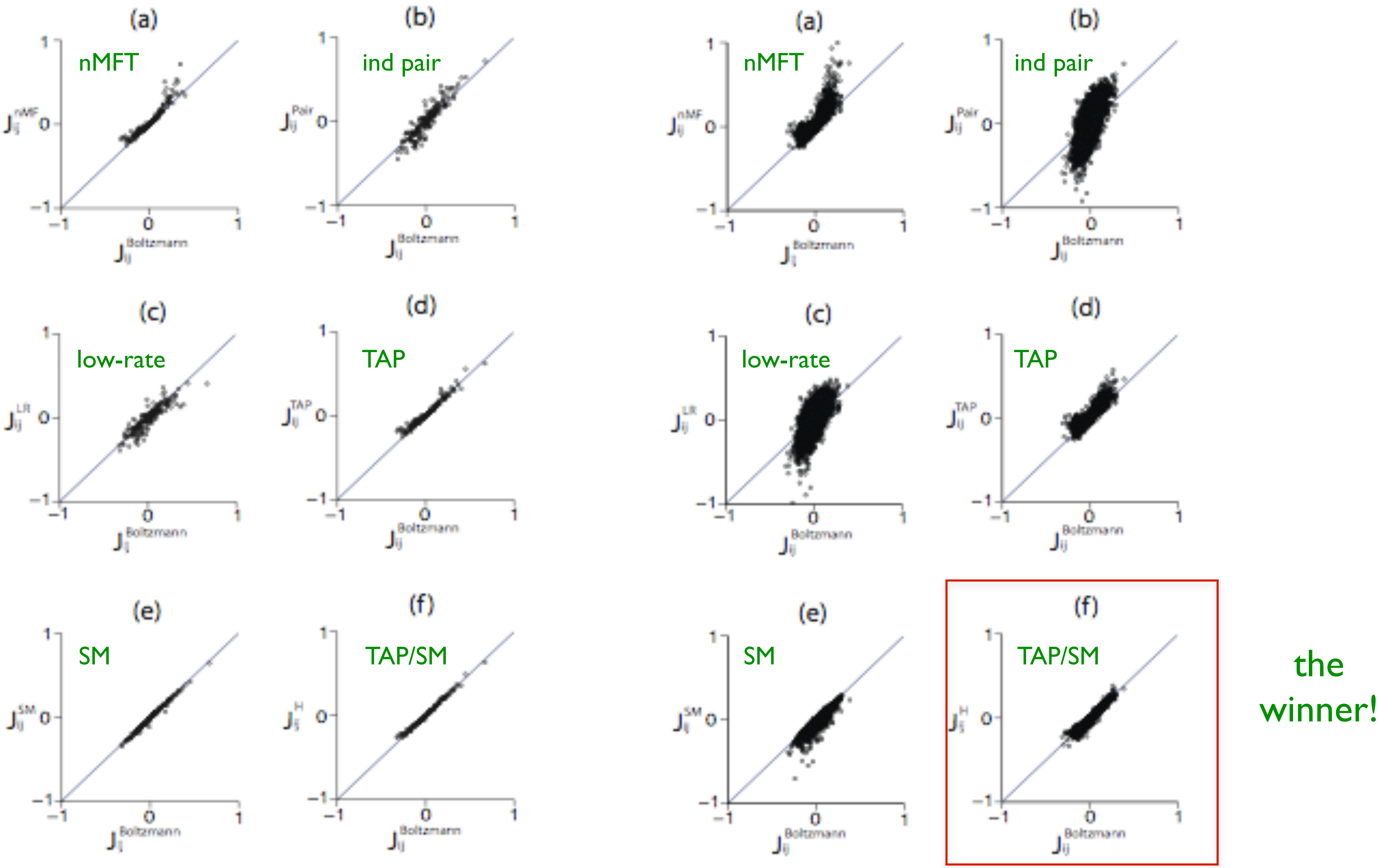
Random connectivity:
Probability of connection between any two neurons is $c = K/N$, where N is the size of the population and K is the average number of presynaptic neurons.

Results here for
$c = 0.1, N = 1000$

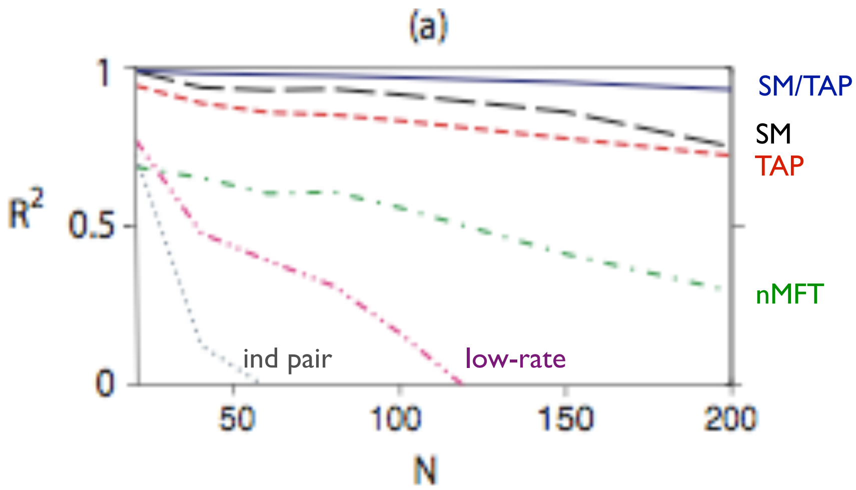


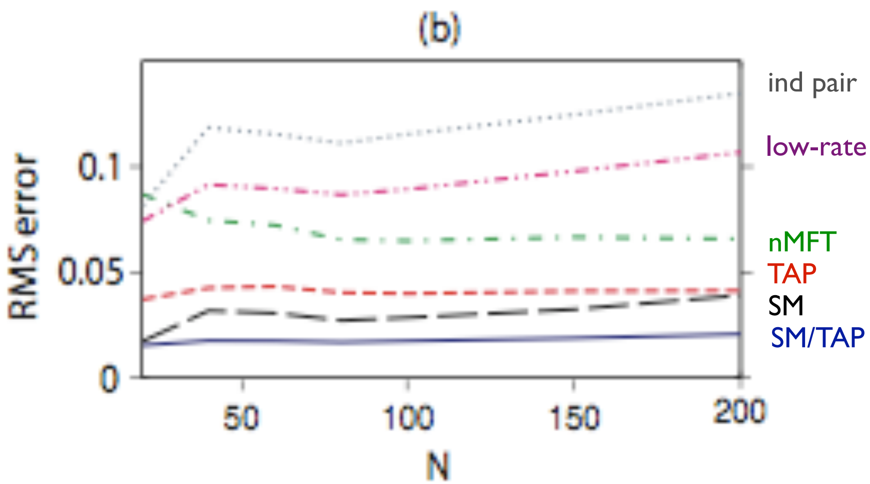
comparing the approximations

N=20 δt=10 ms N =200



N-dependence of error measures



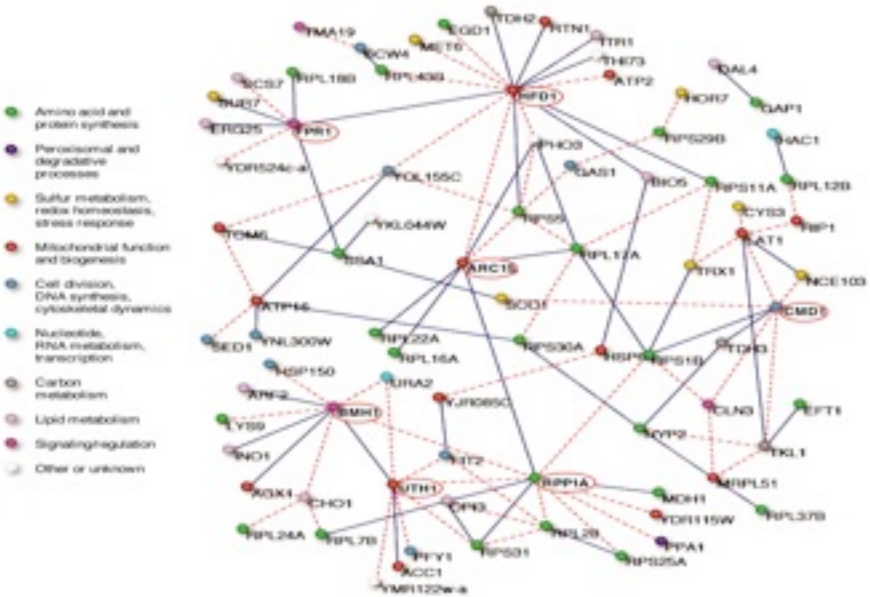


we have fast approximations that can work for large networks

but what can we learn from the inferred connections?

