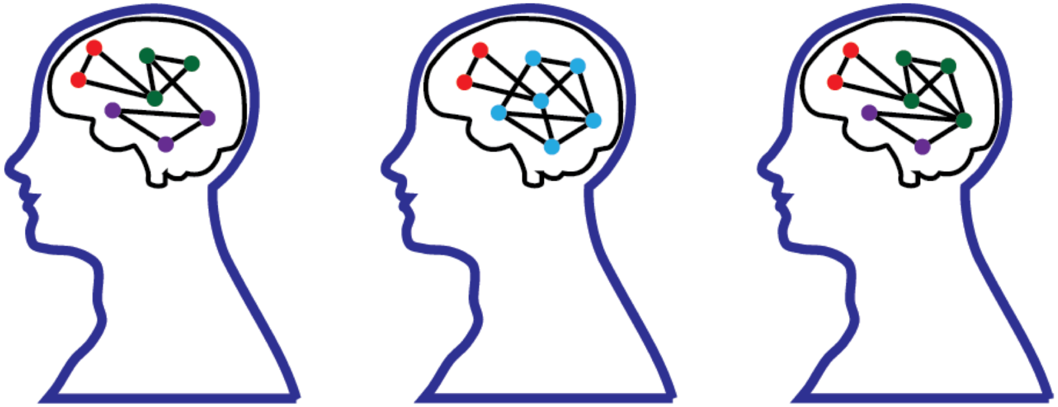
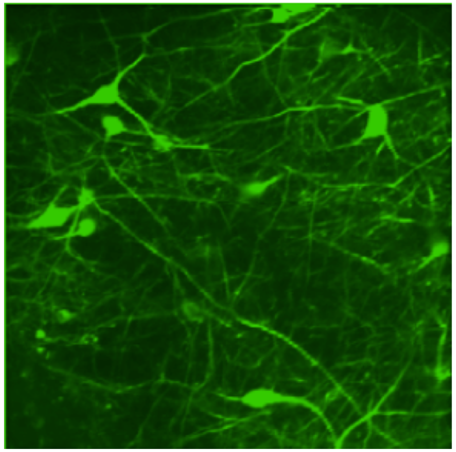
Detecting state changes in evolving functional networks

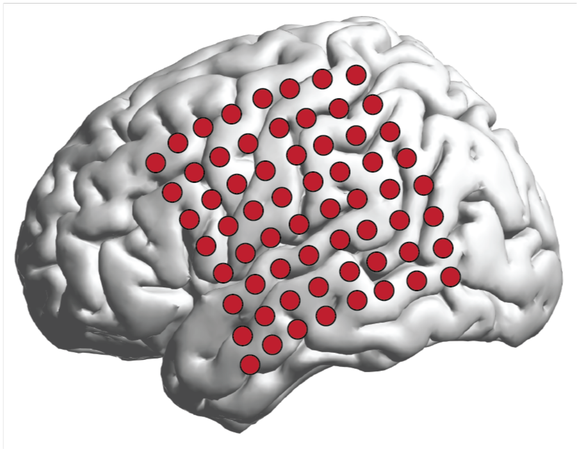


Sarah Feldt Muldoon
Threshold Networks
July 24, 2019

Networks in Neuroscience

Choice of scale determines how networks are built



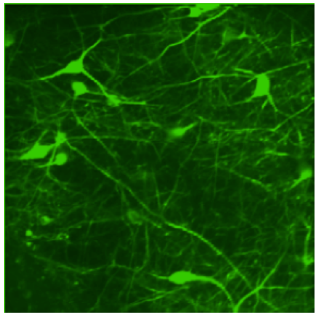


Micro-scale

Macro-scale

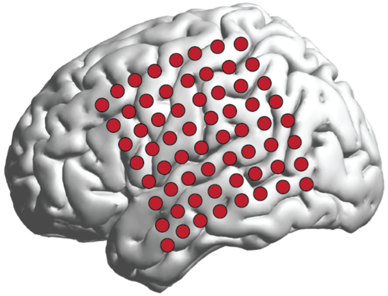
Neurons → Brain Regions

Multi-scale exploration



Micro-scale: calcium imaging data

- Community structure to find functionally similar groups of neurons
- Applications in epilepsy



Meso-scale: sensor data (ECoG/EEG)

- Individual differences
- Brain states in epilepsy

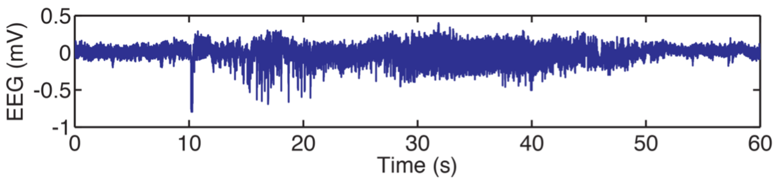
Macro-scale: MRI data (structural/functional)

- Individual differences
- Personalized Brain Network Models (BNM)
- Disease evolution in epilepsy

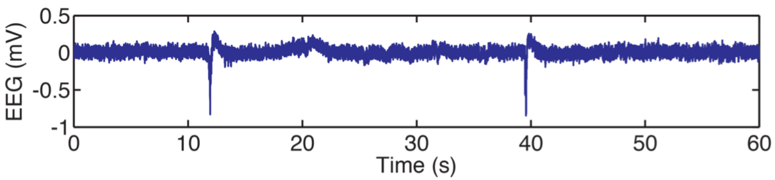
Motivation: Epilepsy

- ~1% of the world population suffers from epilepsy
- Epilepsy is characterized by recurrent seizures

Pathological dynamics: seizures



Pathological dynamics: interictal spikes



- 30% of epilepsy patients don't respond to medication
  - Surgical resection is an option

Very little is known about the underlying causes of epilepsy

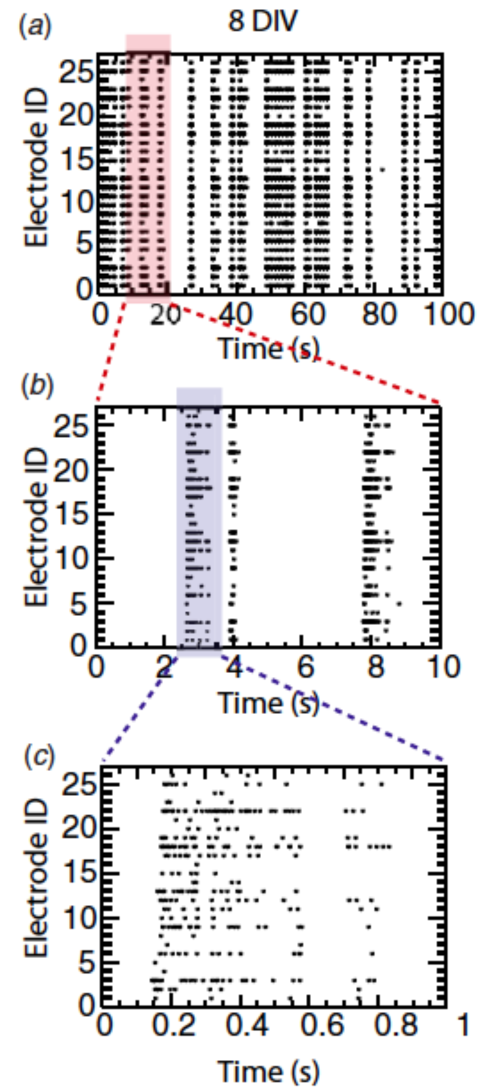
The big question:

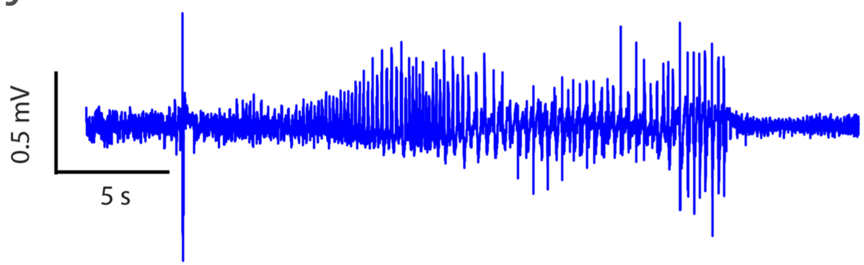
How does micro-scale activity relate to macro-scale brain dynamics?

In epilepsy, we are specifically interested in the role of individual neurons in seizures (interictal spikes).

Seizure = hypersynchronous activity?

- how do we want to define "hypersynchronous"?

