Applied math in Neuroscience

Dynamical systems approaches

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Plan for today

- An example of how dynamical systems can be used in neuroscience
- A short exercise in Jupyter
  - **github.com/kharris/amath50**
  - Please ensure you have `python 3 + jupyter + numpy/scipy`
  - `pip install brian2`

Respiratory control via tunable synchony in networks of bursting neurons

Many behaviors are rhythmic

Locomotion

Chionea (snow fly)

Many behaviors are rhythmic

Fireflies

https://www.youtube.com/watch?v=sROKYelaWbo

Many behaviors are rhythmic

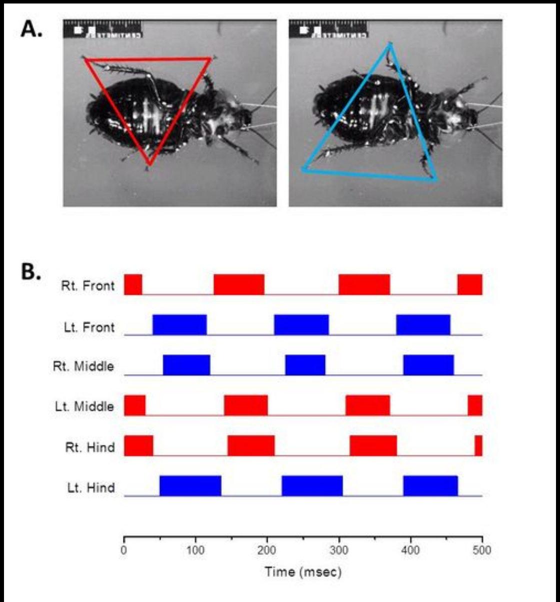
Whisking & **breathing**

Rat

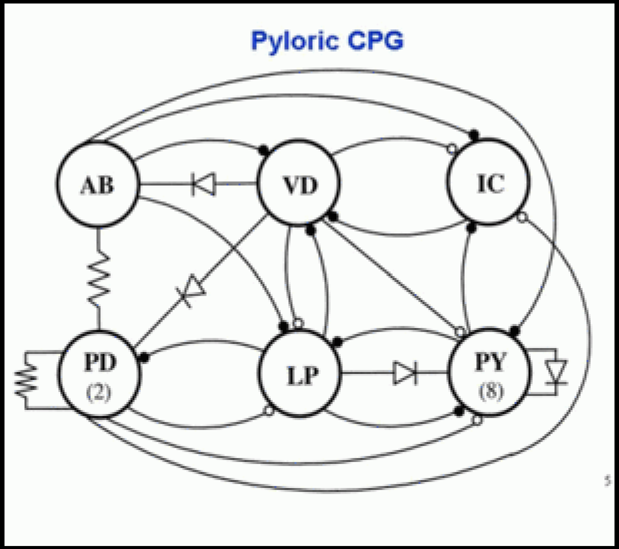
Moore et al. 2013

Video: Martin Deschênes

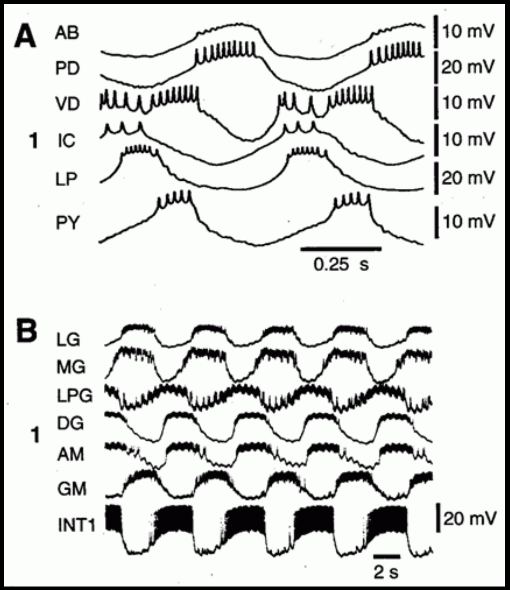
Central pattern generation of rhythms



Locomotion
Ritzmann & Zill (2013)



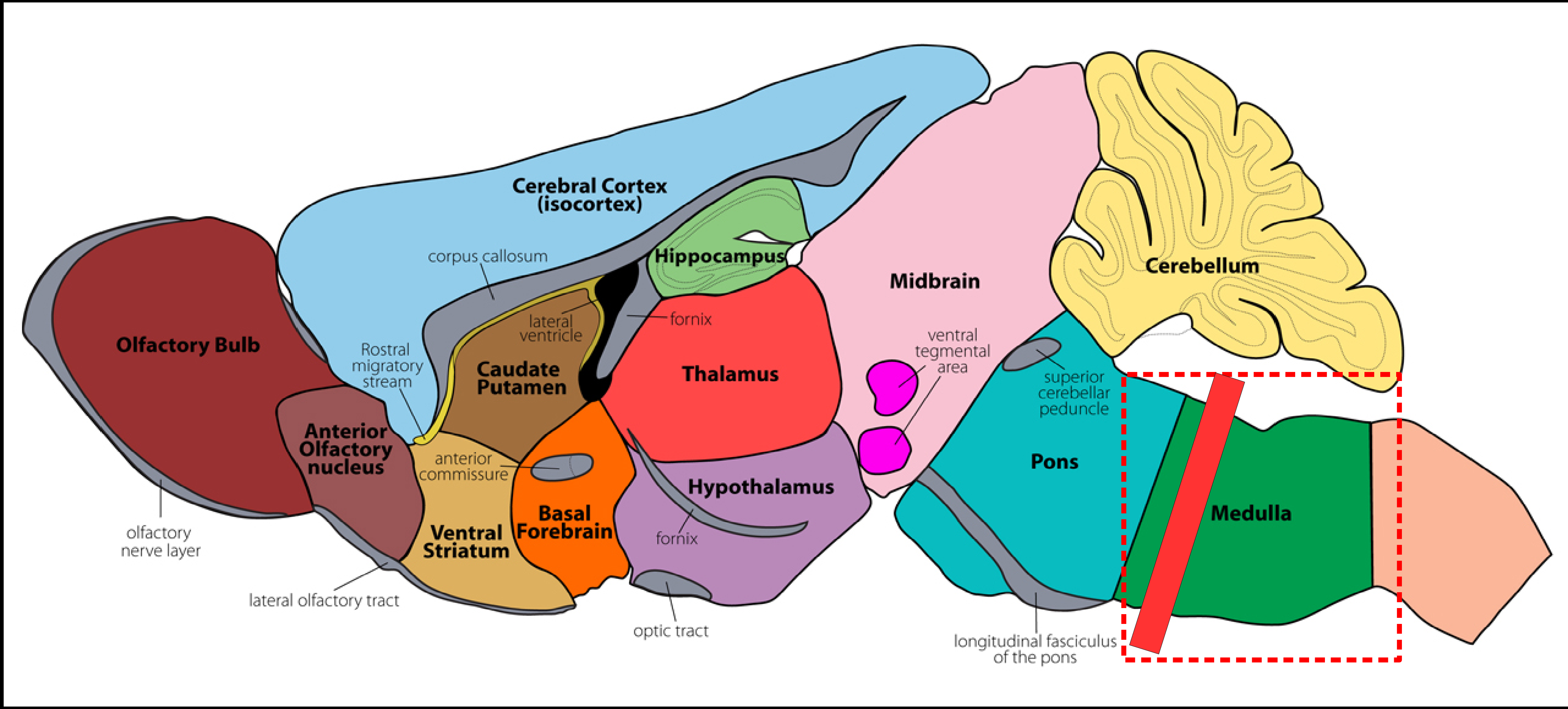
Digestion (crab)
Selverston (2008), Miller & Heinzel, Marder