relation to real network connectivity

~ inferring gene regulatory network



Lazon et al 06

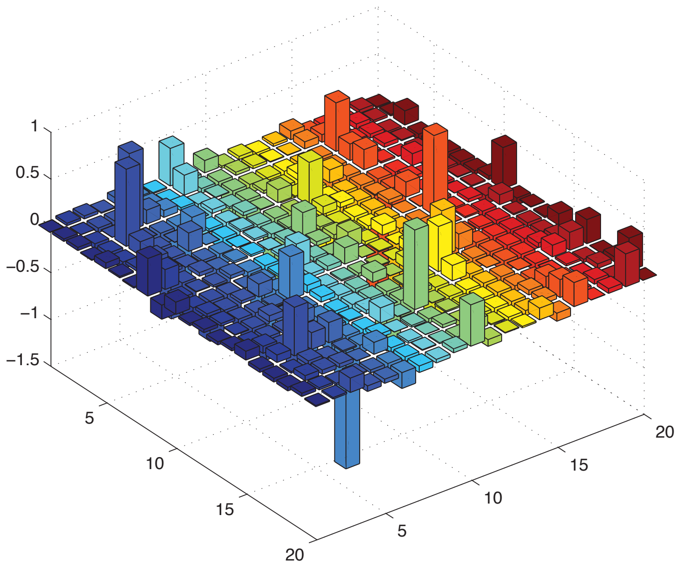
microarray expression data from *Saccharomyces cerevisiae*

~ Reconstructing protein complexes from co-evolution of contacting residues (#a.a. ~ 10^2; #data ~ 10^3-10^4)

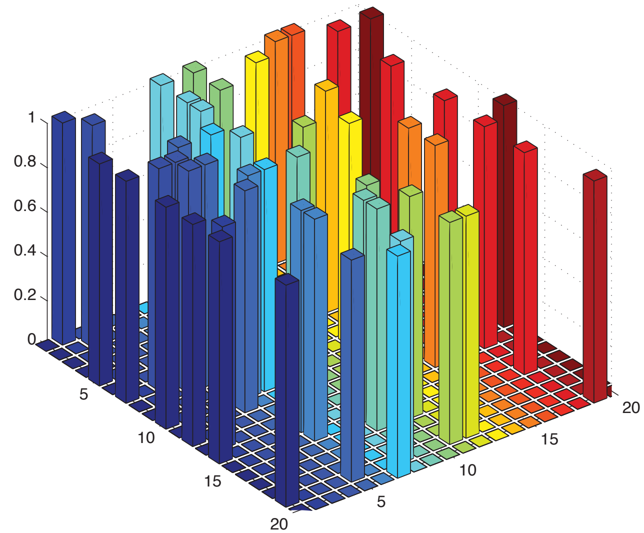
Weigt, White, Szurmant, Hoch, Hwa (PNAS 2009)

neural data

inferred



real



~ forcing the connections to be symmetric

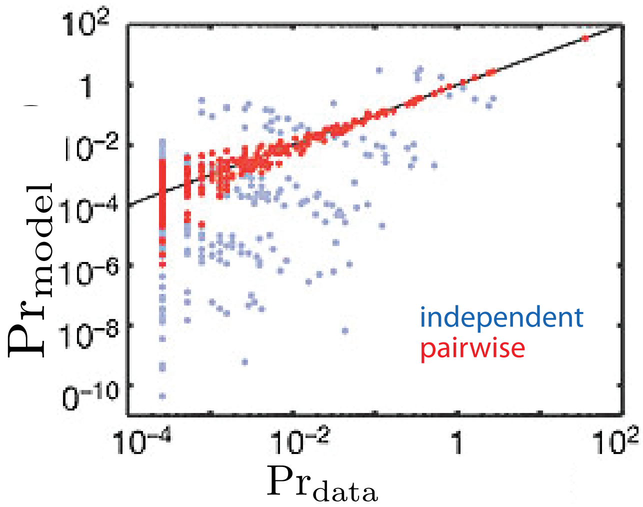
~ equilibrium vs non-equilibrium

- the equilibrium inverse Ising model is not a good model for inferring the connections

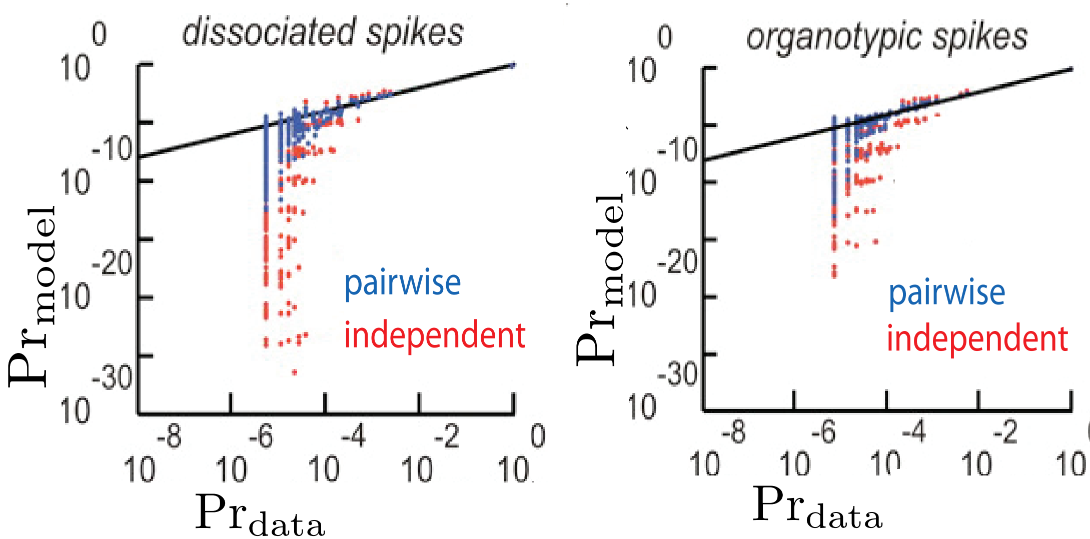
parentheses

- is it a good probability model?

qualitative picture



Schneidman et al, Nature 2006



Tang et al, J. Neuro. 2008

quantitative picture

- Compute $D_{KL}(Pr_{true}||Pr_{pair})$.
- Normalise it by $D_{KL}(Pr_{true}||Pr_{ind})$

$$\Pr_{\text{ind}}(\mathbf{S}) = \frac{1}{Z_{\text{ind}}} \exp\left[\sum_i b_i s_i\right] \qquad b_i = \tanh^{-1}(\langle s_i \rangle_{\text{data}})$$

- pairwise model quality

$$\Delta = \frac{D_{KL}(\Pr_{\text{data}}||\Pr_{\text{pair}})}{D_{KL}(\Pr_{\text{data}}||\Pr_{\text{ind}})} = \frac{\text{Entropy}_{\text{pair}} - \text{Entropy}_{\text{data}}}{\text{Entropy}_{\text{ind}} - \text{Entropy}_{\text{data}}}$$

Δ near zero ====> pairwise model is good

Δ near one ====> pairwise model is bad

- EXPERIMENTAL DATA: $\Delta \approx 0.01 - 0.1$

Schneidman et al, Nature 2006
Shlens et al, J. Neuro. 2006

Tang et al, J. Neuro. 2008
Shlens et al, J. Neuro. 2009

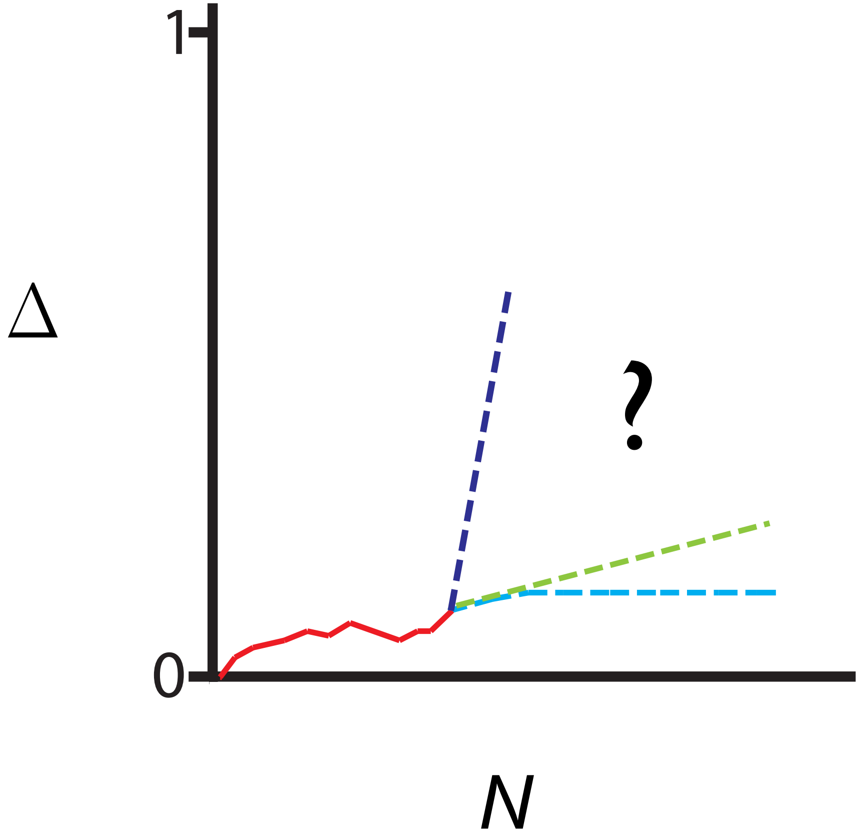
"pairwise models are exceptionally powerful"

This was calculated for small number of neurons $N \leq 10$.