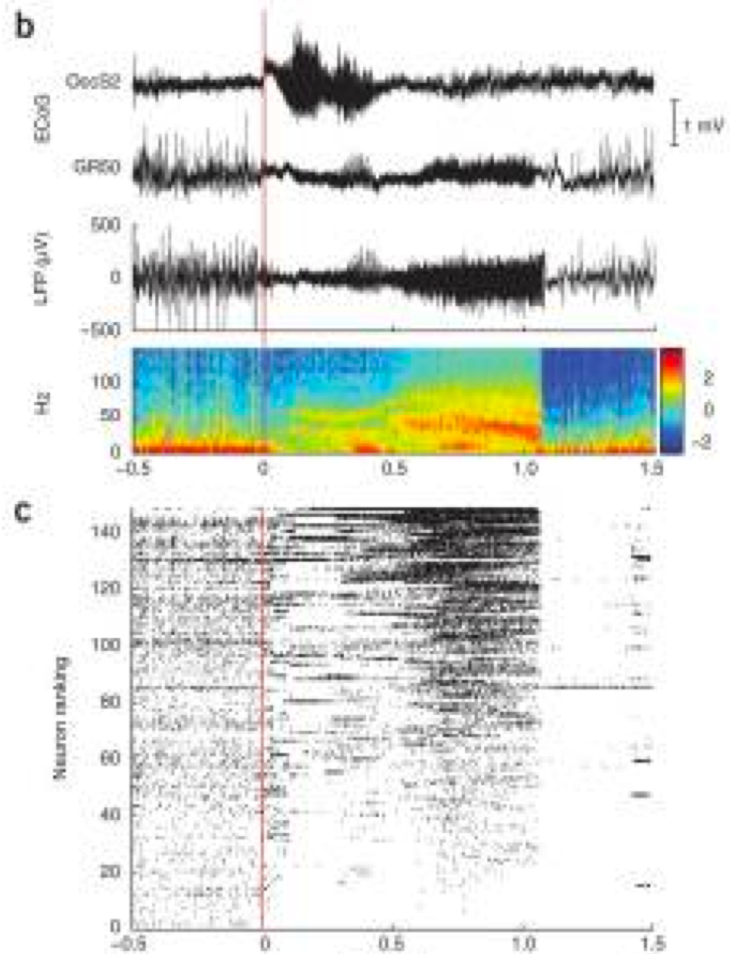




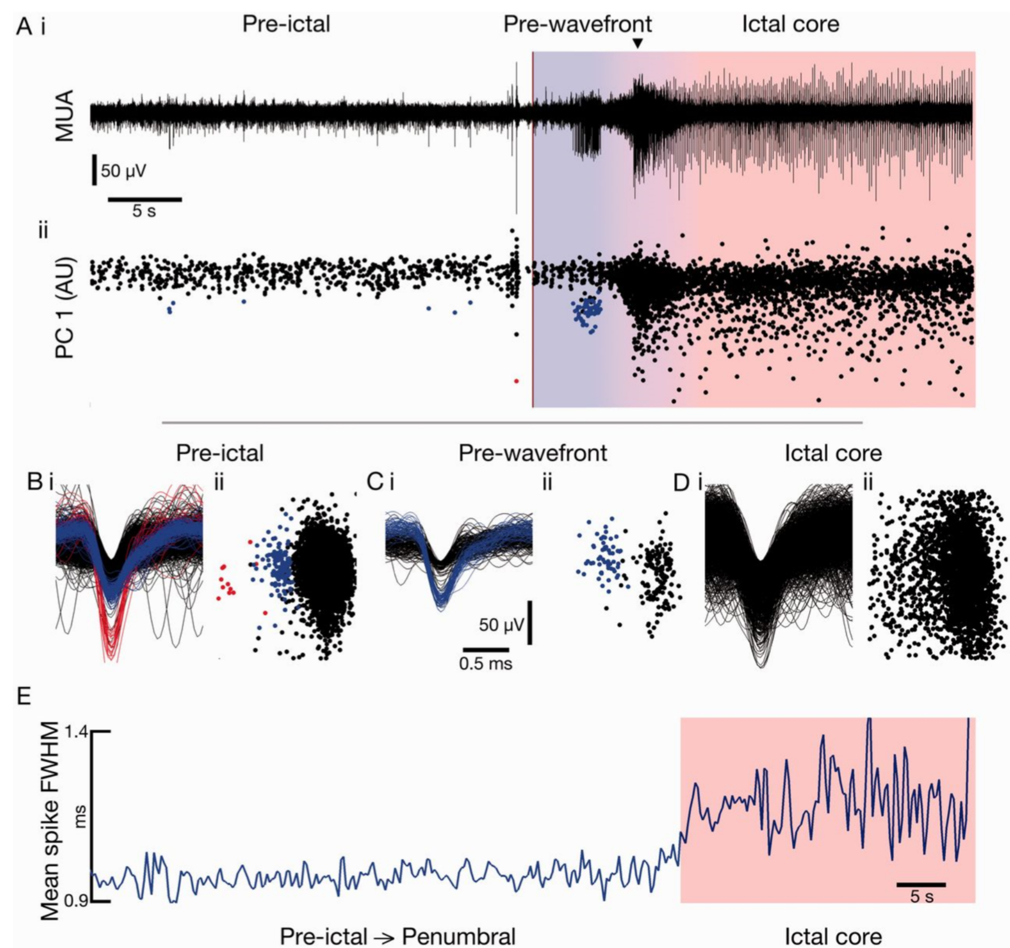
Feldt et al. (2010) Phys Bio

Individual neurons are heterogeneous

Truccolo et al. (2011) Nat Neuro.



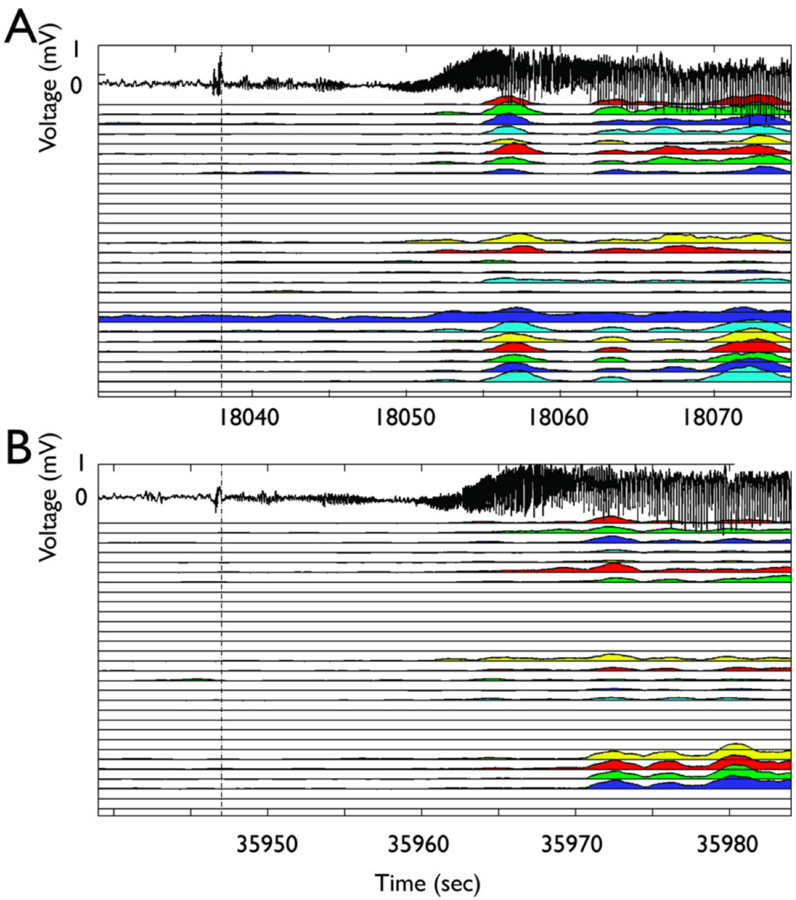
Merricks et al. (2015) Brain



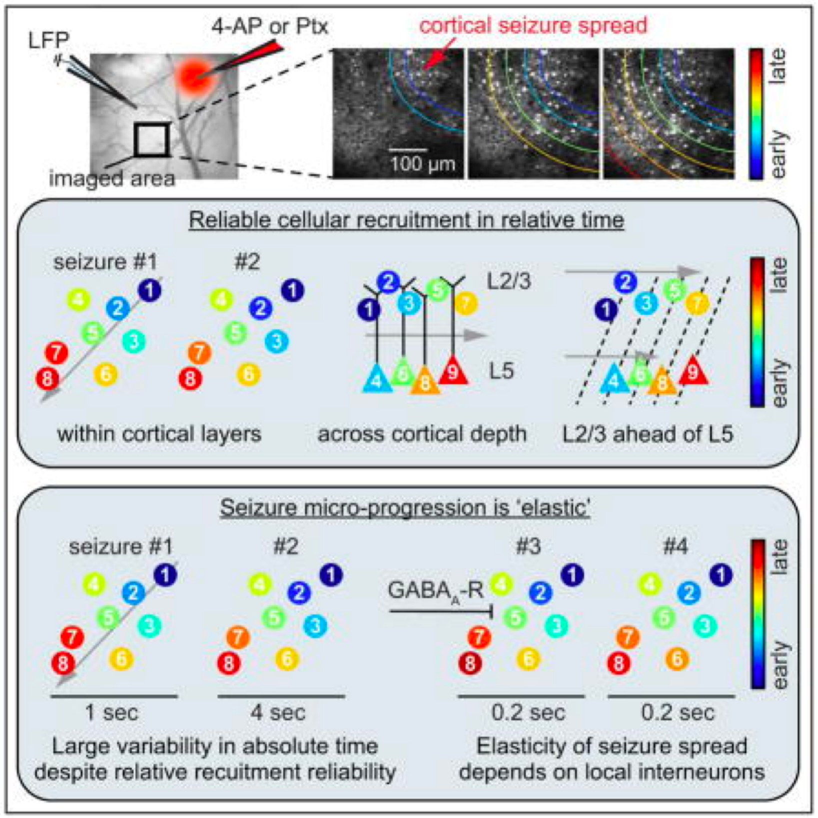
Are all seizures the same?

No! Yes! It depends?

Bower et al. (2012) Epilepsia



Wenzel et al. (2015) Cell Rep



Many factors to consider

When comparing data, publications, methods, etc., the details matter!

- spatial location
- model/type of epilepsy
- modality

Variability can be good, we just need to understand it more

Remember: a seizure is the macro-scale event

We need more tools/techniques

Q: How can we quantify the patterns of neural activity before and during a seizure?

A: Detection of the evolution of cell assemblies

Q: What is a cell assembly?

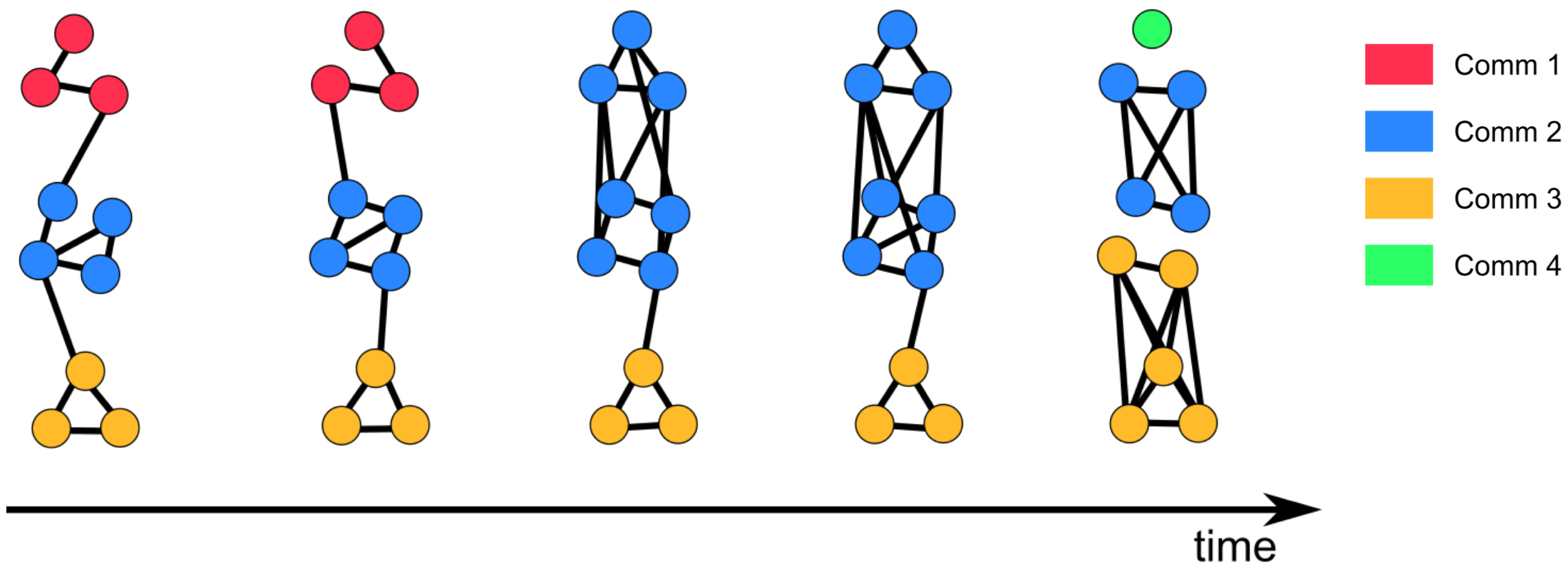
A: A group of neurons with synchronized firing patterns.