… and Breathing

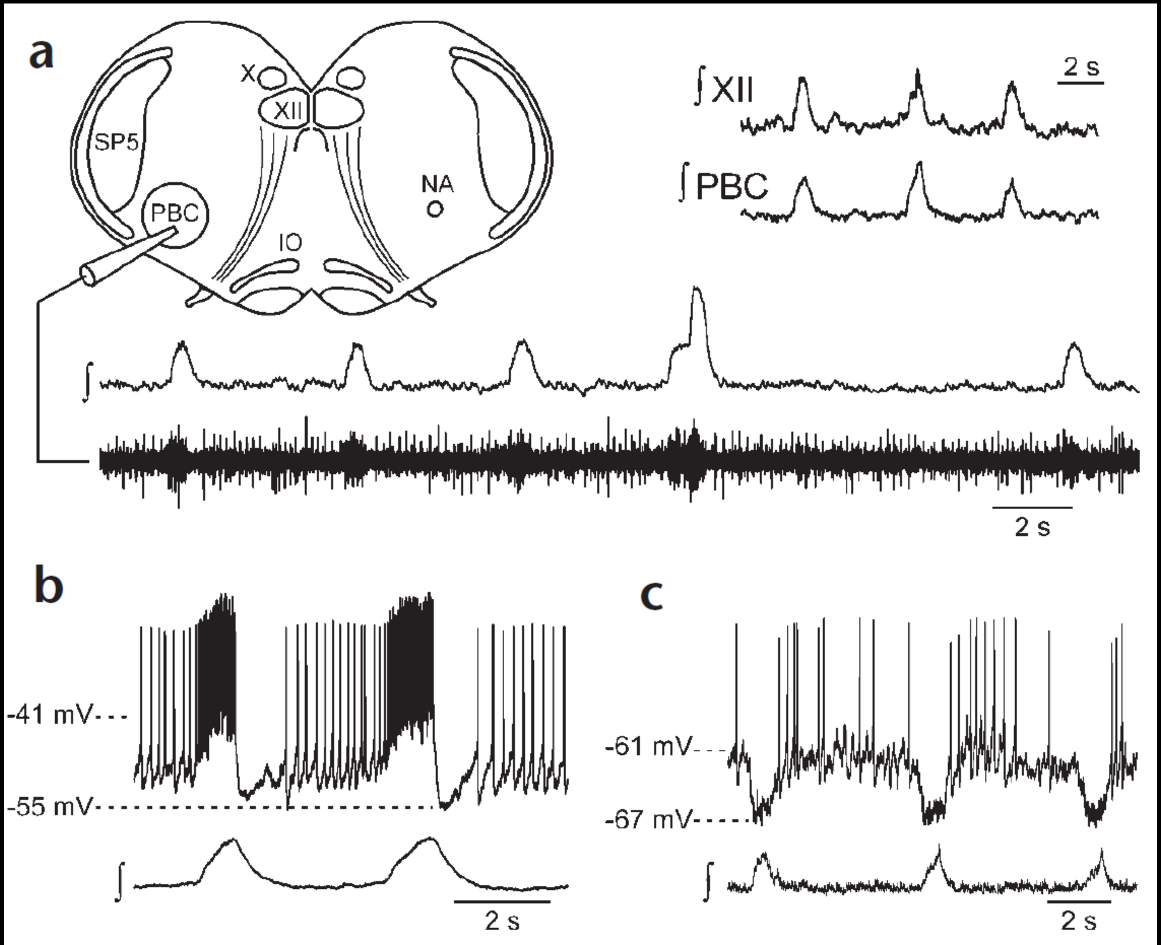
Super important if you want to survive and prosper in the world!

Breathing CPG: Pre-Bötzinger complex



gensat.org

Breathing CPG: Pre-Bötzinger complex



inspiratory cell

expiratory cell

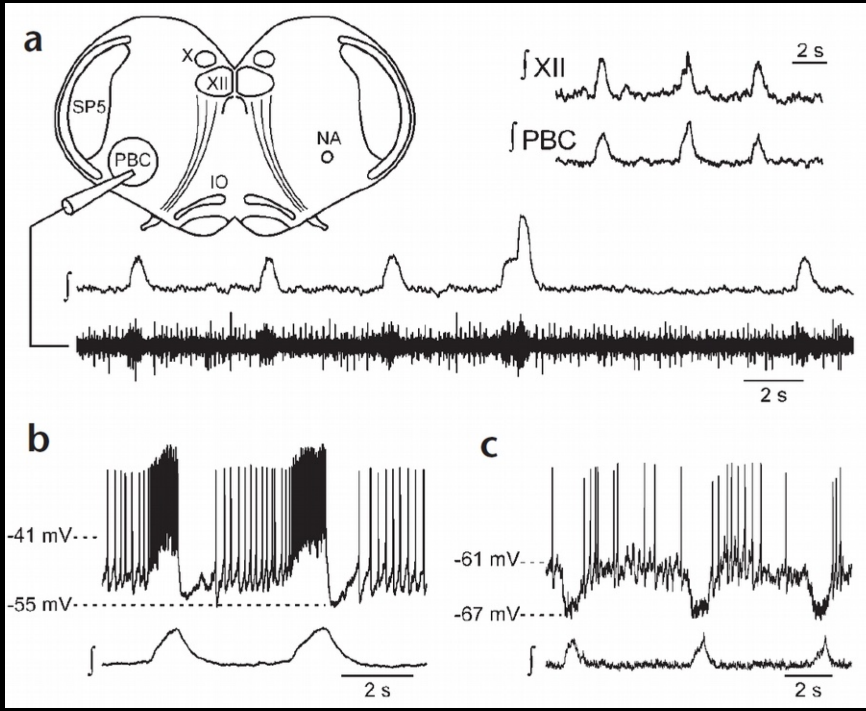
figure: S Lieske, M Thoby-Brisson, P Telgkamp, and J-M Ramirez (2000)

Breathing CPG: Pre-Bötzinger complex

- Properties of the preBot
  - Smith et al. 1991; Ramirez & Richter 1996; Rekling & Feldman 1998; Feldman et al. 2013
  - Heterogeneous: bursters, tonic (periodic) spikers, and quiescent
  - Synchronized population bursts via excitation
  - Sparse network

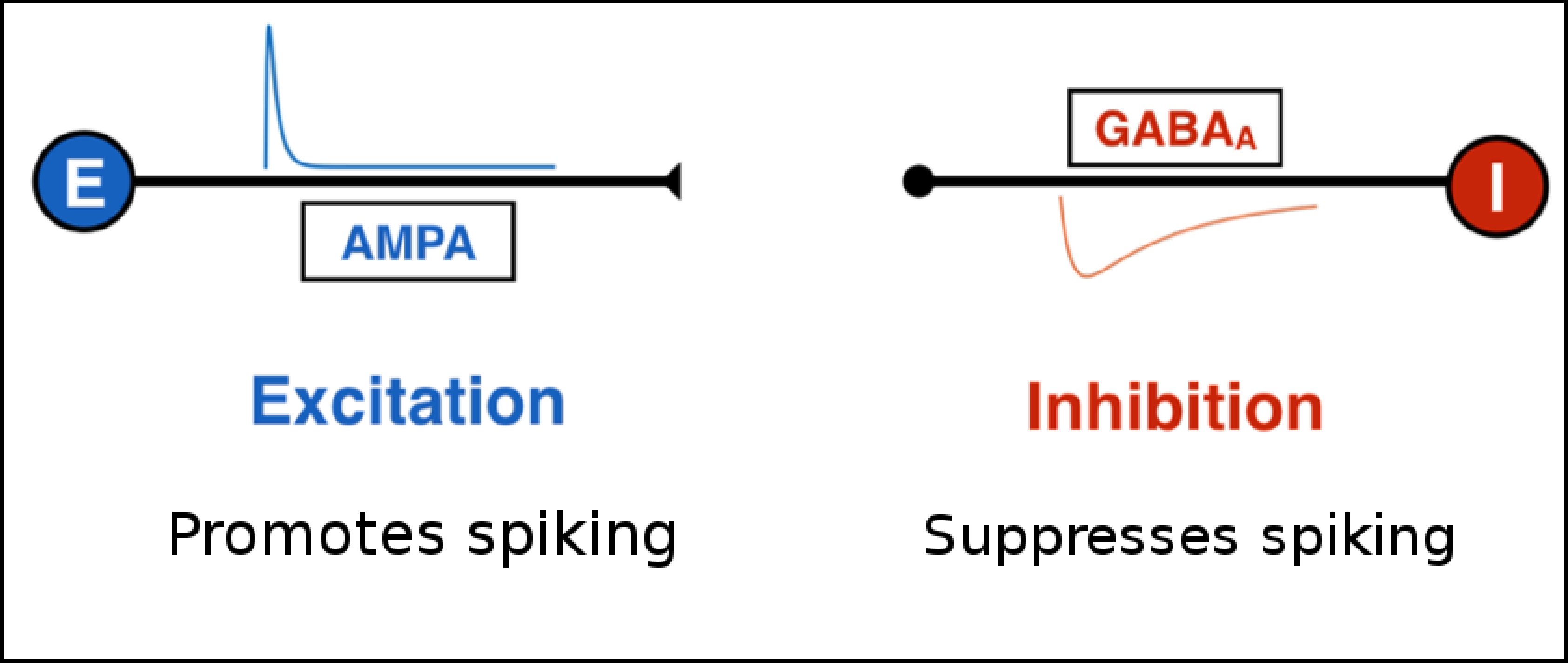
Difference from usual CPGs:

- ~300 neurons... why so many?
- Recurrent E/I network
  - up to 50% inhibitory, Hayes et al. 2012



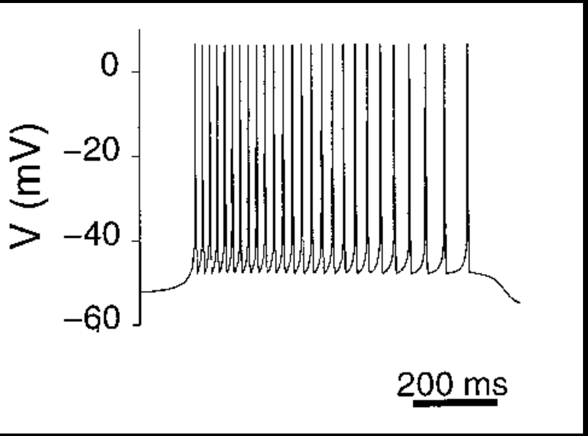
inspiratory cell expiratory

Excitation versus inhibition



We model the effect of inhibitory cells in the population

- Heterogeneous neurons
  - Butera et al. 1999; Best et al. 2005; Rubin et al. 2009; Toporikova & Butera 2011; Park & Rubin 2013
- Embedded in sparse network (N=300, avg deg k = 3 – 6)
  Gaiteri & Rubin 2011; Carroll & Ramirez 2013
- Vary fraction of inhibitory cells p_I
- Look for:
  - Effects on synchrony
  - Rhythm properties
  - Functional role for inhibition?