- can we conclude that pairwise models are good for real sized systems?

Roudi et al, PLoS Comp. Biol., 2009
Roudi et al, Phys. Rev. E., 2009
Roudi et al, Frontiers in CN, 2009

extrapolation problem



perturbation for small $N\delta$

N number of neurons

δ average number of spikes per bin

- assume $N\delta \ll 1$.

experiments were done in this regime.

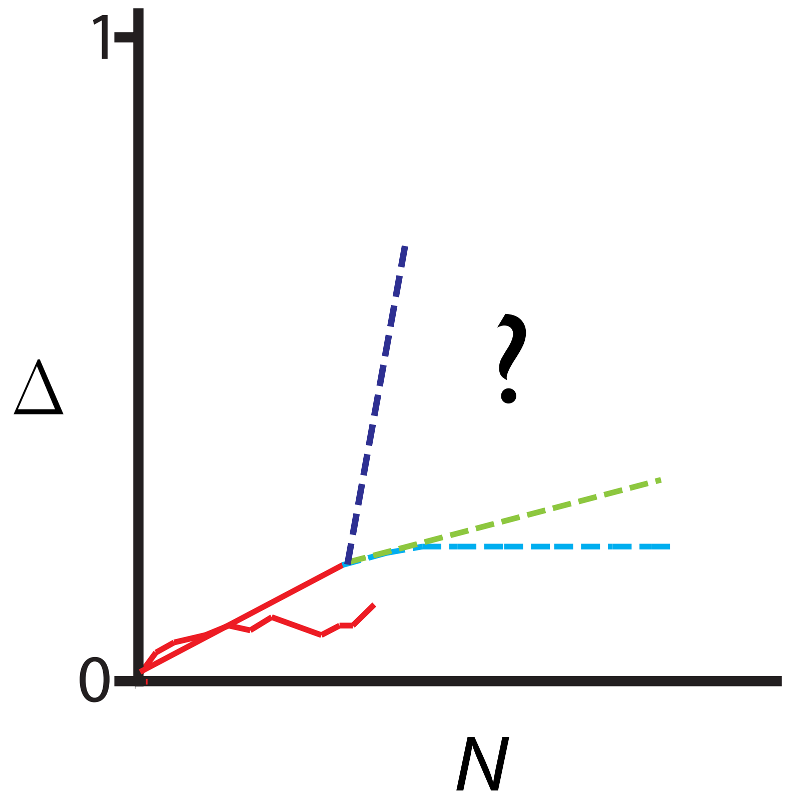
- compute $D_{KL}(P_{true}||P_{pair})$ and $D_{KL}(P_{true}||P_{ind})$ perturbatively.

$$D_{KL}(P_{true}||P_{ind}) \propto N\,(N-1)\,\delta^2$$

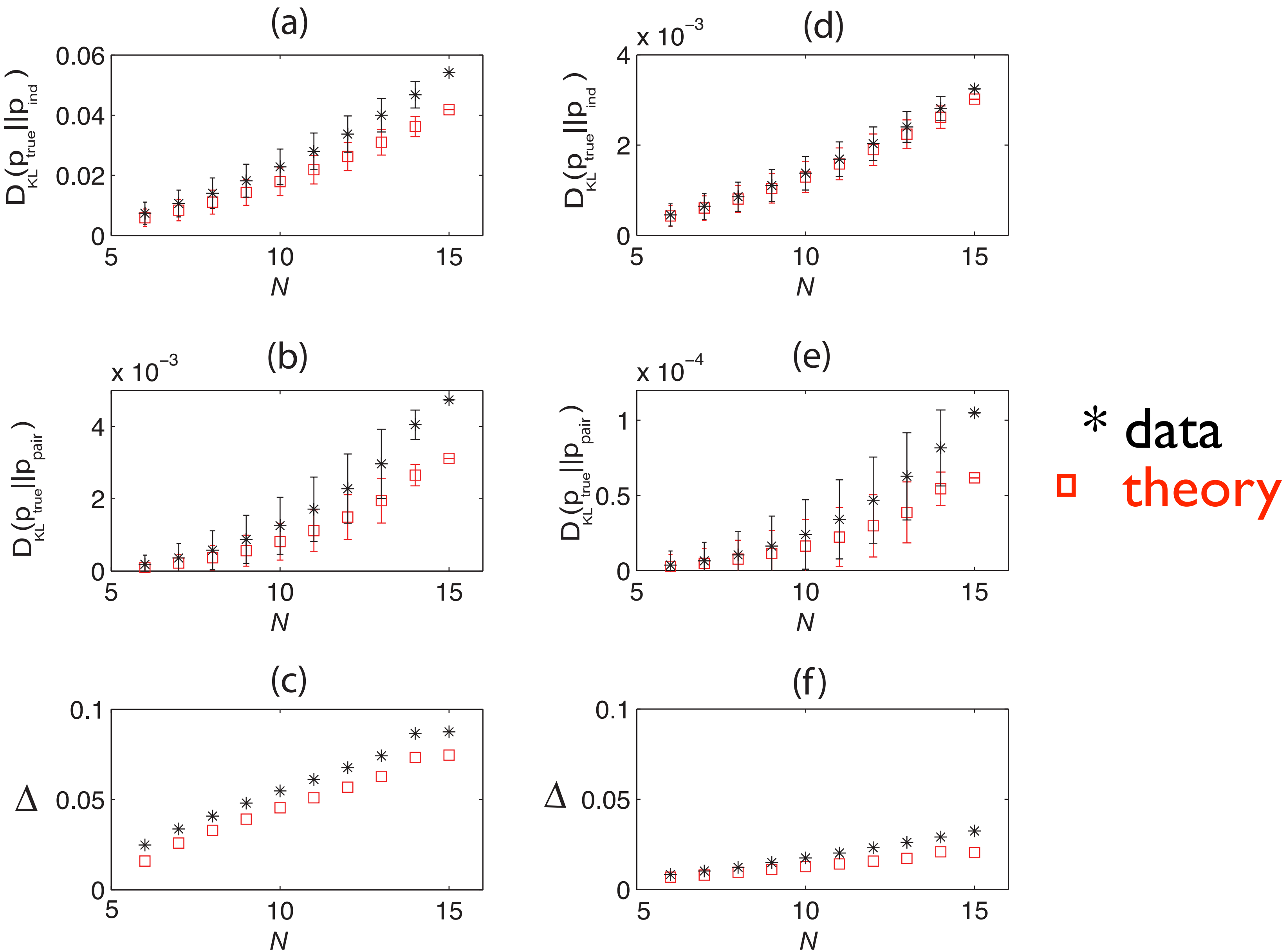
$$D_{KL}(P_{true}||P_{pair}) \propto N\,(N-1)\,(N-2)\,\delta^3$$

$$\boxed{\Delta \propto (N-2)\ \delta \ll 1}$$

Δ is guaranteed to be small for small subsystems, but it has no predictive power.



the experimentally observed power of pairwise models **cannot be extrapolated** to large systems.



δ =0.073

δ t=10 ms

δ =0.019

δ t=2 ms

- equilibrium model does not help you find the connections.

- it is not a good probability model for data unless you're dealing with a brain of N~10-20.