Q: Why was I told this was a talk about networks?

A: Cell assemblies = Communities in a functional neuronal network

Goal

We want to study the evolution of community structure in functional temporal networks.

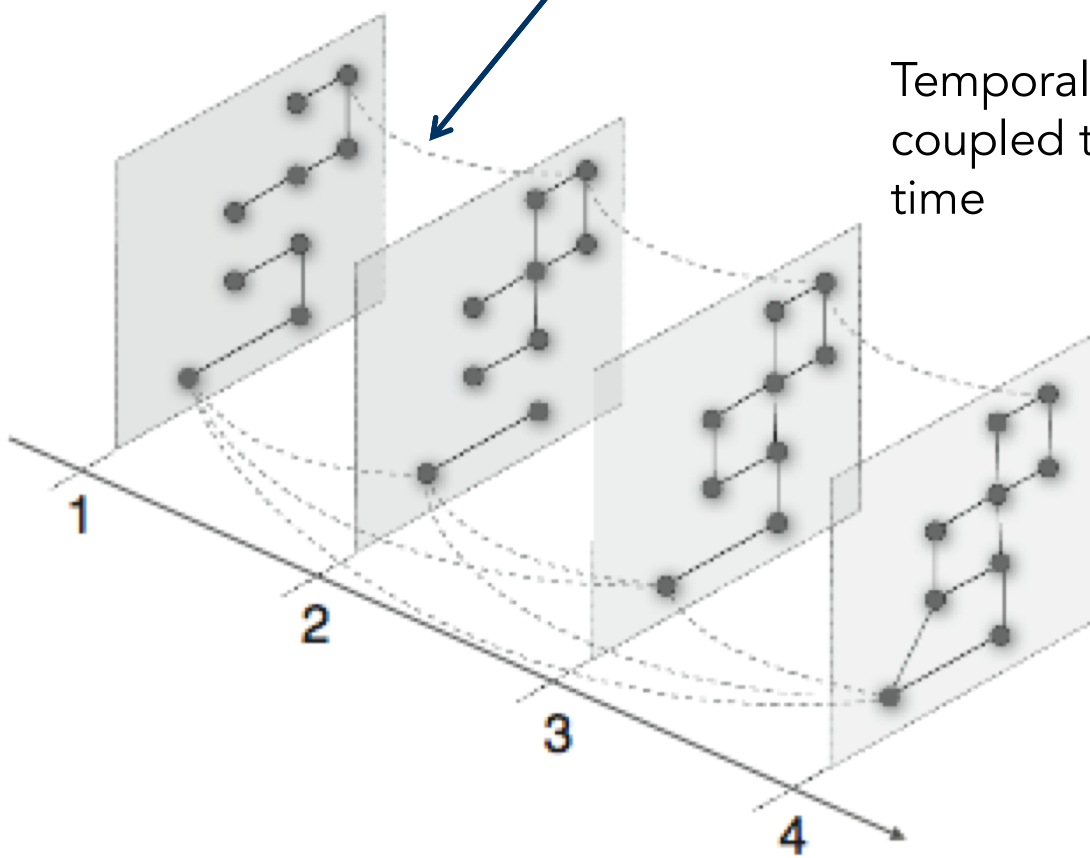


Multilayer networks – temporal networks

Sequential graphs : time ordered snapshots of structure

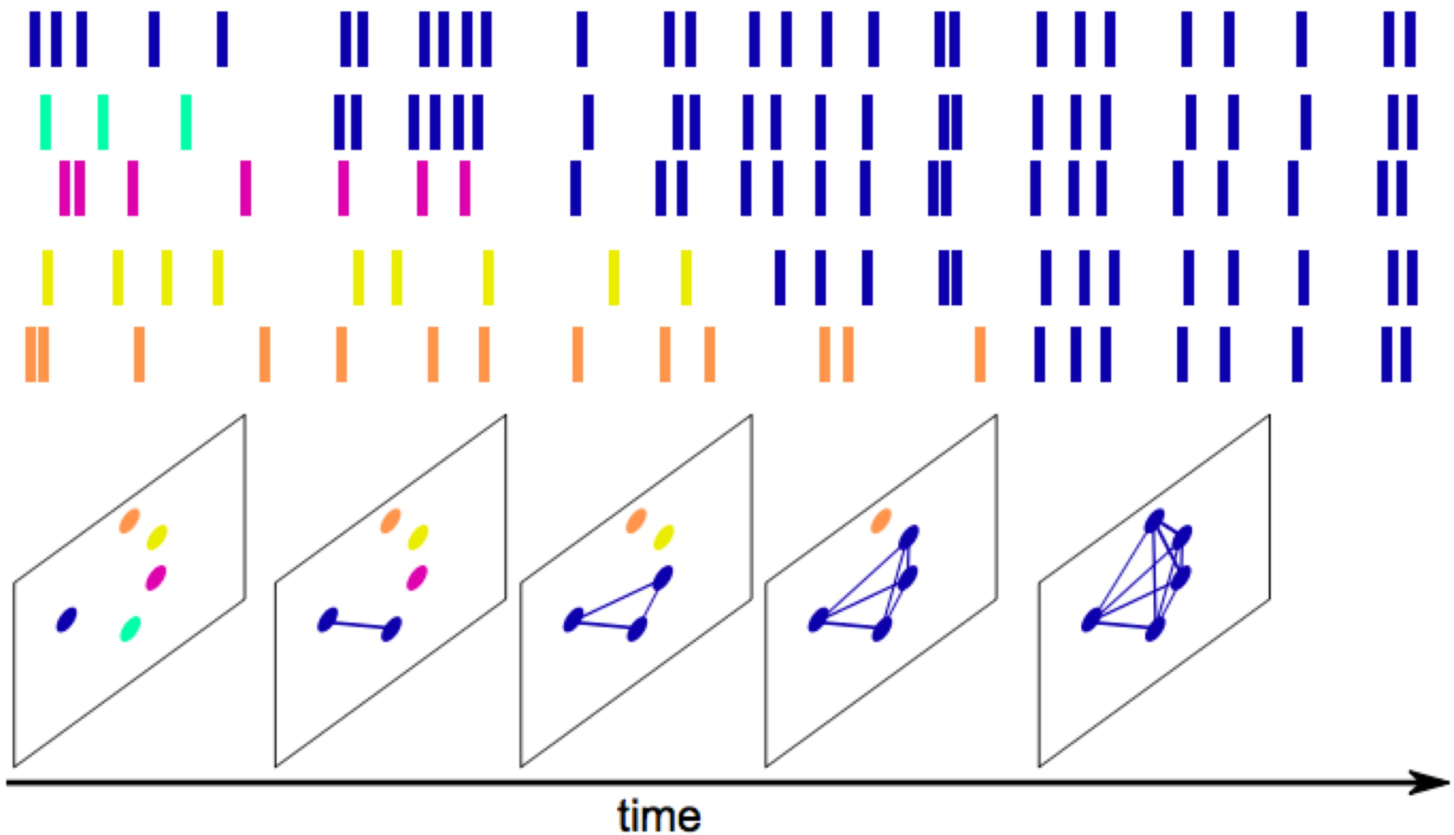
Inter-layer
identity links

Temporal data: layers
coupled to layers adjacent in
time



Mucha et al. (2010) Science

Model neuron firing as a network



Multilayer community detection

Multilayer modularity maximization

$$P = \{C_1, C_2, \ldots, C_n\}$$

Sum over layers

Adjacency Matrix

Resolution Parameter For Module Size

Community i in time layer t

Community i in time layer t

$$Q(P) = \sum_{t}^{L} \sum_{ij} (A_{ijt} - \gamma R_{ijt}) \delta(c_{i_t}, c_{j_t}) + \sum_{t}^{L-1} \sum_{i} 2 B_{it} \delta(c_{i_t}, c_{i_{t+1}})$$

Null Model Adjacency Matrix

Community j in time layer t

Community i in time layer t+1

Interlayer self-identity links

Interlayer links

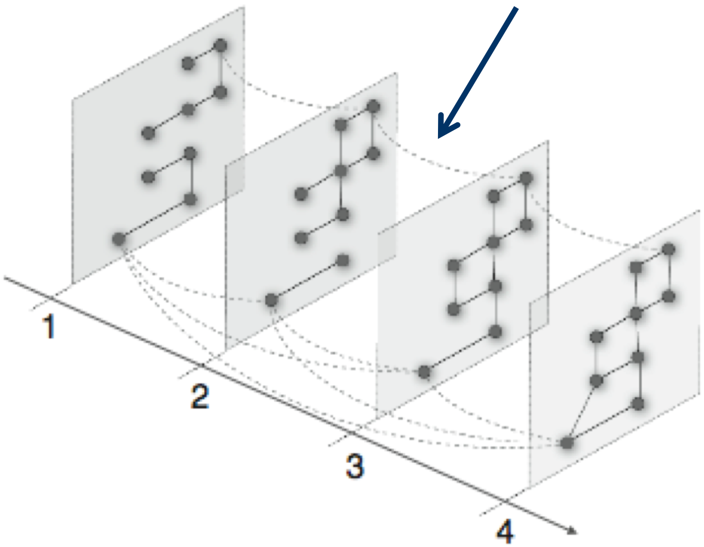
Connect a node to itself over time

How do we determine the strength of these links?