Biophysical model details

- “Butera model 1” for cells

$$\dot{V} = -\left(I_{\mathrm{L}} + I_{\mathrm{K}} + I_{\mathrm{Na}} + I_{\mathrm{NaP}} + I_{\mathrm{syn}}\right)/C_m$$

$$\dot{n} = \left(n_\infty(V) - n\right)/\tau_n(V)$$

I_K activation

$$\dot{h} = \left(h_\infty(V) - h\right)/\tau_h(V)$$

I_{NaP} inactivation

- 1st order synaptic kinetics

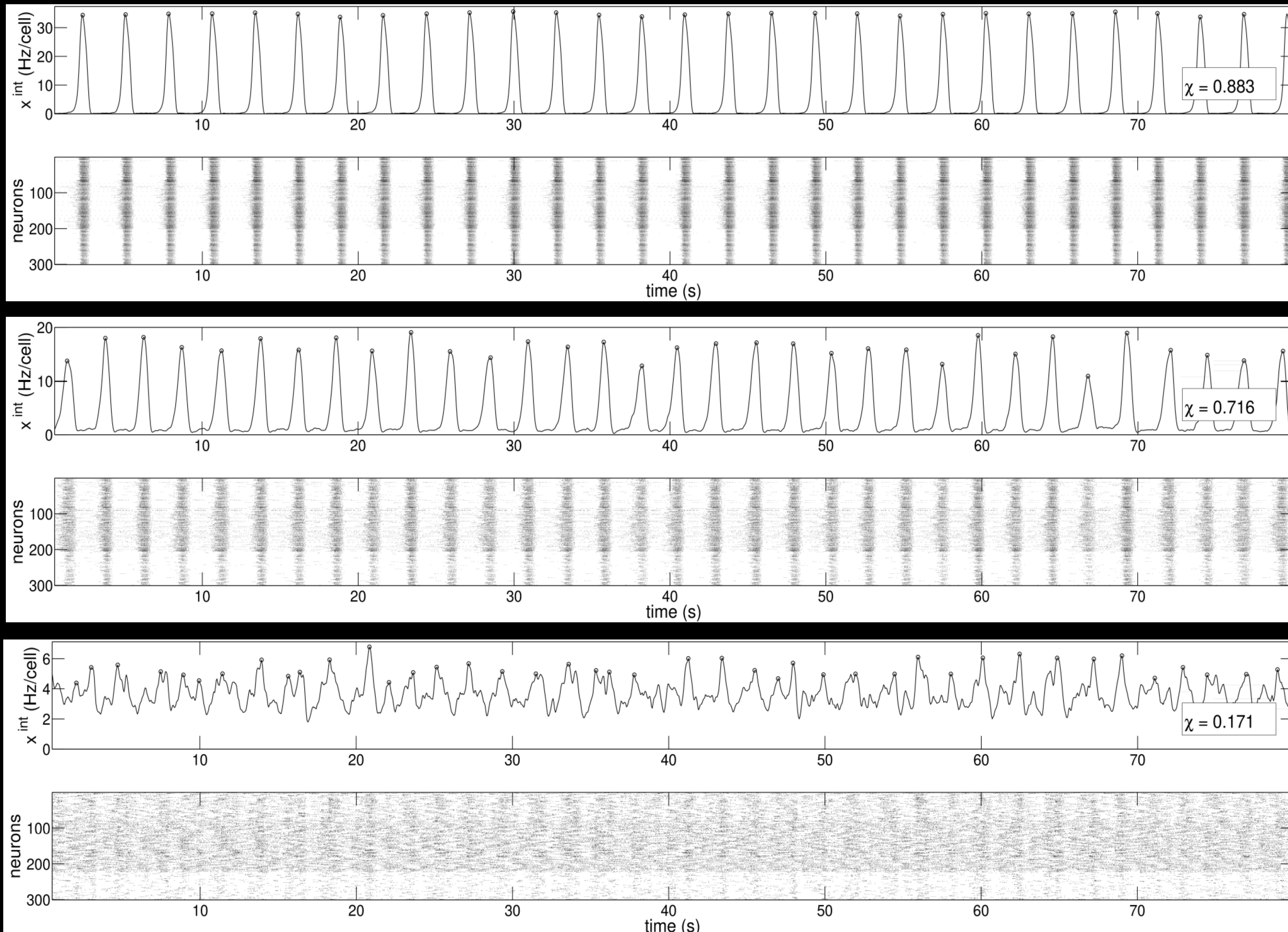
$$\dot{s} = \left[(1 - V_{\mathrm{post}})s_\infty(V_{\mathrm{pre}}) - kV_{\mathrm{post}}\right]/\tau_s$$

$$I_{\mathrm{syn}} = \left(\sum_{i:i\to j} g_{ij}s_i\right)(V_j - V_{\mathrm{syn}})$$

Input current for neuron j

Avg degree = 6, $g_E = g_I = 2.0$ nS

Increasing inhibition

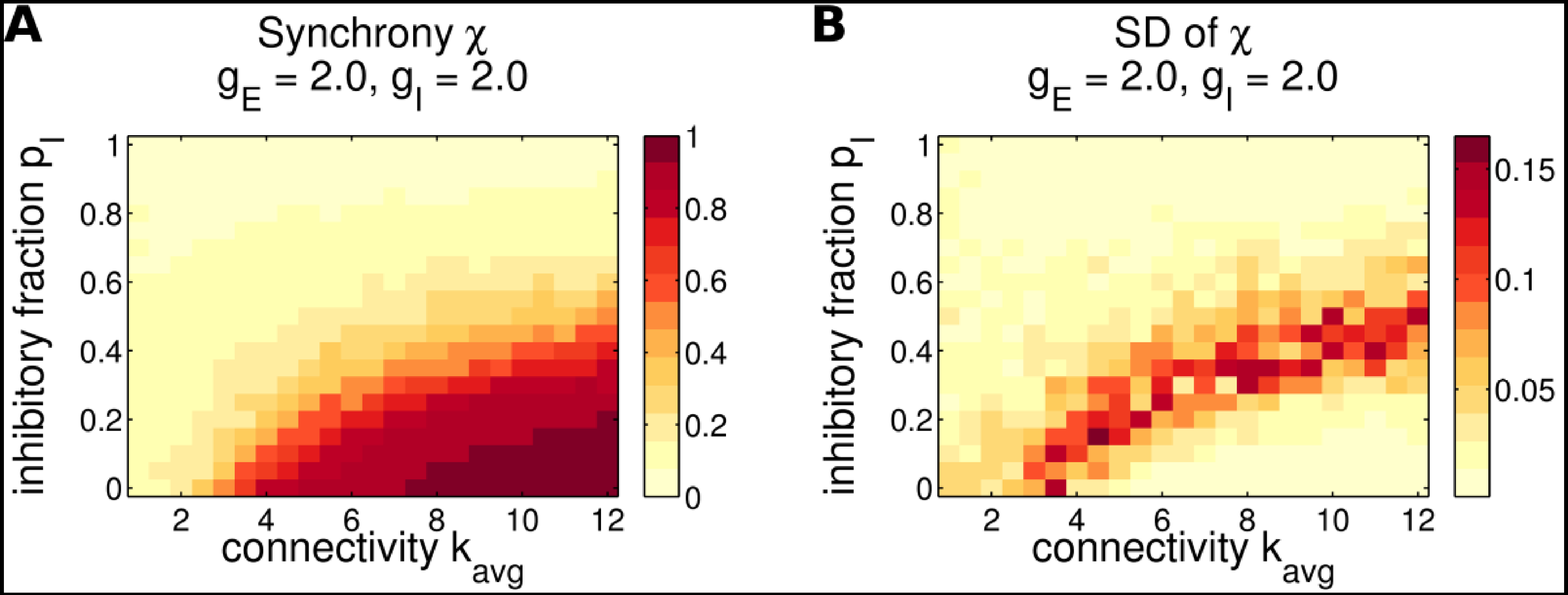


Sparsity & inhibition both degrade the rhythm – (E/I balance)