~ forcing the connections to be symmetric

~ equilibrium vs non-equilibrium

study kinetic models

GLM models

network of IF neurons

kinetic Ising model

synchronous discrete time β=1

$$\Pr(\{s_i(t+1)\}|\{s_i(t)\}) = \prod_i \frac{\exp\left[\beta s_i(t+1)h_i(t) + \sum_j \beta J_{ij} s_i(t+1) s_j(t)\right]}{2\cosh\left[\beta h_i(t) + \sum_j \beta J_{ij} s_j(t)\right]}$$

asynchronous, continuous time

$$s_i \to -s_i \quad \text{with probability} \quad \gamma\delta t \left[1 - s_i \tanh(\beta h_i + \sum_j J_{ij} s_j)\right]$$

suppose we have observed R repeats each of length L

$$\boldsymbol{s}^r(t) = \{s_1^r(t), \cdots, s_N^r(t)\},\ r = 1 \ldots R.$$

log likelihood of this data is

$$\mathcal{L}(\mathbf{h}, \mathsf{J}) = \sum_{t,r,i} \left[\, h_i s_i^r(t+1) + \sum_j J_{ij} s_i^r(t+1) s_j^r(t) - \log 2\cosh(h_i(t) + \sum_j J_{ij} s_j^r(t))\right].$$

exact learning by maximizing the likelihood by gradient decent

$$\delta h_i = \eta_h \frac{\partial \mathcal{L}}{\partial h_i} \qquad \delta J_{ij} = \eta_J \frac{\partial \mathcal{L}}{\partial J_{ij}}$$

$$\delta h_i(t) = \eta_h \{ \langle s_i(t+1) \rangle_r - \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t))] \rangle_r] \}$$

$$\delta J_{ij} = \eta_J \{ \langle s_i(t+1) s_j(t) \rangle - \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t)] s_j(t) \rangle \}$$

like (batch version) delta-rule for N independent perceptrons

Much faster than Boltzmann learning for the symmetric case because it doesn't need long Monte Carlo runs to evaluate the second term

Exact algorithm: mean square error ~ 1/L

Weak- coupling limit: $\left\langle \left(J_{ij}^{calculated} - J_{ij}^{true} \right)^2 \right\rangle = \frac{1}{\left(1 - m_i^2\right) L}$

Mean field theory for the kinetic learning

I do this for the stationary case first for simplicity

$$\delta J_{ij} = \eta_J \left\{ \langle s_i(t+1) s_j(t) \rangle - \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t)] s_j(t) \rangle \right\}$$

after the learning is converged $\delta J_{ij} = 0$

$$\langle s_i(t+1) s_j(t) \rangle = \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t)] s_j(t) \rangle$$

$$S_i = m_i + \delta S_i$$

$$m_i = \langle s_i \rangle$$

expanding 1st order in δs and assuming $m_i = \tanh(h_i + \sum_j J_{ik}^{\mathrm{MF}} m_k)$

$$\langle \delta s_i(t+1) \delta s_j(t) \rangle = (1 - m_i^2) \sum_k J_{ik}^{\mathrm{MF}} \langle \delta s_k(t) \delta s_j(t) \rangle.$$

$$\mathsf{J}^{\mathrm{MF}} = \mathsf{A}^{-1} \mathsf{D} \mathsf{C}^{-1}$$

$$C_{ij} = \langle \delta s_i(t) \delta s_j(t) \rangle \qquad D_{ij} = \langle \delta s_i(t+1) \delta s_j(t) \rangle$$

$$\delta J_{ij} = \eta_J \{ \langle s_i(t+1) s_j(t) \rangle - \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t)] s_j(t) \rangle \}$$

after the learning is converged $\delta J_{ij} = 0$

$$\langle s_i(t+1) s_j(t) \rangle = \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t)] s_j(t) \rangle$$

$$S_i = m_i + \delta S_i$$
$$m_i = \langle s_i \rangle$$

expanding 3rd order in δs and assuming

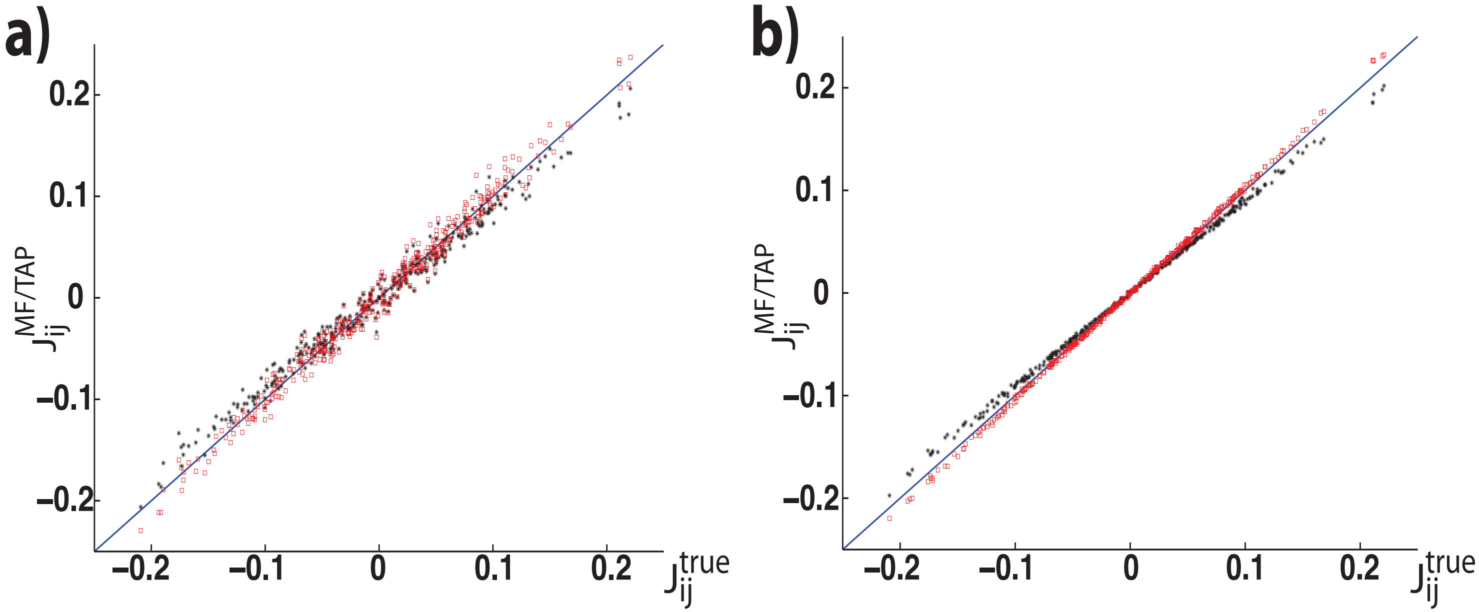
$$m_i = \tanh[h_i + \sum_k J_{ik}^{\mathrm{TAP}} m_k - m_i \sum_k (J^{\mathrm{TAP}})_{ik}^2 (1 - m_k^2)]$$

$$J_{ij}^{\mathrm{TAP}} = \mathrm{A}^{\mathrm{TAP}^{-1}} \mathrm{DC}^{-1} = J_{ij}^{\mathrm{MF}} / (1 - F_i)$$

$$A_{ii}^{\mathrm{TAP}} = (1 - m_i^2)(1 - F_i), \qquad F_i (1 - F_i^2) = (1 - m_i^2) \sum_j (J^{\mathrm{MF}})_{ij}^2 (1 - m_j^2).$$

$$C_{ij} = \langle \delta s_i(t) \delta s_j(t) \rangle \qquad D_{ij} = \langle \delta s_i(t+1) \delta s_j(t) \rangle$$

MF and TAP tested on data generated from a kinetic Ising model:



L = 10^4 L = 10^6

L time steps, generated by a model with random couplings:

$$\langle J_{ij} \rangle = 0 \qquad \langle J_{ij}^2 \rangle = \frac{g^2}{N}$$

(asymmetric Sherrington-Kirkpatrick model)

quantifying the errors

exact algorithm is satisfied when

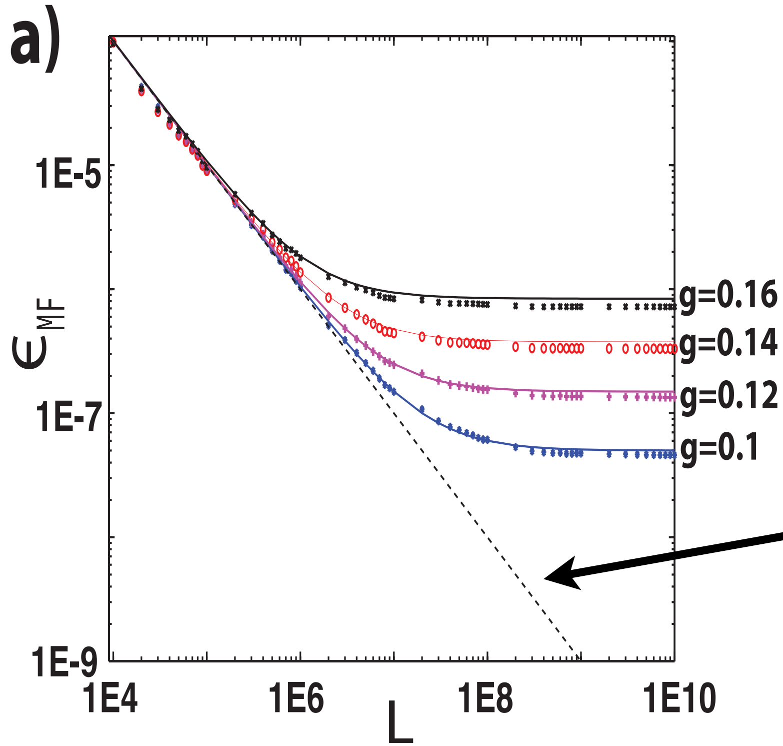
$$D_{ij} = \langle \tanh[h_i(t) + \sum_k J_{ik} s_k(t)] s_j(t) \rangle$$