- Common assumption: Set all interlayer links to the same constant value across all layers

$$B_{it} = \omega$$

Inter-layer identity links



Simplifying assumption still not simple

Modularity function is still dependent on the choice of 3 parameters:

Null Network

$$Q(P) = \sum_{t}^{L} \sum_{ij} (A_{ijt} - \gamma R_{ijt}) \delta(c_{i_t}, c_{j_t}) + \sum_{t}^{L-1} \sum_{i} 2\omega \delta(c_{i_t}, c_{i_{t+1}})$$

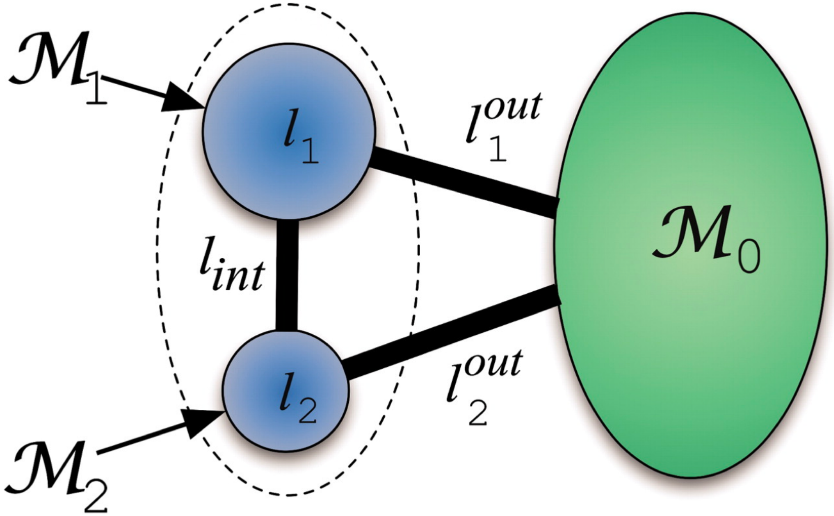
Intralayer resolution parameter

Interlayer coupling parameter

Problems with multilayer modularity

Single layer resolution limit

- Modularity maximization won't necessarily detect small communities
- γ parameter added to mitigate effects of resolution limit



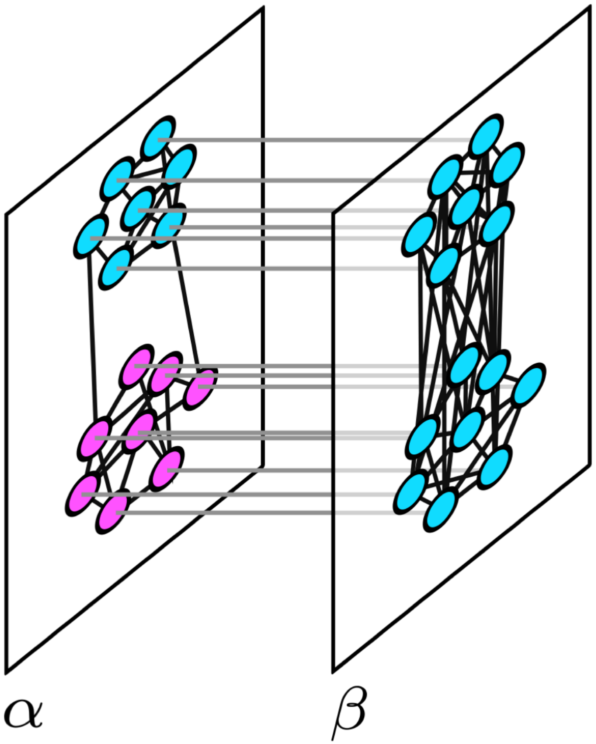
Also a multilayer resolution limit!

Fortunato and Barthélemy (2007) PNAS

Community mergers

Upper bound (Ω) on ω beyond which communities cannot be detected

- Related to γ and R

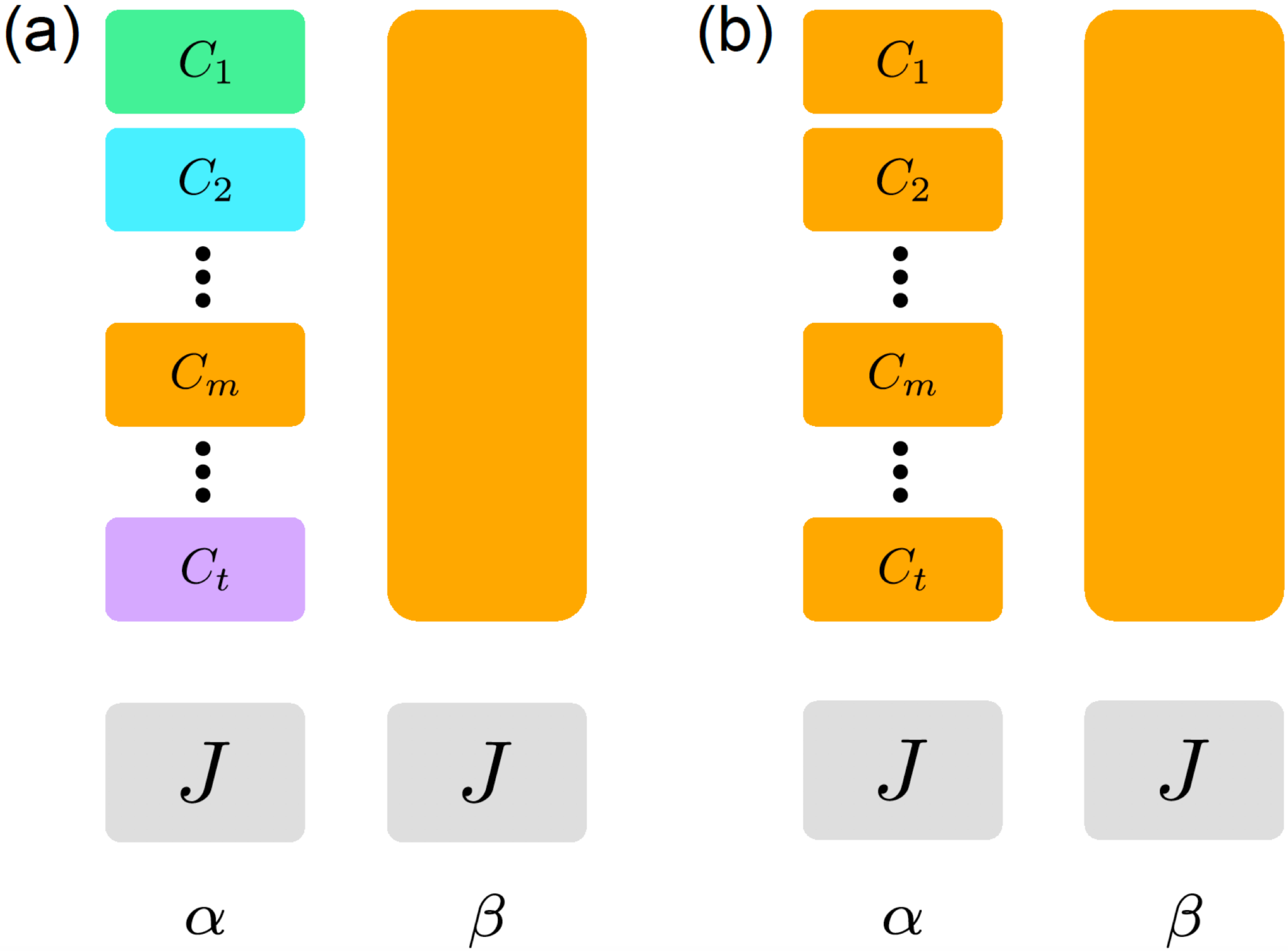


$$\Omega_t = \sum_{\substack{ij \in K \\ \delta(c_{i_t}, c_{j_t}) = 0}} \frac{1}{2\theta}(\gamma R_{ijt} - A_{ijt})$$

$$\theta = |K| - |C_{max}|$$

K is the subset of nodes that participate in the merger, C_{max} is the largest community

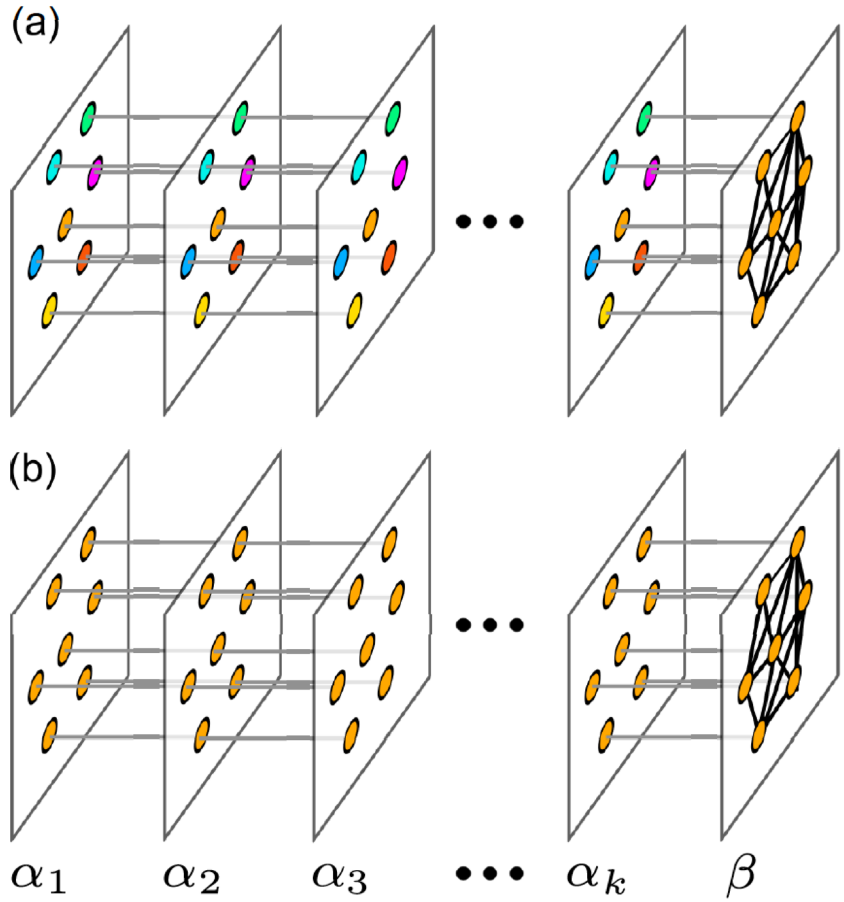
Multilayer resolution limit



Vaiana and Muldoon (2018) arXiv

Multilayer resolution limit

Important if you have unconnected nodes

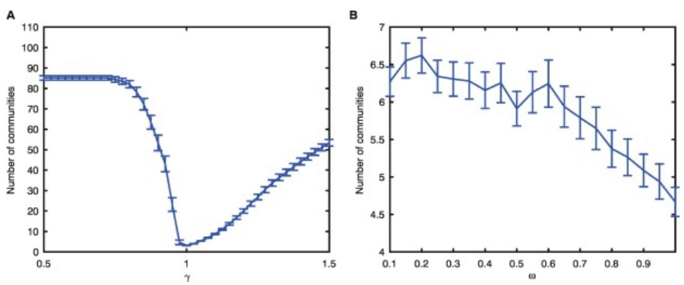


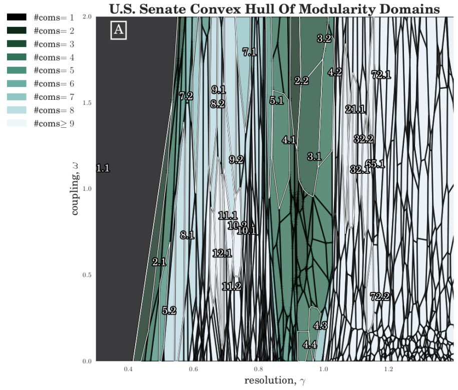
Vaiana and Muldoon (2018) arXiv

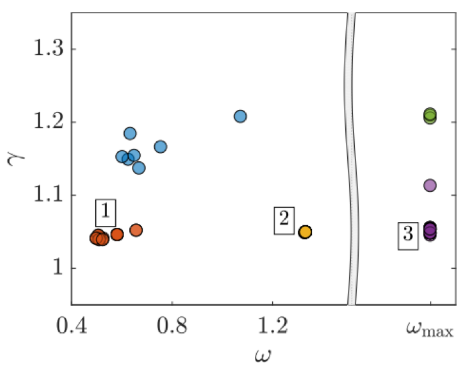
Problems with multilayer modularity

Still need to choose parameters

- Parameter sweeps – look for stability (Muldoon et al. 2018)
- CHAMP Algorithm: explore γ-ω landscape (Weir et al. 2017)
- Map to stochastic block model (Pamfil et al. 2018)
  - Gives layer dependent values!