- Synchronous network oscillation from excitatory interactions
- Stronger with more/stronger connections
- Same effect changing g_E / g_I... E/I balance what matters

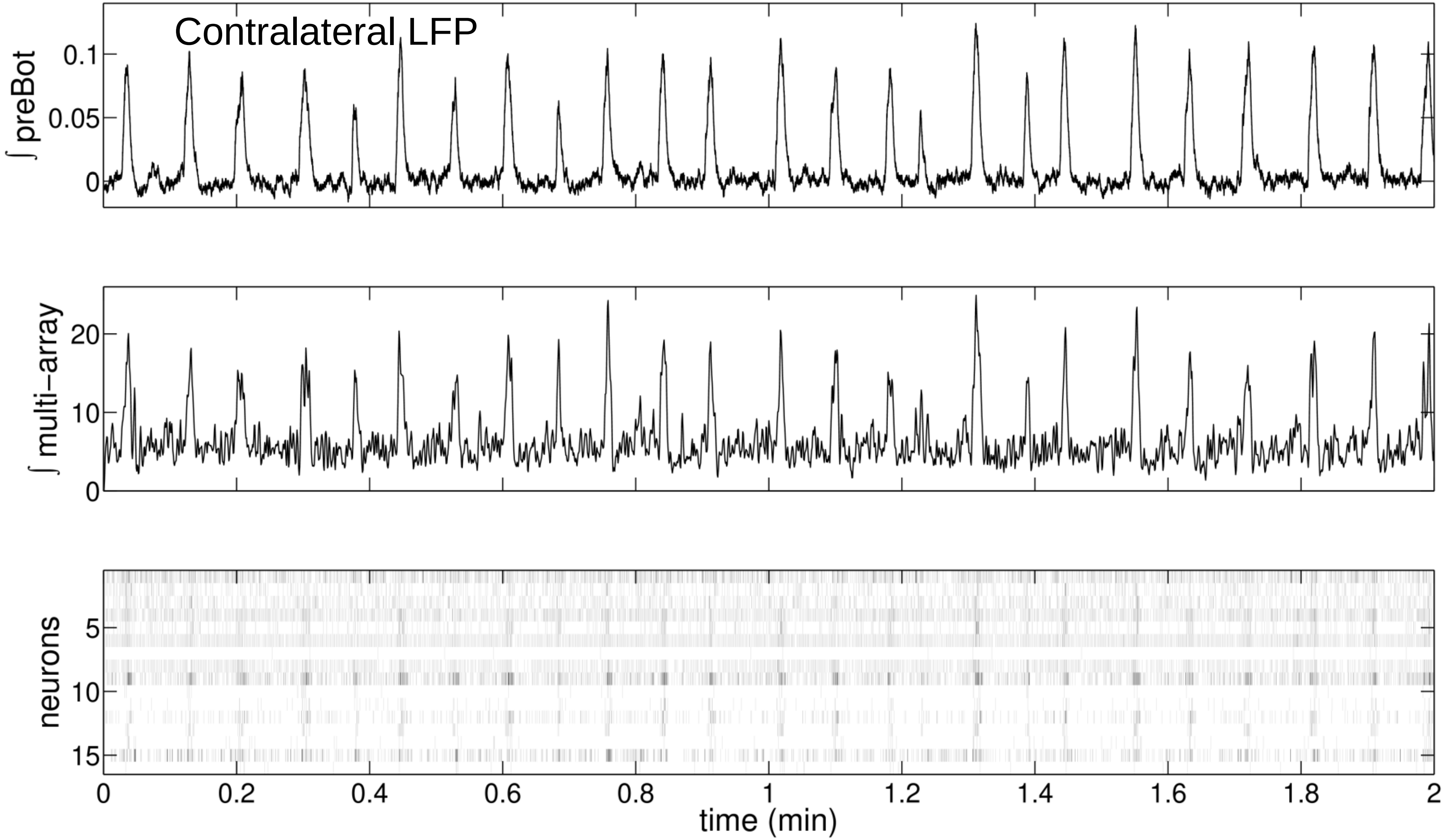
Autocorrelation measure

Variance across network realizations



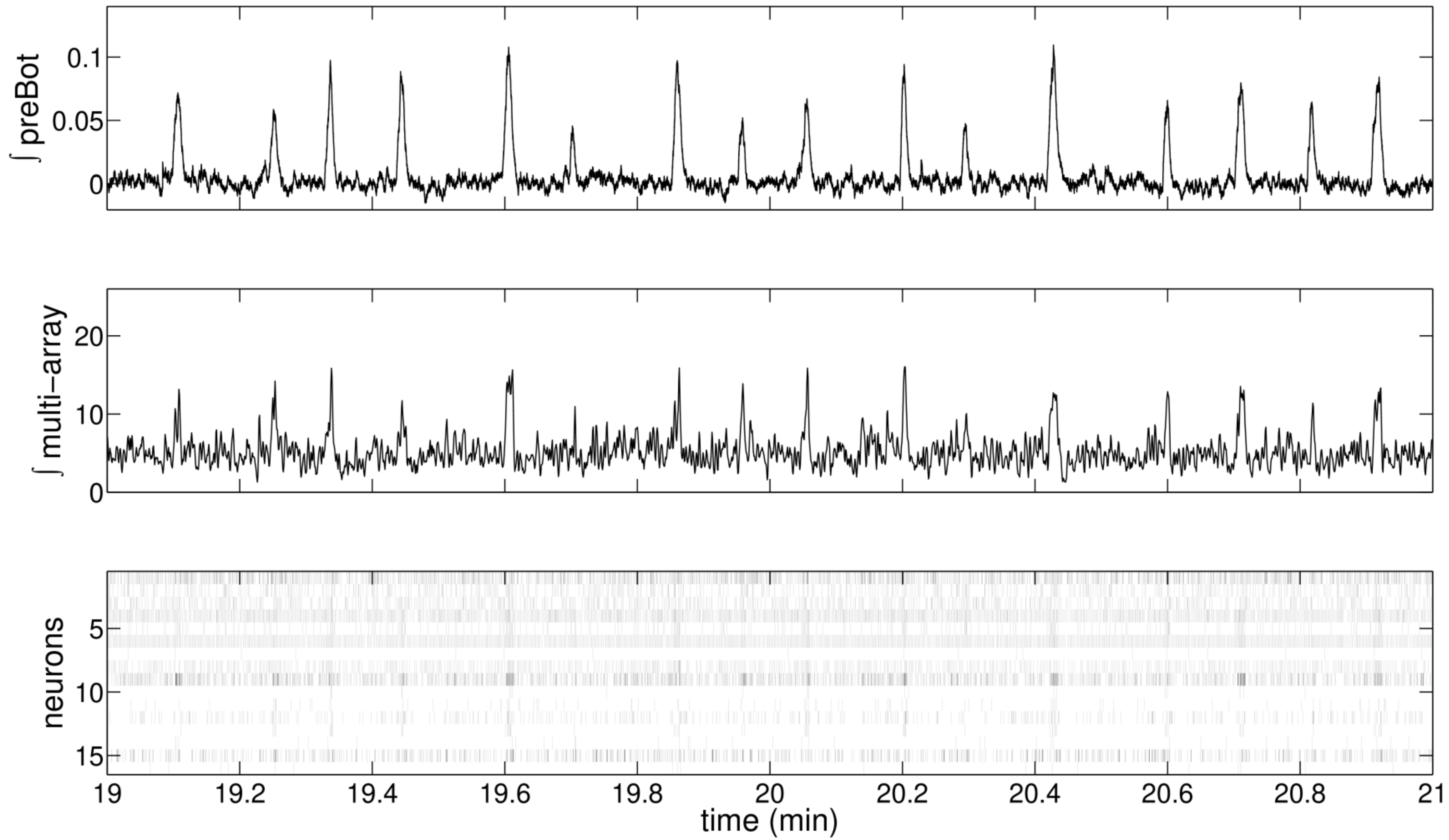
Experiments confirm E/I balance determines synchrony