at zero field $$D_{in} = \sum_k J_{ik} \langle s_k s_n \rangle - \tfrac{1}{3} \sum_{klm} J_{ik} J_{il} J_{im} \langle s_k s_l s_m s_n \rangle + \cdots$$

using $\mathrm{J}^{\mathrm{MF}} = \mathrm{A}^{-1} \mathrm{D} \mathrm{C}^{-1}$ yields $$J_{ij}^{\mathrm{MF}} = J_{ij} - \sum_k J_{ik}^2 J_{ij}$$

$$\left\langle \left(J_{ij} - J_{ij}^{MF} \right)^2 \right\rangle = \left\langle \sum\nolimits_k J_{ik}^2 \right\rangle^2 \left\langle J_{ij}^2 \right\rangle = \left(g^2 \right)^2 \cdot \frac{g^2}{N}$$

$$= \frac{g^6}{N}$$

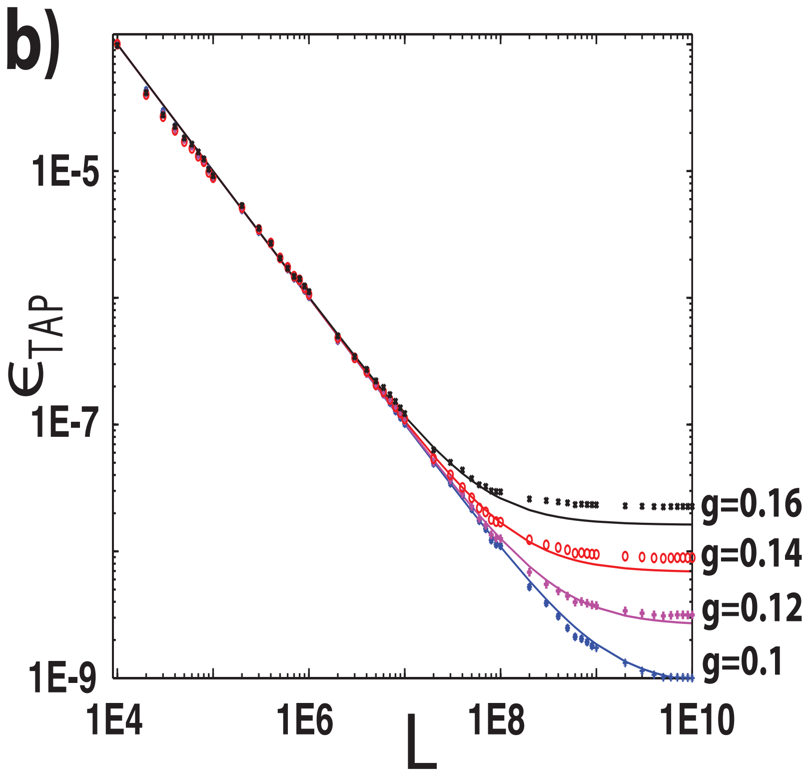


exact
algorithm

TAP error

$$4g^{10}/N.$$

much smaller than what simulations show



$$4g^{10}/N + (20g^6)/(3N^3).$$

finite size effect
negligible only for N>>1/g^2

Nonstarionary

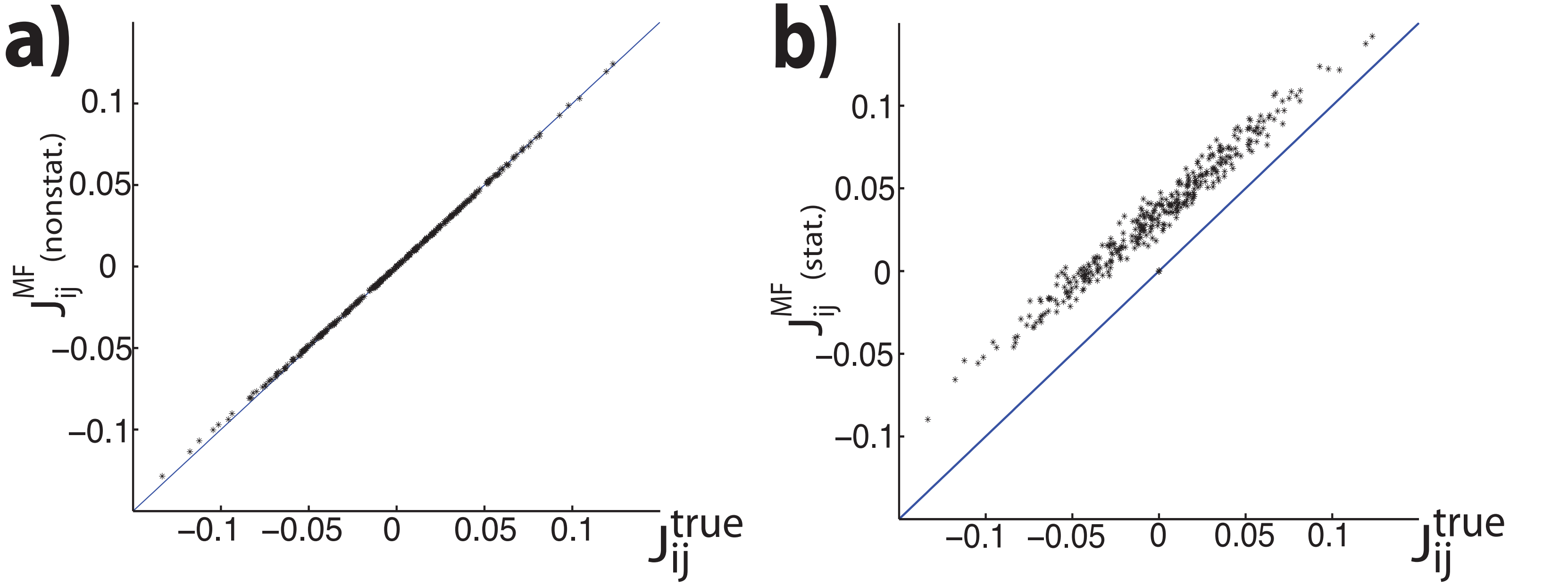
MF

$$m_i(t+1) = \tanh[h_i(t) + \sum_i J_{ij}^{\mathrm{MF}} m_j(t)].$$

TAP

$$m_i(t+1) = \tanh[h_i(t) + \sum_j J_{ij}^{\mathrm{TAP}} m_j(t) - m_i(t+1) \sum_j (J^{\mathrm{TAP}})_{ij}^2 (1 - m_j^2(t))]$$

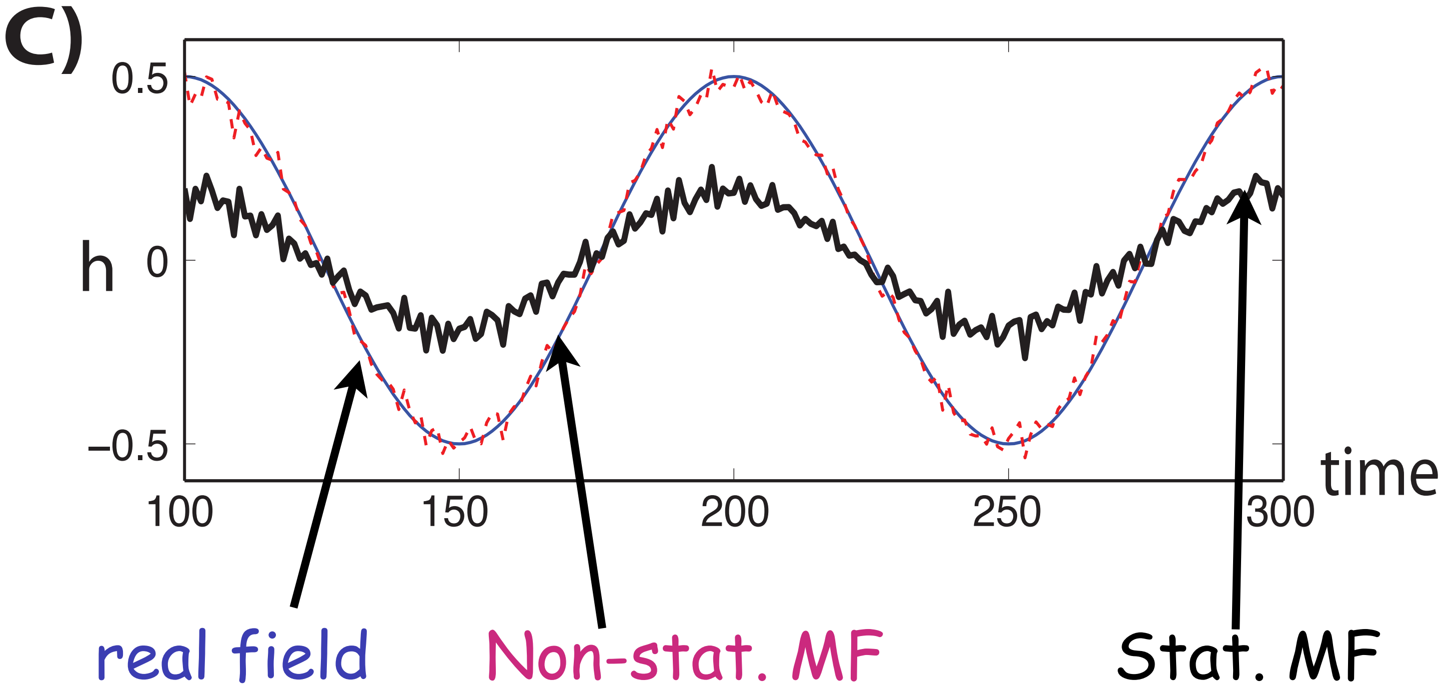
sinusoidal field applied to all spins



nonstationary MF inference applied to nonstationary data

stationary MF inference applied to nonstationary data after we inferred the couplings, we can infer the fields