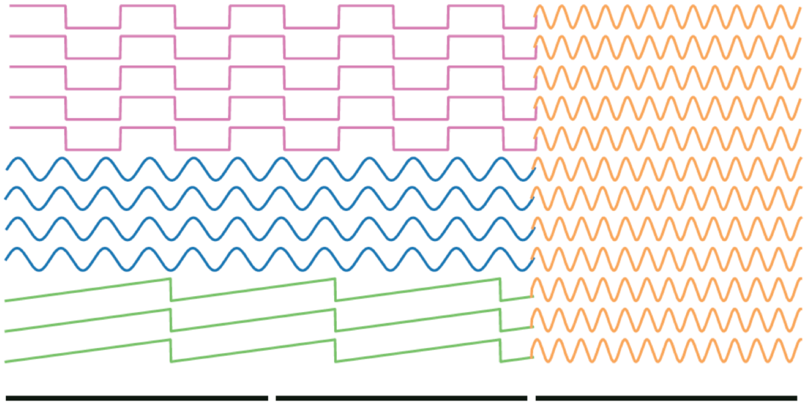
(a) Scatter plot of fixed points

Modeling physical systems

Simplifying assumption of ω = constant is rather arbitrary

What does ω represent in our model?
- Self-identity link

How similar is a node to itself from one layer to the next?
- Functional networks – nodes are dynamic!

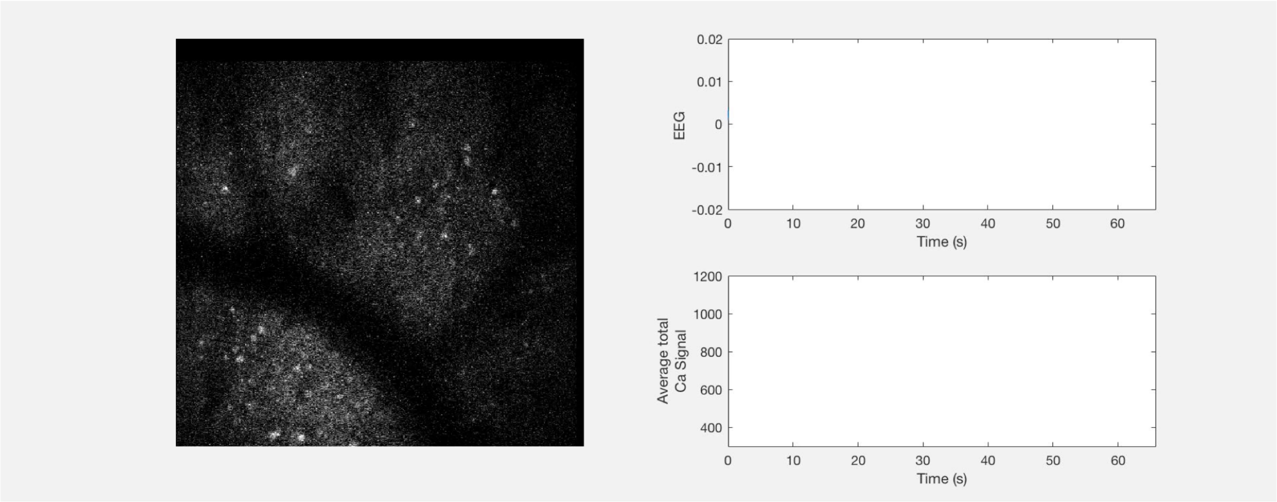


System can have state changes

Back to thinking about epilepsy

We want to be detect large scale state changes (transition to seizures)

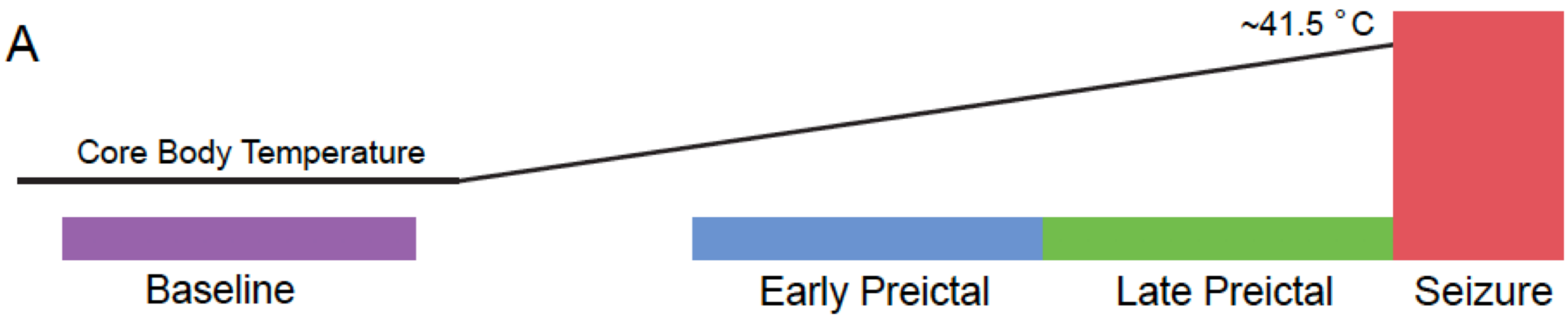
- Don’t understand relationship between single neuron state changes and system level state changes



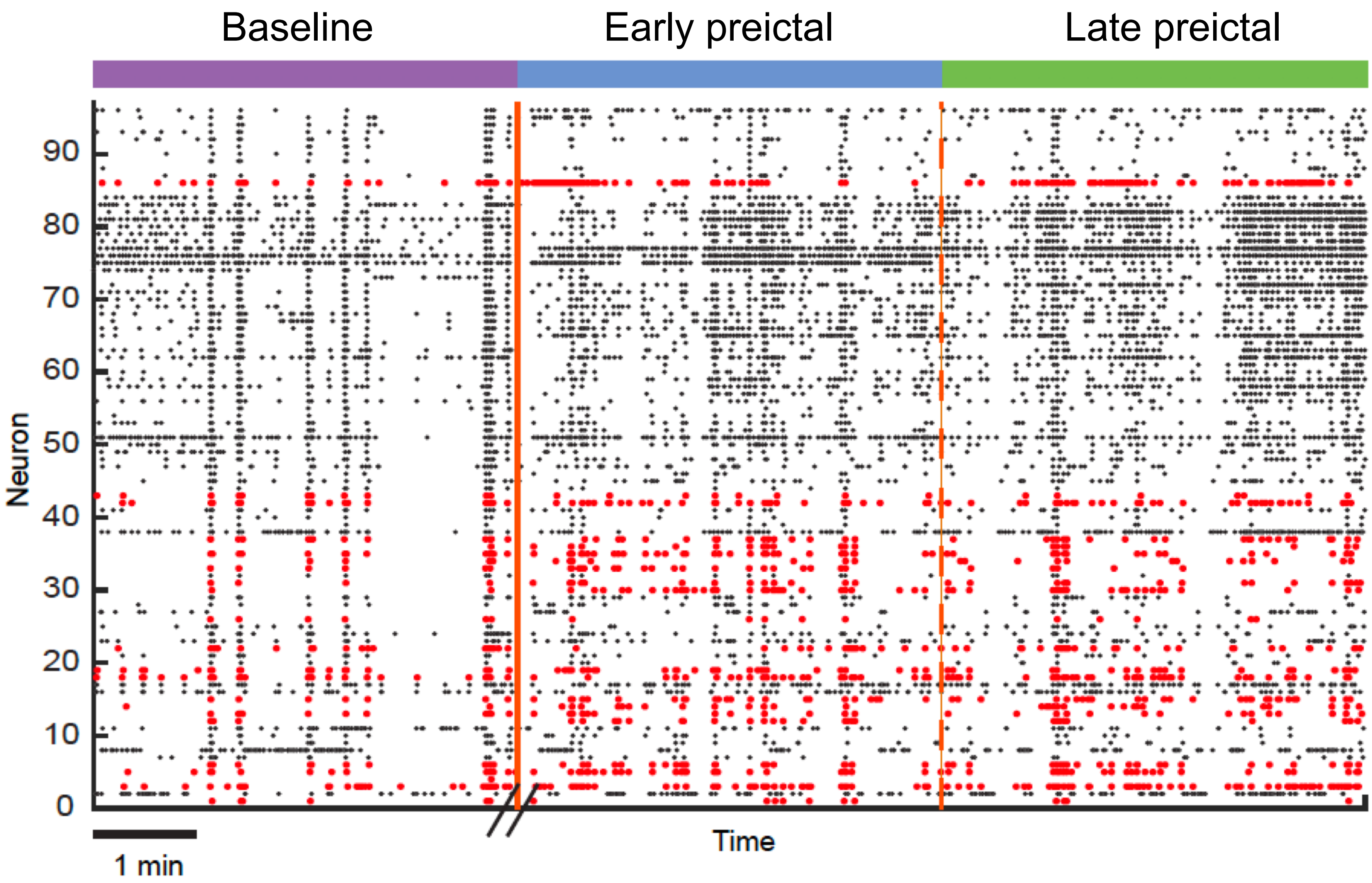
Data from Ethan Goldberg, CHOP/Penn

Focus on preictal period

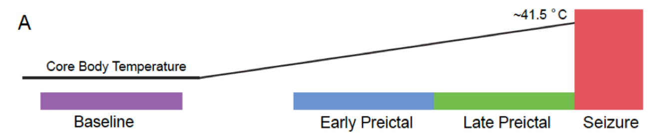
Mouse model of Dravet Syndrome: temperature dependent seizures