Control: χ=0.56



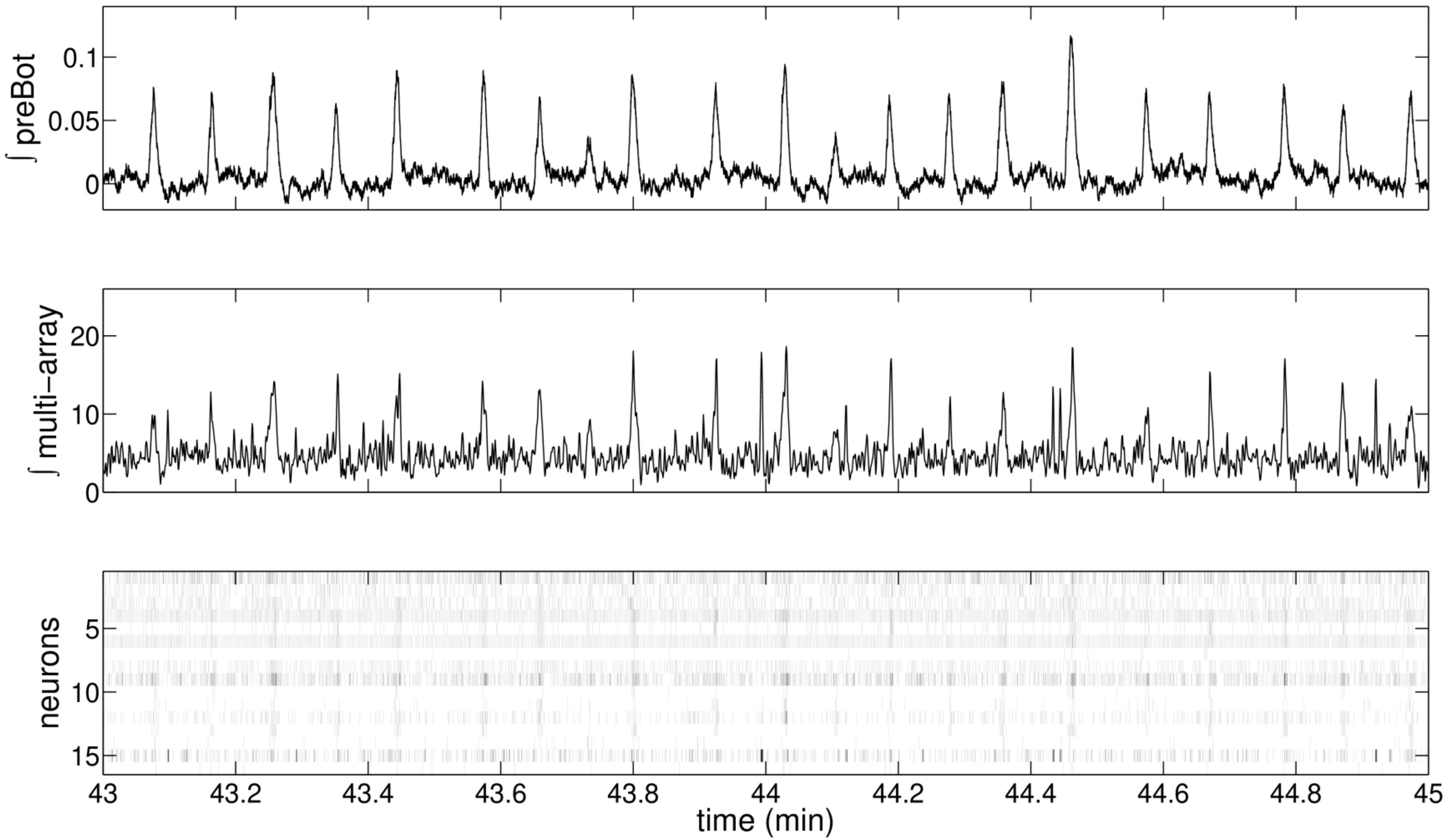
Experiments confirm E/I balance determines synchrony

DNQX @ 0.7 μM: χ=0.43



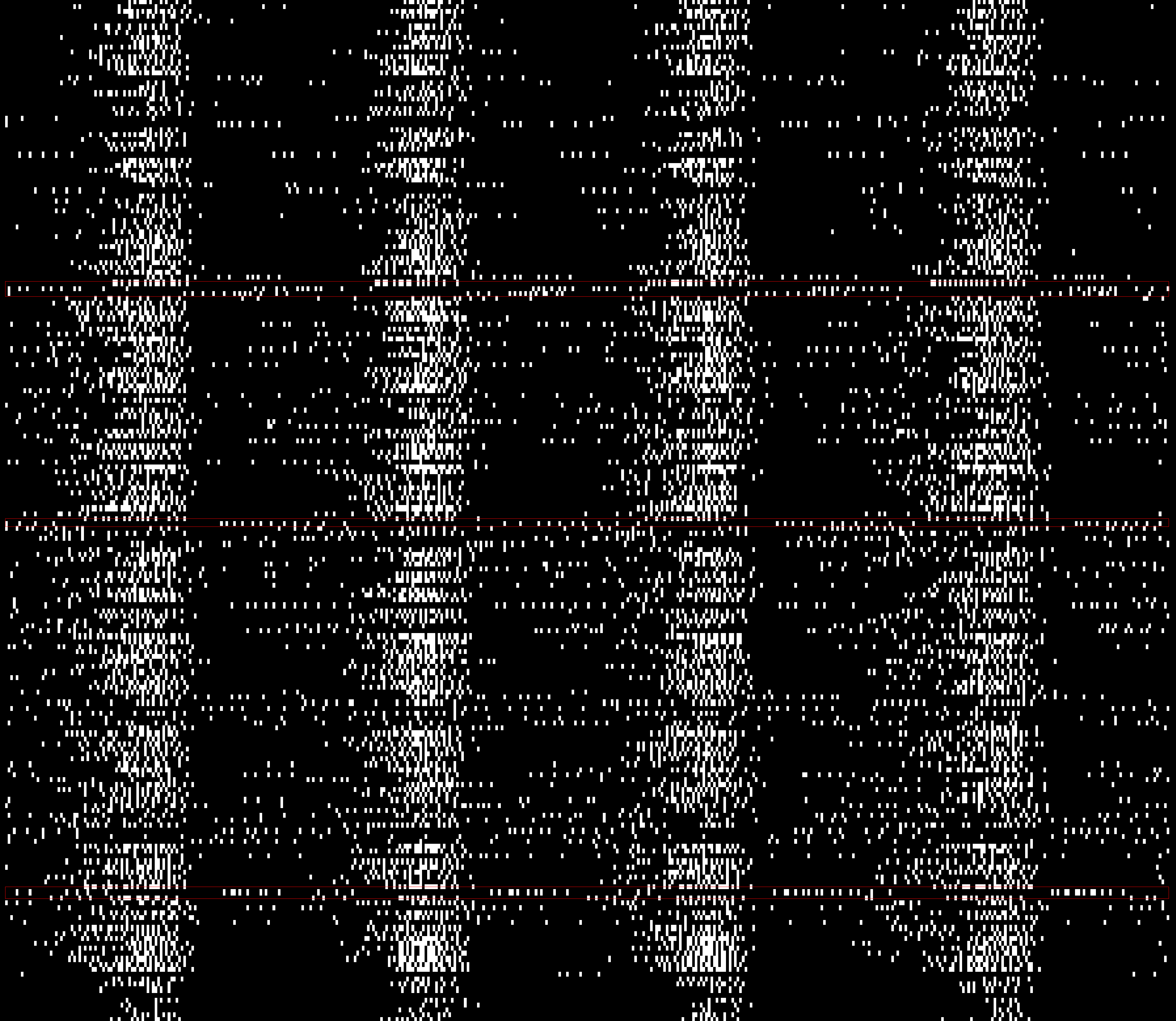
Experiments confirm E/I balance determines synchrony