$$m_i(t+1) = \tanh[h_i(t) + \sum_j J_{ij}^{\mathrm{MF}} m_j(t)].$$



real data

- for *in vivo* and *in vitro* real data, we don't know the connectivity
- so we use in silico real data.

simplified model of circuitry in a small (~0.5 mm) region of neocortex

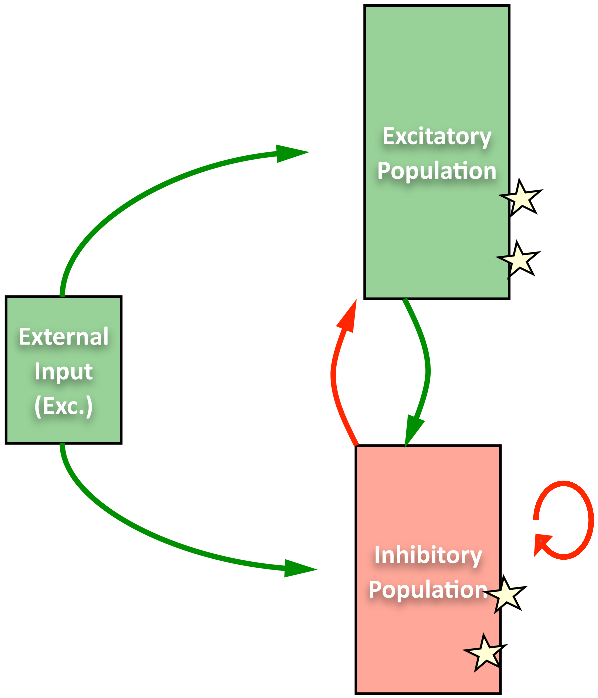
2 populations in network:
Excitatory, Inhibitory

Excitatory external drive ("rest of brain")

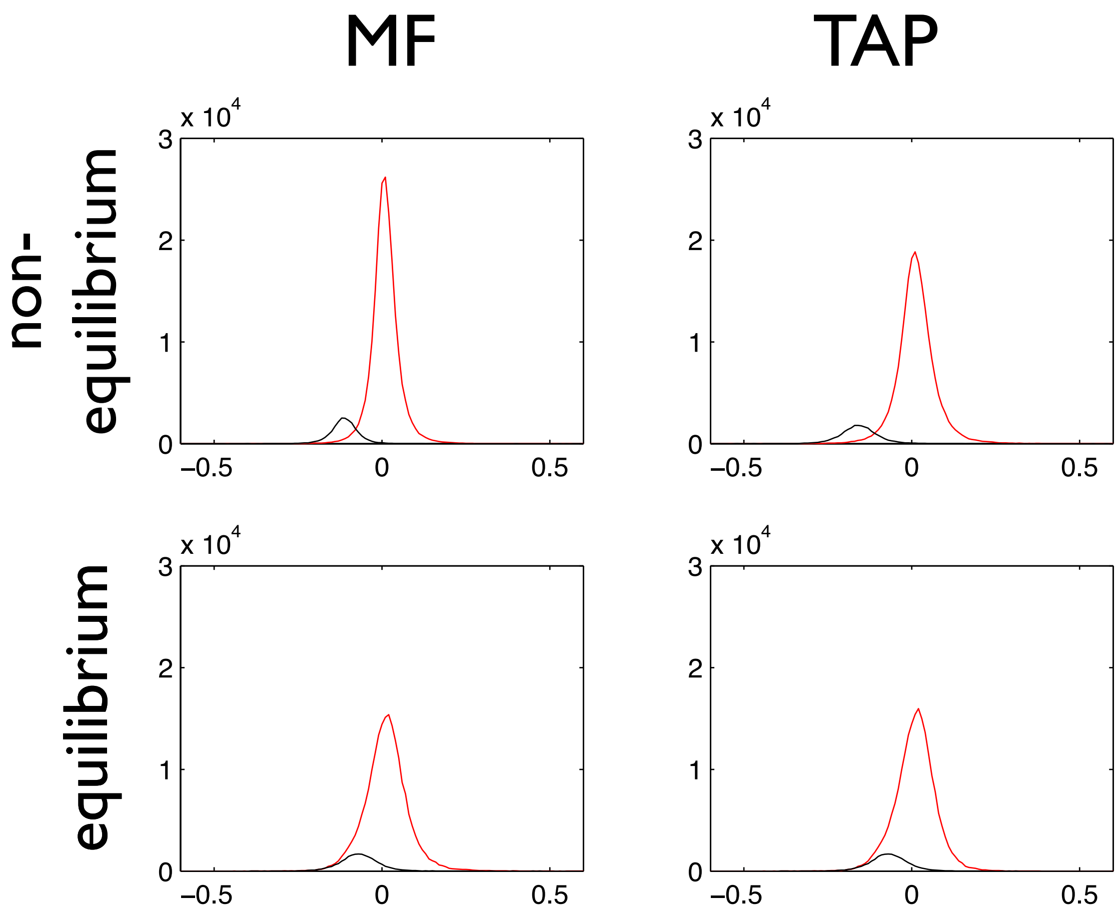
realistic modeling: Hodgkin-Huxley-like neurons, conductance-based synapses

Random connectivity:
Probability of connection between any two neurons is $c = K/N$, where N is the size of the population and K is the average number of presynaptic neurons.