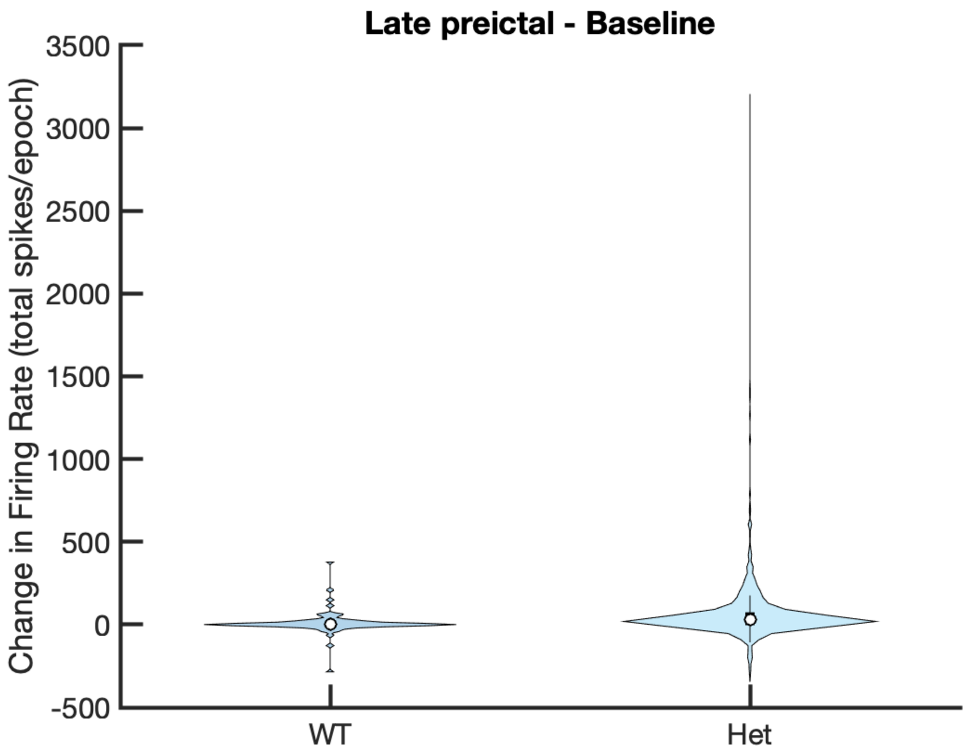
Single neuron firing before seizure



Firing rate changes



Heterogeneous changes in firing patterns



Neurons dynamics change over time

Modeling interlayer links

Choose strength of ω based on how similar a node is to itself from one layer to the next

"Similar" will necessarily be application dependent

For neuronal networks – look at change in firing rate

Represent self-similarity of node i between layers t and t+1 as $s(i_t, i_{t+1})$

Vaiana et al. (2018) J Complex Networks

Algorithm for "updating interlayer edges"

1. Choose ω_{global} and set $B_{it} = \omega_{\text{global}}$ for all i and t.
2. For each i and t if $s(i_t, i_{t+1})$ is 'small', then set $B_{it} = \rho\omega_{\text{global}}$.

How do we define small? – Application dependent

- Local threshold (over all nodes between two consecutive layers)
- Global threshold (over all nodes and all layers)

How do we choose ω_{global}? – Parameter sweep/consensus

- Fix choice of (γ,ω) and run consensus over multiple runs of algorithm
- Choose a grid of (γ,ω) values and run a consensus over a sweep of these values

Vaiana et al. (2018) J Complex Networks

Compare 4 methods

1. Fixed consensus. Choose a fixed value of (γ,ω) and run a consensus over multiple runs of the algorithm. DO NOT update interlayer edges.
2. Sweep consensus. Choose a grid of points in the (γ,ω) plane and run a consensus over a single run of the algorithm for each combination of these parameters. DO NOT update interlayer edges.
3. Fixed consensus with updates. Choose a fixed $(\gamma, \omega_{global})$ and run a consensus on multiple runs of the algorithm. During each run, additionally update interlayer edges.
4. Sweep consensus with updates. choose a grid of points in the $(\gamma, \omega_{global})$ plane and run a consensus over a single run of the algorithm for each combination of these parameters. For each choice of $(\gamma, \omega_{global})$, additionally update interlayer edges.

Vaiana et al. (2018) J Complex Networks

Example: Simulated neuronal data

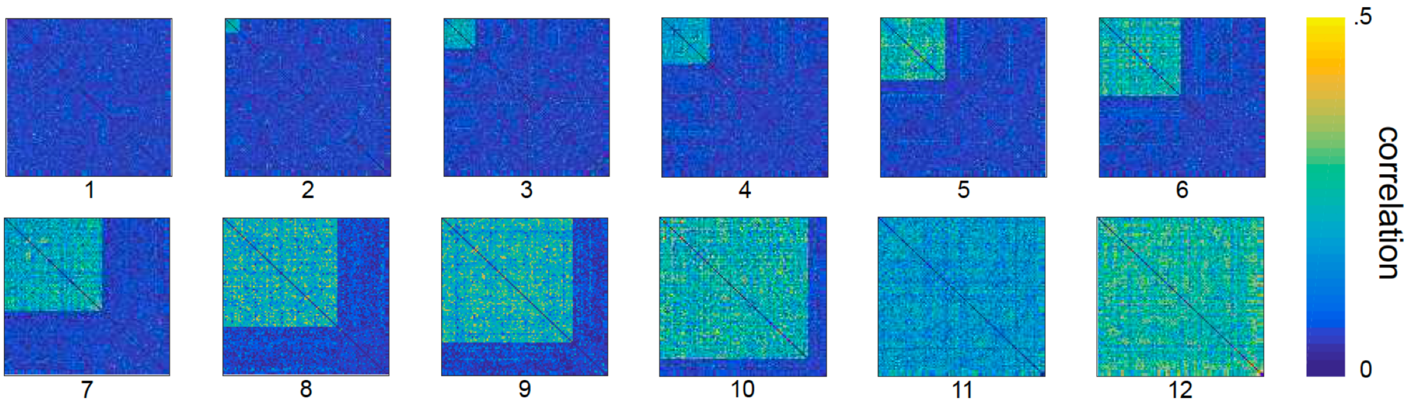
- 100 neurons modeled by Poisson process
- 12 seconds of activity
- Seconds 1-2: all neurons uncorrelated with firing rate 10 spikes/second
- Seconds 2-3: 10 neurons increase firing rate to 30 spikes/seconds and synchronize
- Seconds 3-4 10 more neurons increase firing rate and synchronize with others
- Continue until all neurons have increased firing rates and are synchronized

Vaiana et al. (2018) J Complex Networks

Spikes to networks

Build functional networks based on activity patterns of neurons – measure edge weight based on absolute value of Pearson correlation between firing patterns over some window

- Matching (1 second window)
- Disjoint (1.5 second window)
- Large (2 second window)



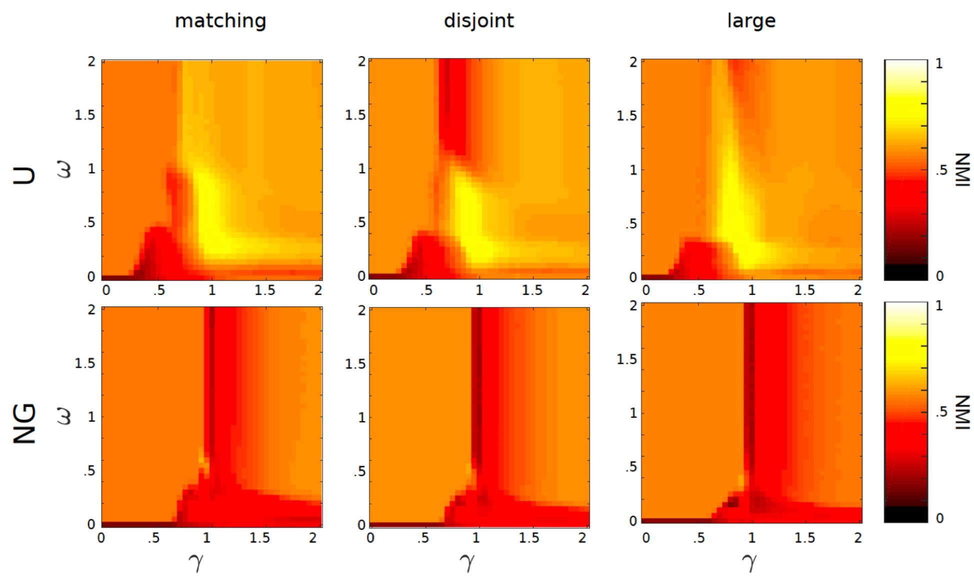
Vaiana et al. (2018) J Complex Networks

Extracting evolving communities

First determine "optimal" (γ,ω)

- 100 synthetic networks
- Examine (γ,ω) in [0,2] x [0,2], step size 0.05
- Compare detected community evolution with ground truth using Normalized Mutual Information (NMI)
- Do this for both Newman-Girvan (NG) null network and Uniform (U) null network