DNQX @ 0.7 μM, PTX @ 20 μM: χ=0.50

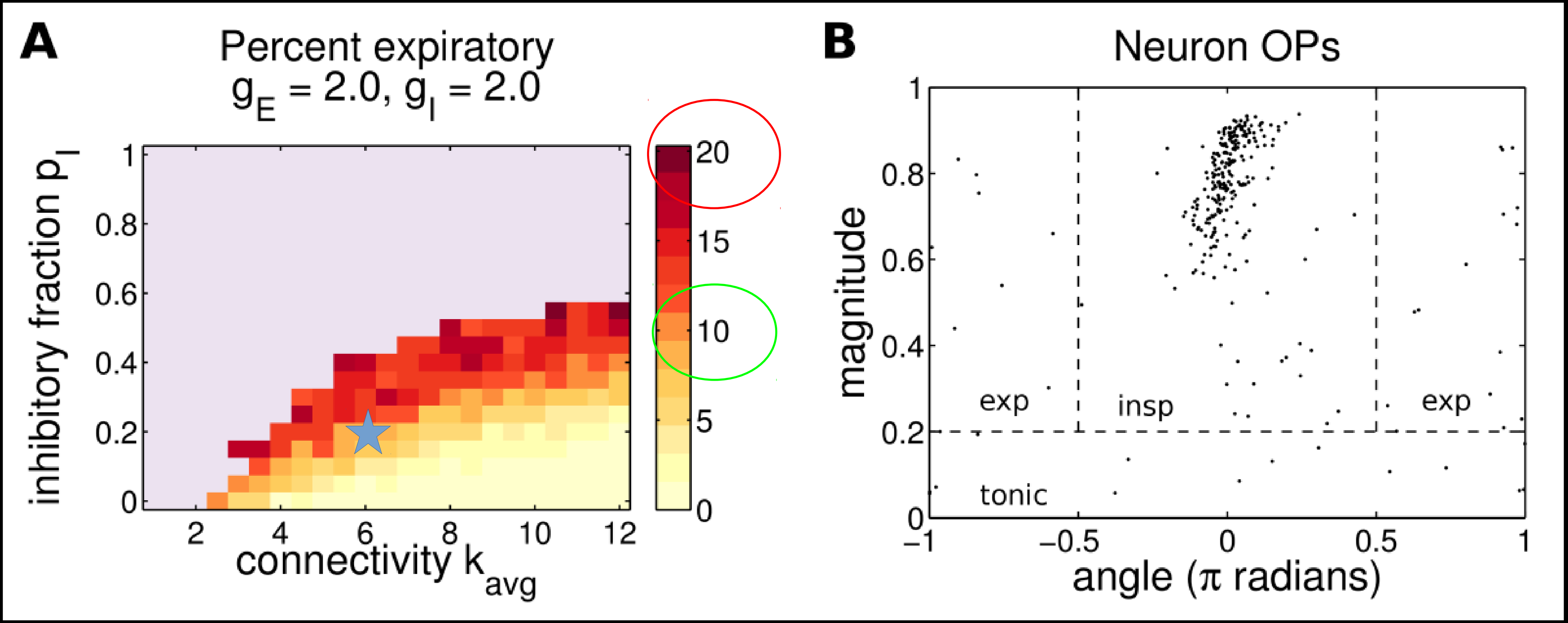


In model, with p_I=0.2

Expiratory cells



Expiratory neurons arise from inhibition

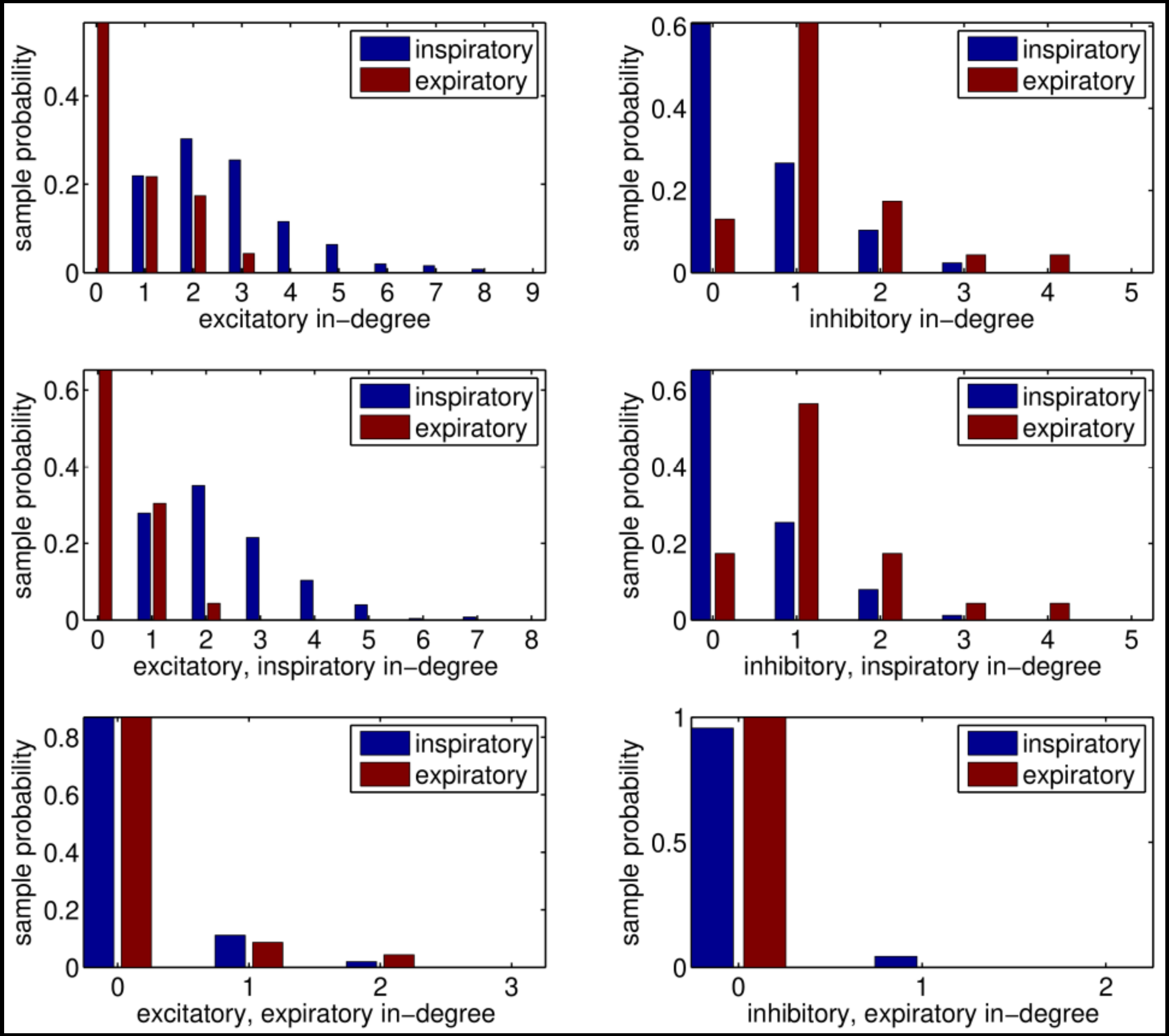


Inputs determine phase

Overall degrees:

Degrees labeled by phase:

- **Expiratory** neurons receive **less excitation**, preferentially **from other expiratory**
- **Expiratory** neurons receive **more inhibition**, preferentially **from inspiratory**
- Inspiratory is reverse

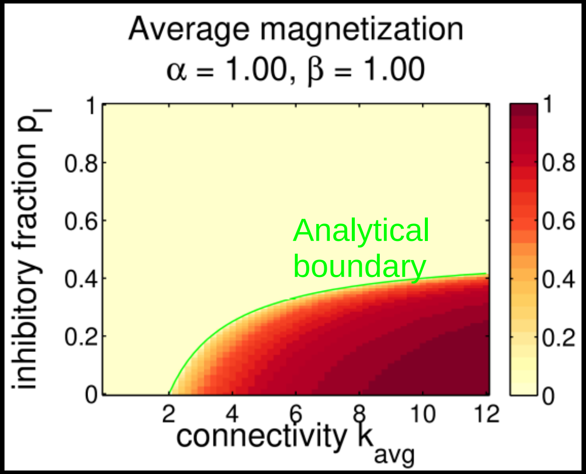


“Phases as spins” model reproduces synchrony phase diagram

Phases align/anti-align based on excitatory/inhibitory inputs
Makes sense with “binary”-like bursting neurons

We construct a spin-type model that includes both effects:

$$H = -\sum_{i<j} A_{ij}^{(\mathrm{E})}\sigma_i\sigma_j + \alpha\sum_{i<j} A_{ij}^{(\mathrm{I})}\sigma_i\sigma_j$$

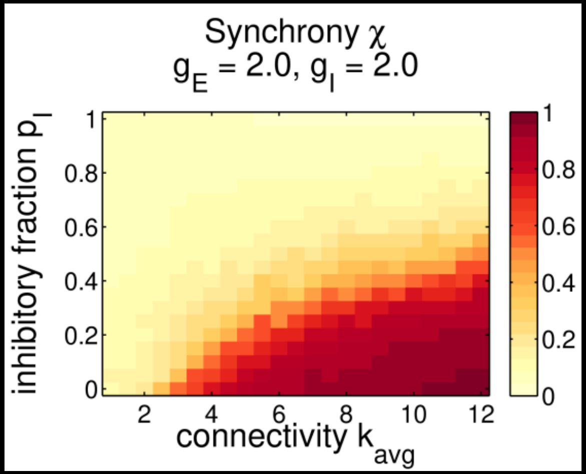


Mean field theory for locally tree-like graphs: sparse ER
[Dembo & Montanari 2010]