Results here for
$c = 0.1, N = 1000$



inhibitory-inhibitory connections

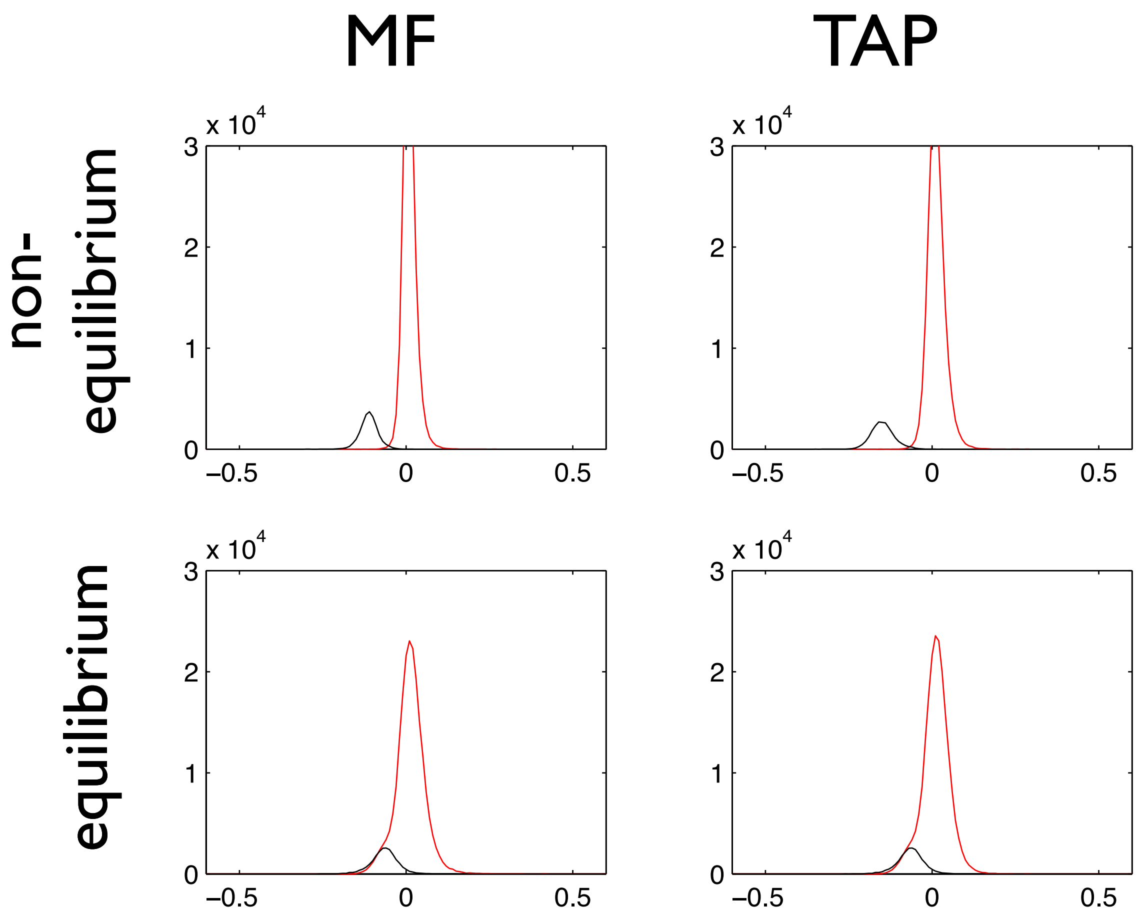


--- : synaptic connection present in original network

--- : synaptic connection absent in original network

L=10000

inhibitory-inhibitory connections

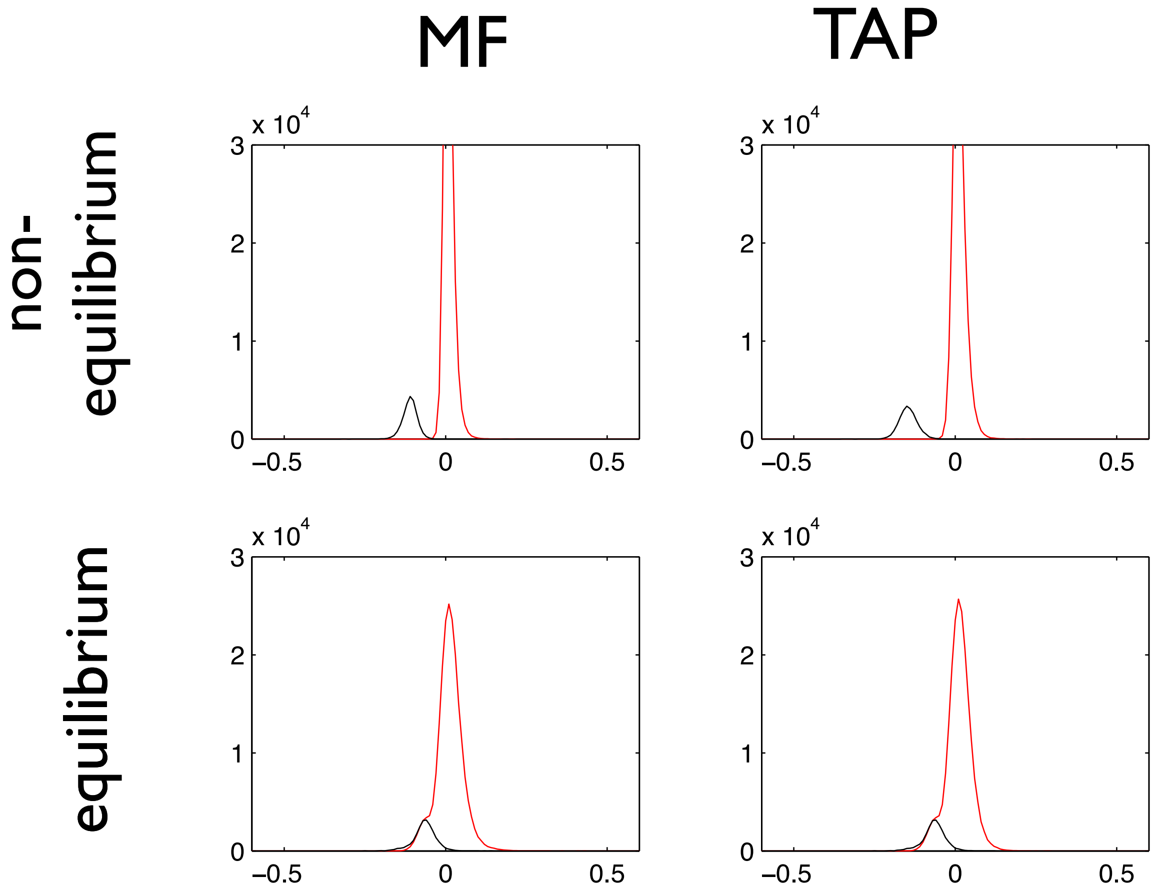


--- : synaptic connection present in original network

--- : synaptic connection absent in original network

L=100000

inhibitory-inhibitory connections



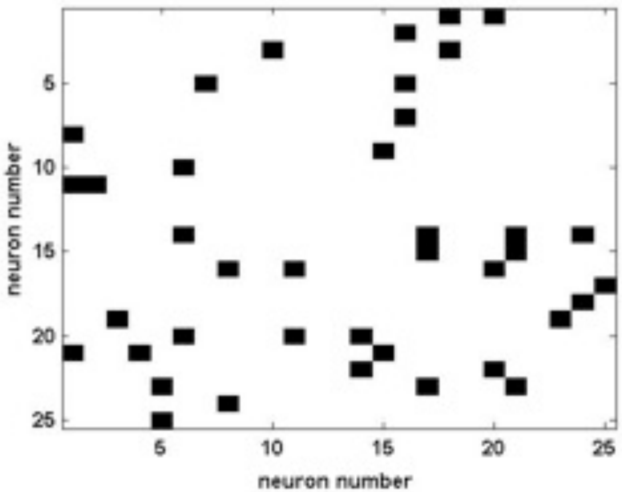
--- : synaptic connection present in original network

--- : synaptic connection absent in original network

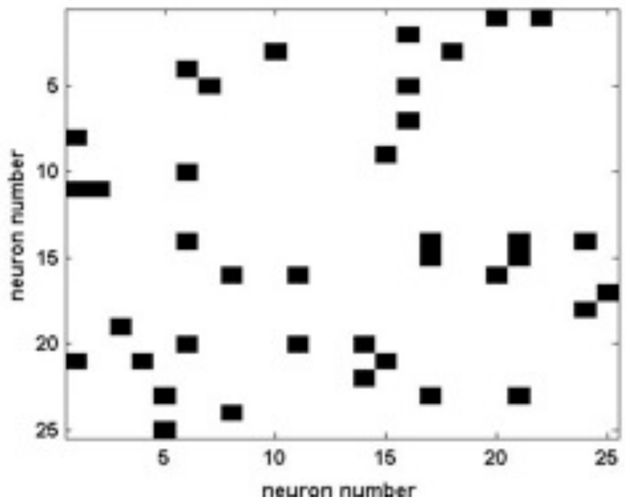
L=1000000

one example: 25 neurons

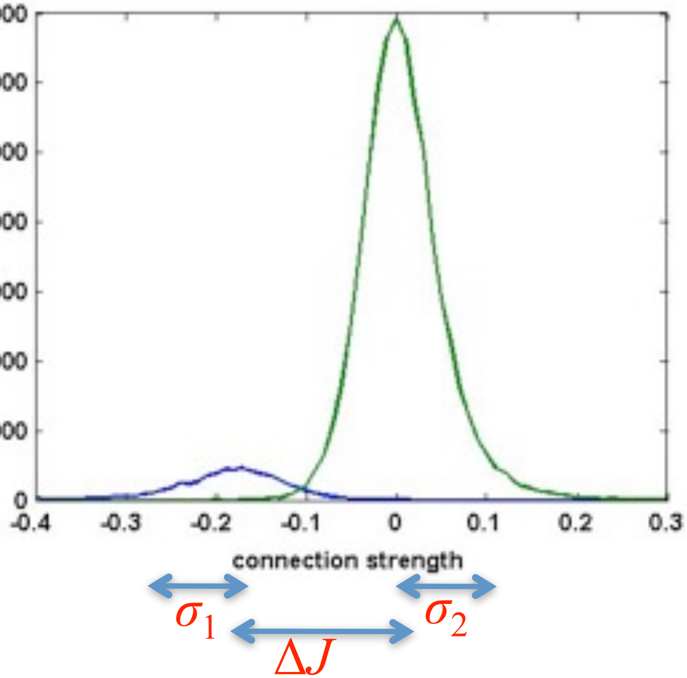
model connections:



inferred connections:



noise/signal ratio

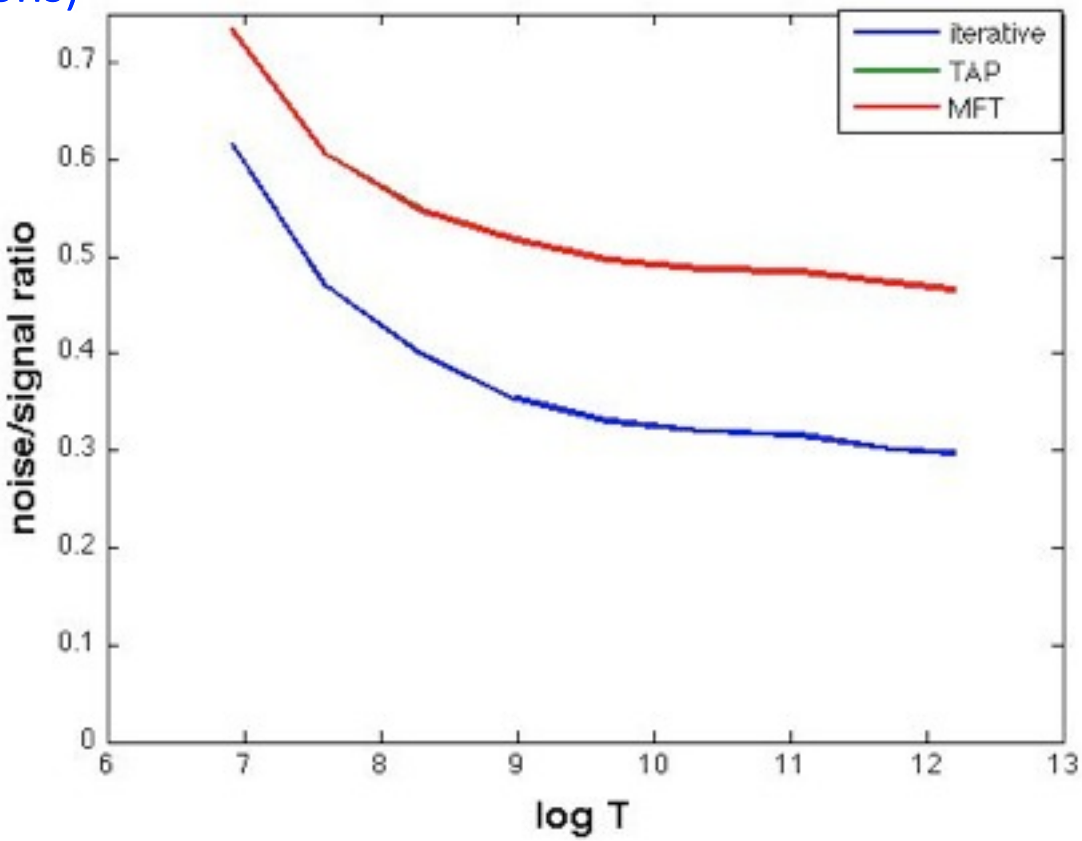


$$\text{nsr} = \frac{\sigma_1 + \sigma_2}{\Delta J}$$

$$= 0.5212$$

nsr as function of data set size

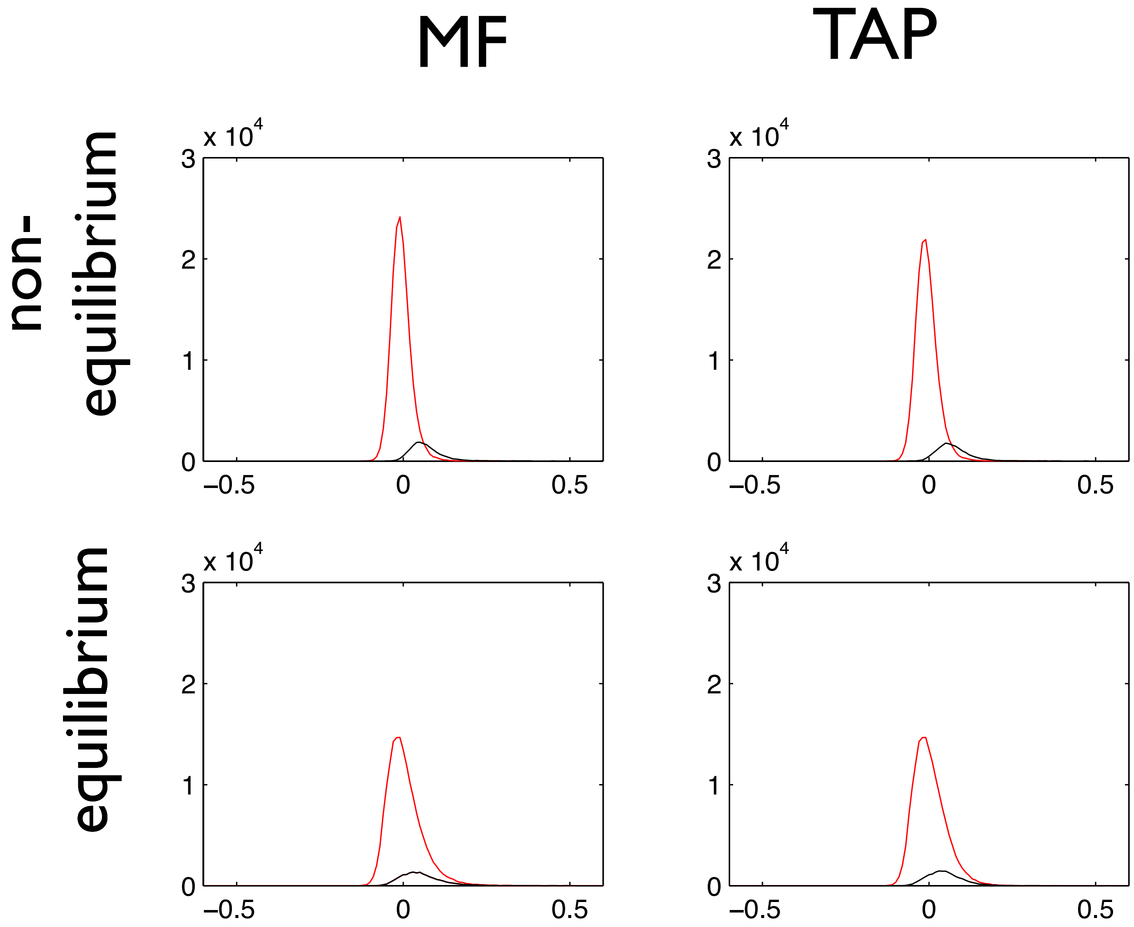
(95 neurons)



TAP and MFT give same results here

(1000-200000 10-ms time bins)

excitatory-excitatory connections



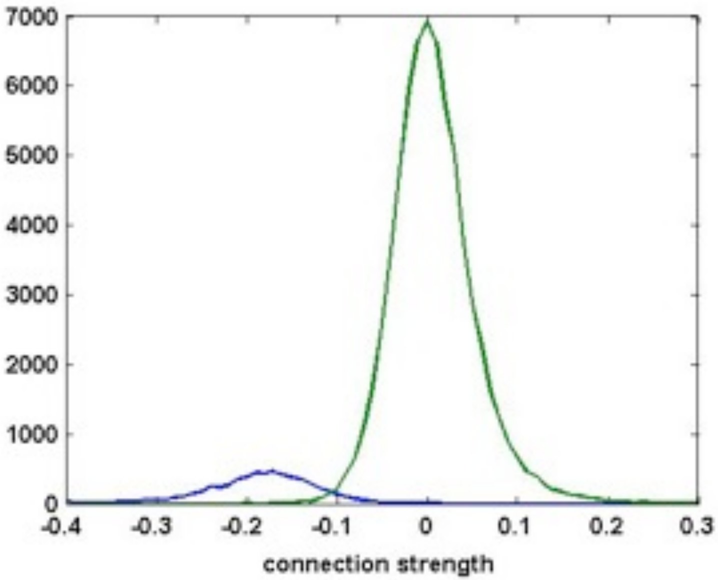
--- : synaptic connection presen
in original network

--- : synaptic connection absent
in original network

L=1000000

summary

- we can develop exact, MF and TAP approximate learning rules for the non-equilibrium case.
- the error can be quantified in the weak couplings (high Y) regime, leading to an asymptotic error of g^6/N for MF and g^10/N for TAP (+ finite size).
- we can also extend everything to the nonstationary regime.
- for simulated data, we can infer the strong connections.



from some point, width of these histograms does not shrink with increasing data set size:

Residual error reflects misfit between original network and Ising model

future

- quantify the error for the non-stationary case.
- the issue of subsampling, i.e. observing only part of the system.
- relation to non-equilibrium FDTs.
- asynchronous (continuous time) dynamics (Erik Aurell et al)

based on

Roudi, Tyrcha, Hertz, 2009, Phys. Rev. E

Roudi, Aurell, Hertz, 2009, Frontiers. C. N.

Roudi, Nirenberg, Latham, 2009, PLoS C. B.

Hertz, Roudi et al, 2010, BMC Neur.

Aurell, Olions, Roudi, EPJ B, 2010

Roudi & Hertz, 2010, arXiv:1009.5946

in collaboration with

John Hertz

Peter Latham

Erik Aurell

Joanna Tyrcha

Sheila Nirenberg

financial Support

THE KAVLI FOUNDATION

NORDITA