Note: VERY computationally expensive



Vaiana et al. (2018) J Complex Networks

Specify updating rule

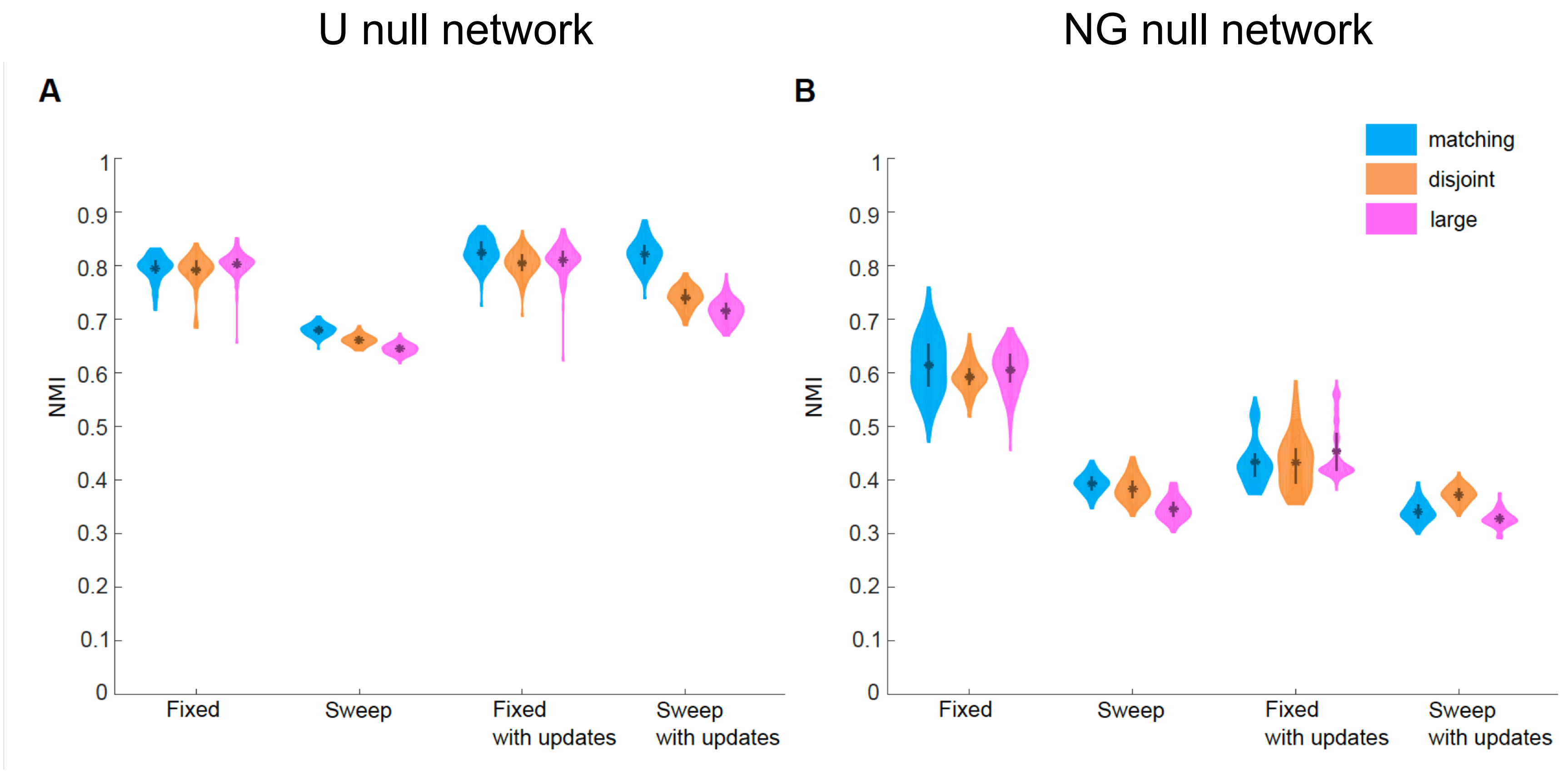
1. Choose ω_{global} and set $B_{it} = \omega_{\text{global}}$ for all i and t.
2. For each i and t if $s(i_t, i_{t+1})$ is 'small', then set $B_{it} = \rho\omega_{\text{global}}$.

How do we define "small"?

Local threshold:

- For each consecutive pair of layers calculate change in firing rate
- If a neuron's change in firing rate is τ = 2 or more standard deviations from the mean, update the interlayer edge for that neuron based on the above rule
- Use ρ=0.1 (smaller is better)

Comparing methods



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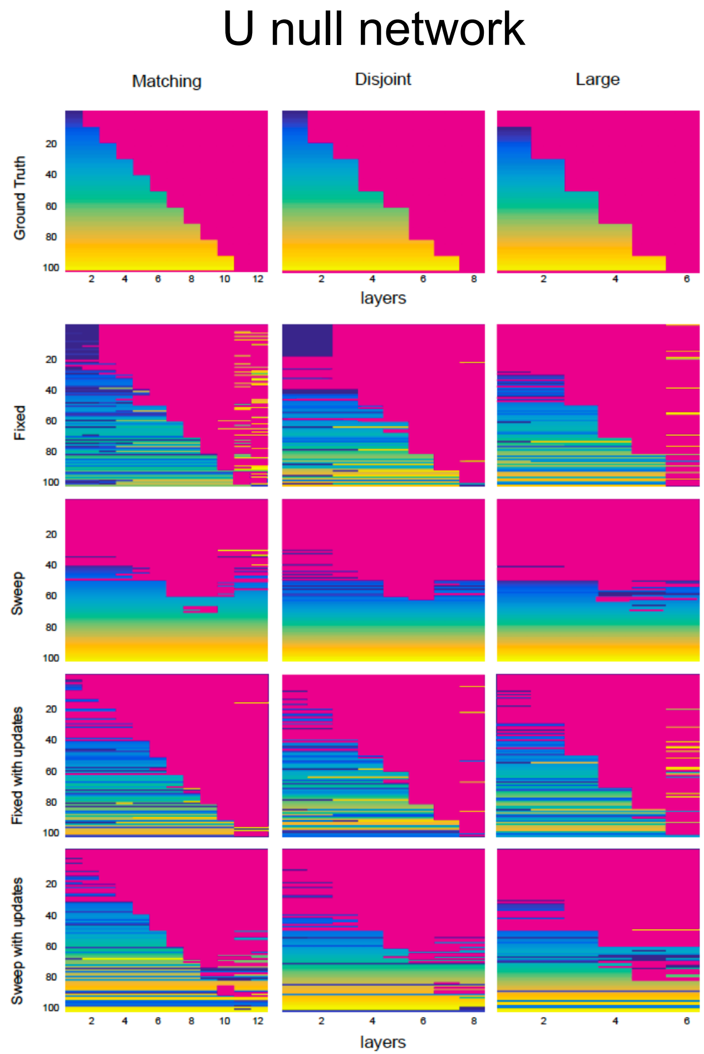
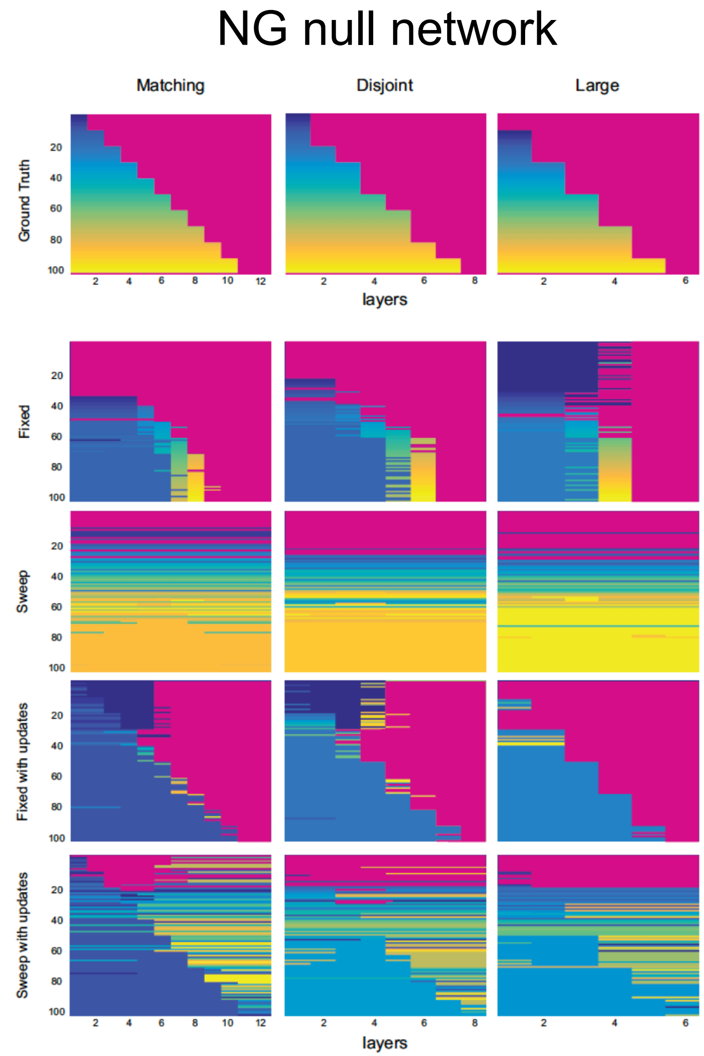
Comparing methods

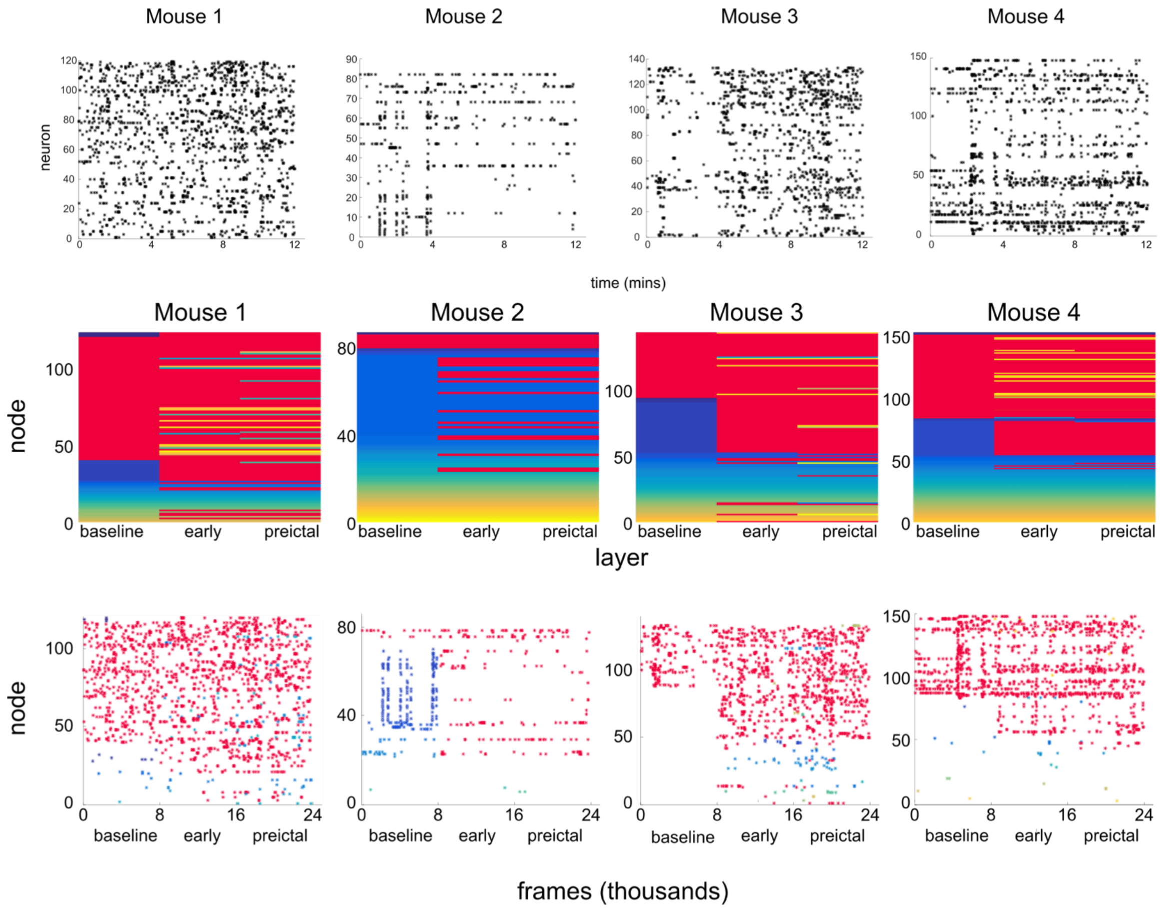




Vaiana et al. (2018) J Complex Networks

What about real neurons?