MF synchronization

$$\bar{m} = \sum_k P(k)\tanh\left(\beta(1-p_I-\alpha p_I)k\bar{m}\right)$$

versus



Implicit equation for amount of synchronization

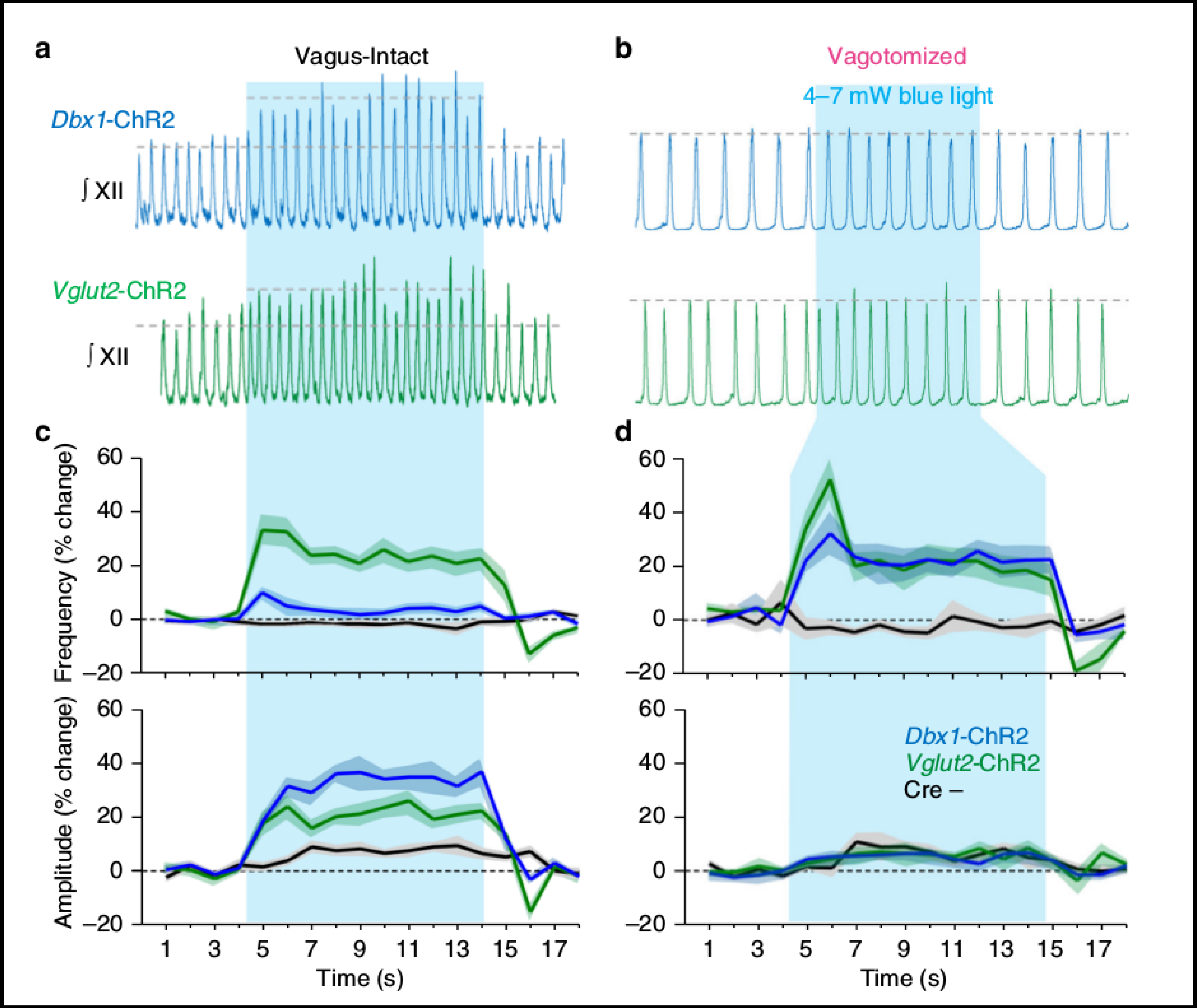
Yields phase boundary:

$$p_I < \frac{1}{1+\alpha}\left(1-\frac{1}{\beta k_{\mathrm{avg}}}\right)$$

So what good is inhibition?

- Diversity of cell types: expiratory cells
- Shapes the rhythm – broader than w/o
- A control knob
  - Sherman et al. (2015) deactivate rhythm w/ strong optogenetic input to Gly2 cells in vivo
  - Work by Baertsch et al.
- Gain control [e.g., Azim], dynamic range

Control knob: stimulating I population



Optogenetic experiments *in vivo*
Baertsch, Baertsch, Ramirez (2018)

Thank you! Acknowledgments

- Harris, Dashevskiy, Mendoza, Garcia III, Ramirez, Shea-Brown. Different roles for inhibition in the rhythm-generating respiratory network. J Neurophysiology 118(4), 2070-2088. 2017.
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  - Alfredo J. Garcia III
  - Jan-Marino Ramirez
- University of Washington Applied Math
  - Eric Shea-Brown
  - Joshua Mendoza (now at PNNL)
- NSF Grant #1122106, Boeing fellowship, Big Data Training Grant

Exercise: neurons & synchrony

- A short exercise in Jupyter
  - **github.com/kharris/amath50**
  - `python 3 + jupyter + numpy/scipy`
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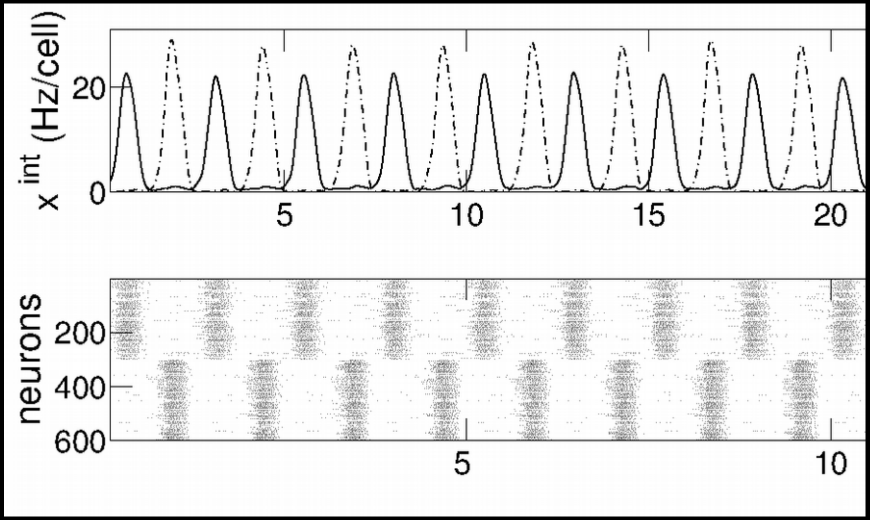
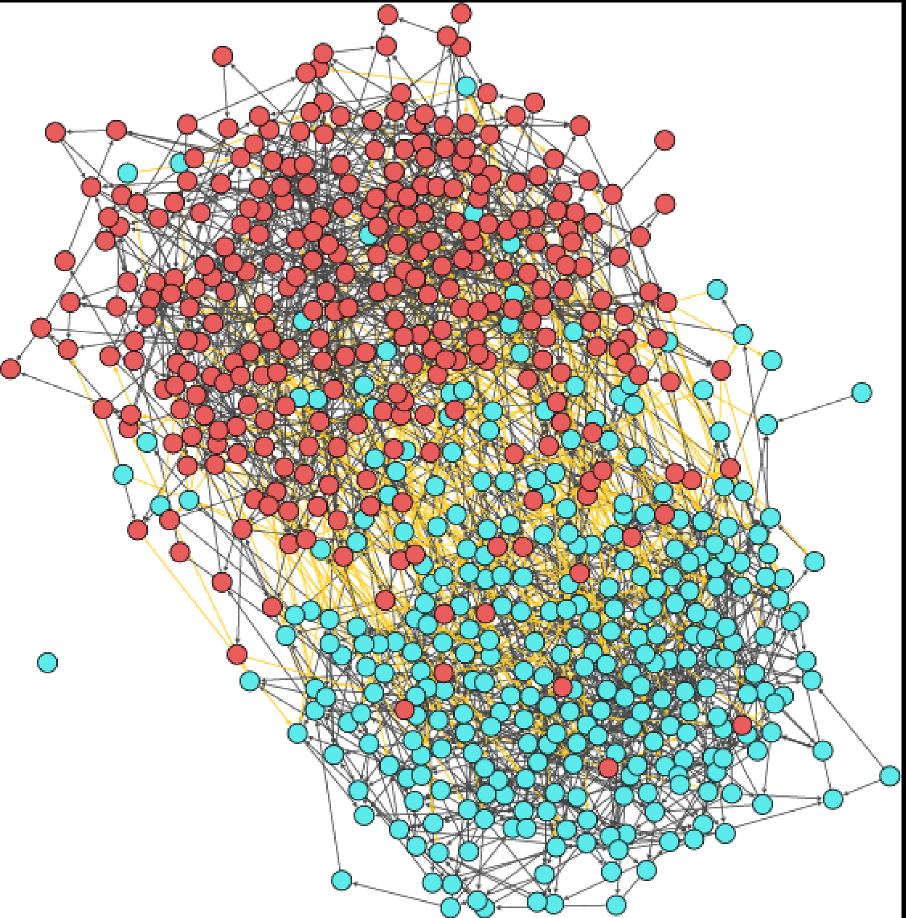
How to get 50% expiratory neurons?

- PreBot & Botzinger complexes (inspiration + active expiration)
- **Add structure to network**





2-block stochastic block model

Work with undergraduate
Joshua Mendoza

Synchrony measure

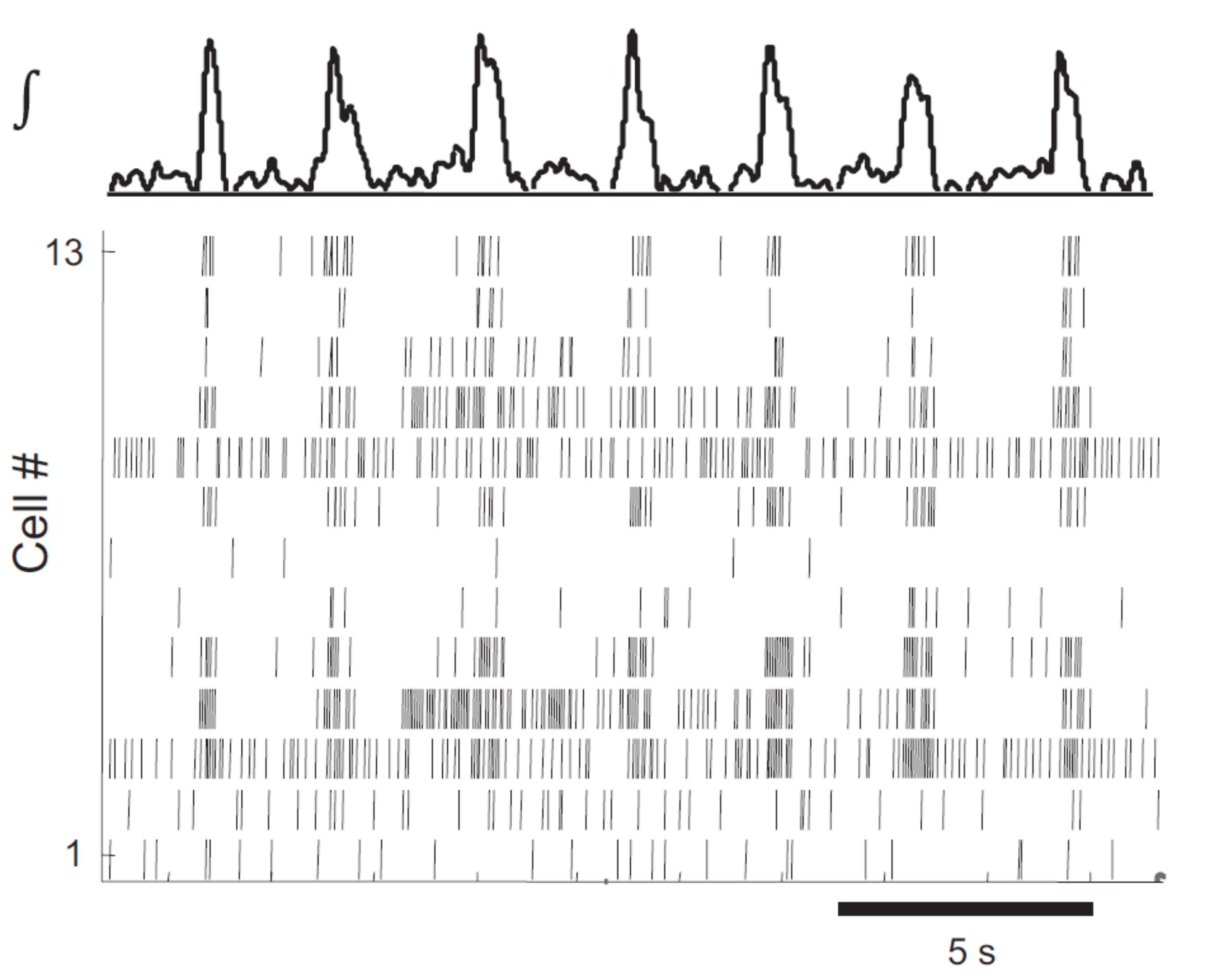
$$\chi = \left(\frac{\langle \bar{x}^{\mathrm{filt}}(t)^2 \rangle_t - \langle \bar{x}^{\mathrm{filt}}(t) \rangle_t^2}{\frac{1}{N} \sum_{i=1}^{N} \left[\langle x_i^{\mathrm{filt}}(t)^2 \rangle_t - \langle x_i^{\mathrm{filt}}(t) \rangle_t^2 \right]} \right)^{1/2}$$

Square root of ratio of

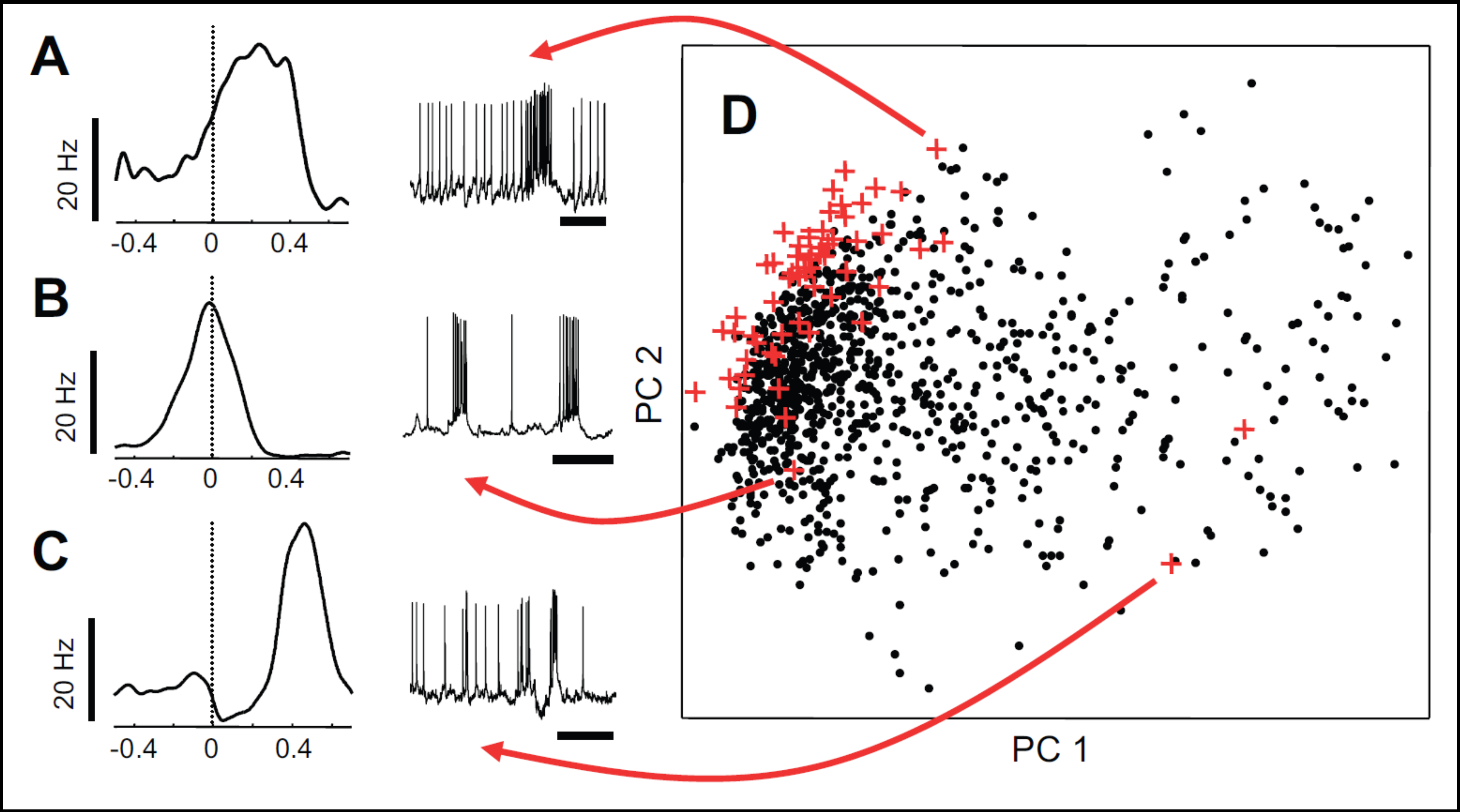
- MS deviations of pop average to
- pop average of MS deviations

Stochastic assembly

Cycle-cycle role of individual neurons is variable



Carroll, Viemari, Ramirez. J Neurophysiol (2013).



Red dots = intracellular recordings
Black dots = multielectrode

Carroll, Viemari, Ramirez. J Neurophysiol (2013).