No ground truth for comparison – can only speculate about what is "correct"

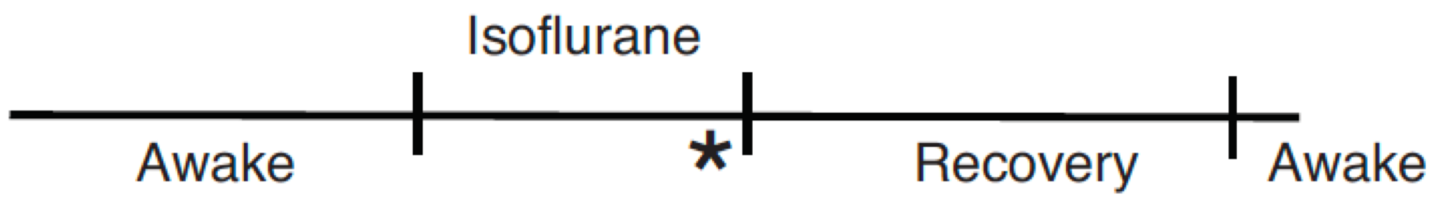


Vaiana (2018) Dissertation

Transition from awake to anesthetized

Experimental paradigm

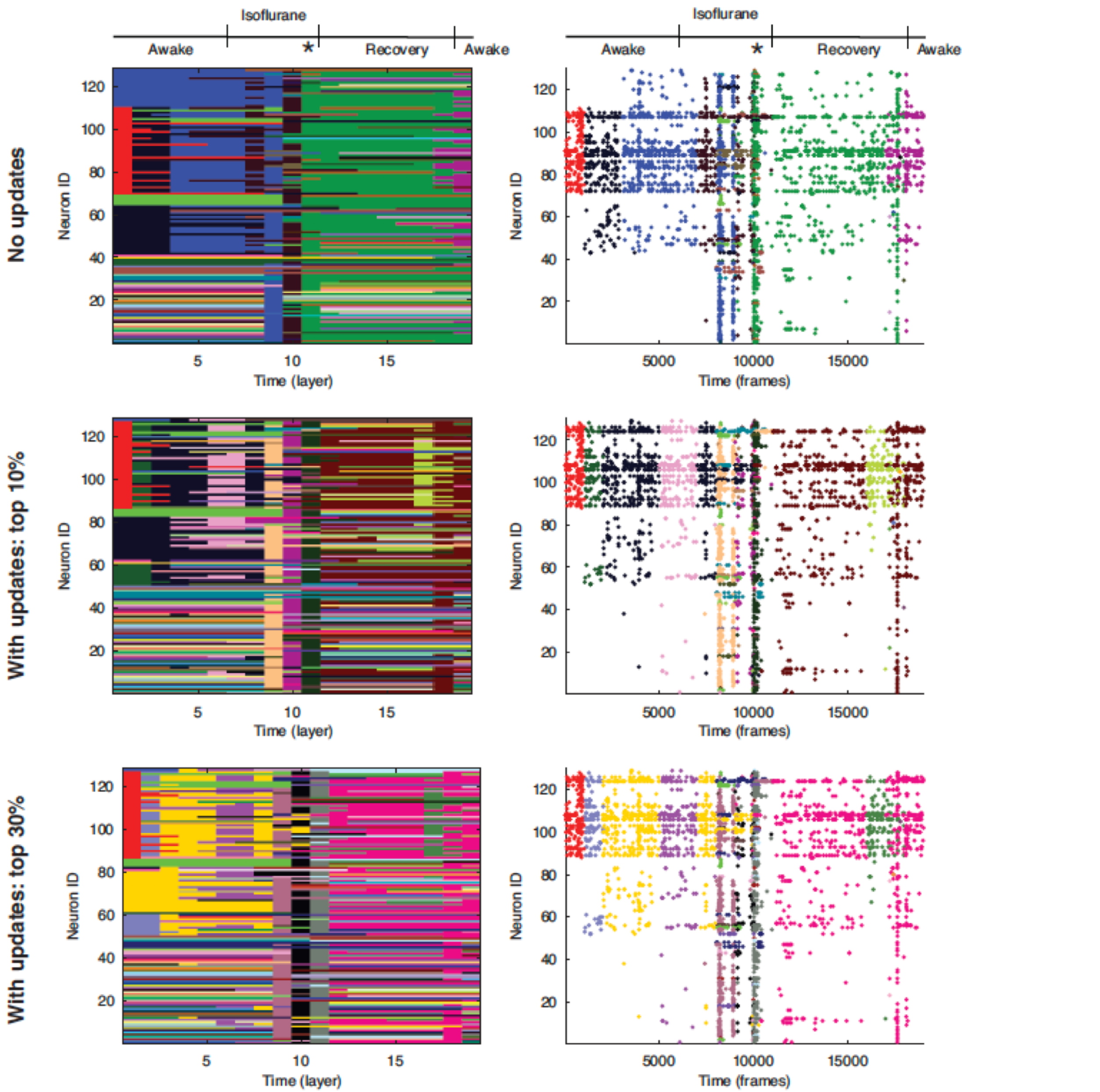
- Mouse starts in awake state. Turn on flow of isoflurane. At some point mouse becomes deeply anesthetized (variable between mice). Turn off isoflurane. Allow mouse to recover.



New updating rule

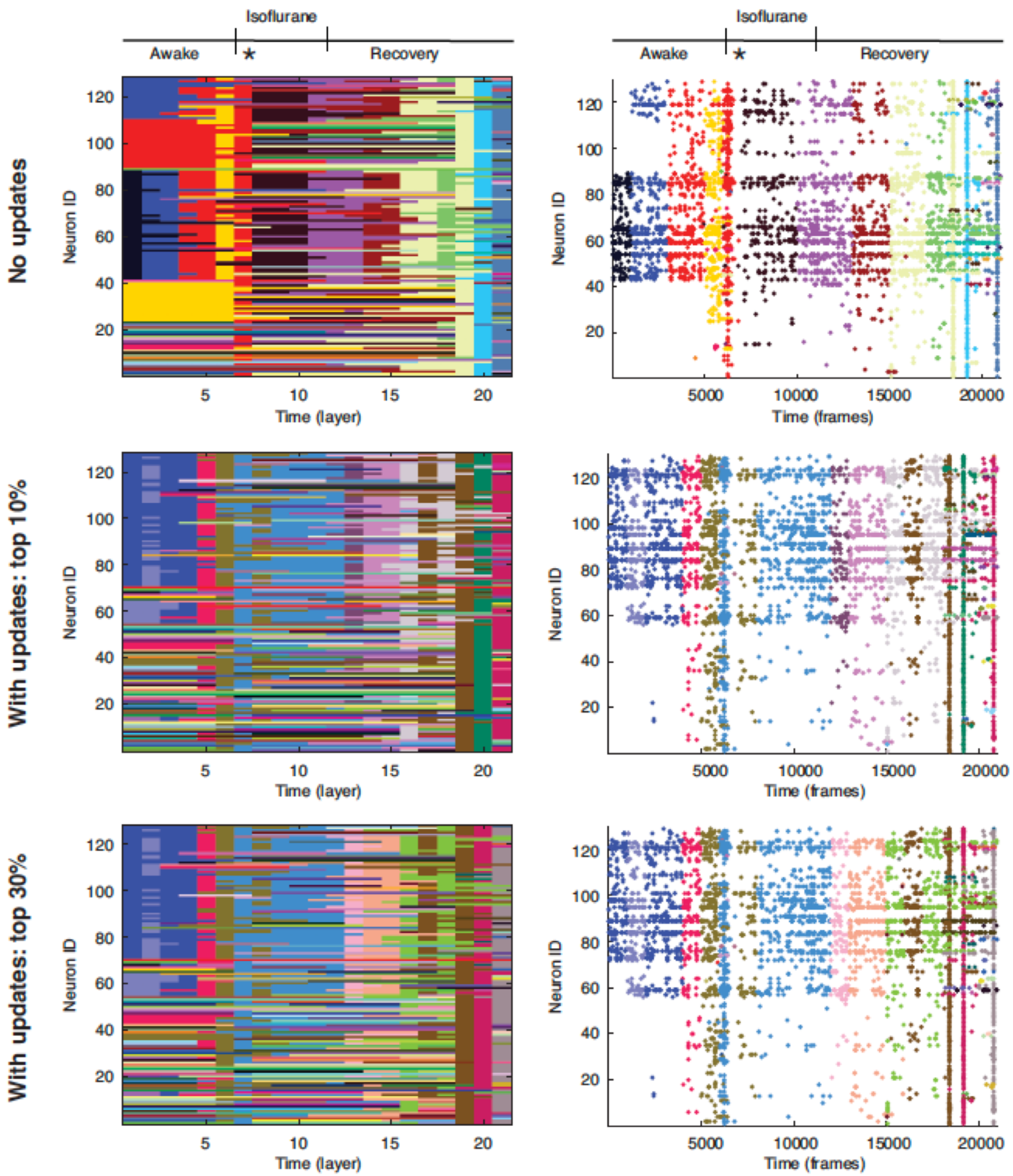
- Global threshold: examine distribution of firing rate changes across all layers and update if change is in the top X% of the distribution
- Use ρ=0.1

Mouse 1



Vaiana et al. (2018) J Complex Networks

Mouse 2



Isoflurane
Awake
*
Recovery
No updates
With updates: top 10%
With updates: top 30%
Neuron ID
Time (layer)
Time (frames)
120
100
80
60
40
20
5
10
15
20
5000
10000
15000
20000

Conclusions

- To be sensitive to system level state changes, we need to be sensitive to node level state changes
- For multilayer networks – reflected in how we model interlayer links
- Increased sensitivity to state changes if update interlayer links based on measures of self-similarity

Thanks to…

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- Cameron Brooks
- Ulgen Kilic

Collaborators:

- Ethan Goldberg, Penn/CHOP
- Conny Tran, Penn/CHOP

Funding:

Come join us!

- Looking for PhD students (current undergraduate or masters students)

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Questions?