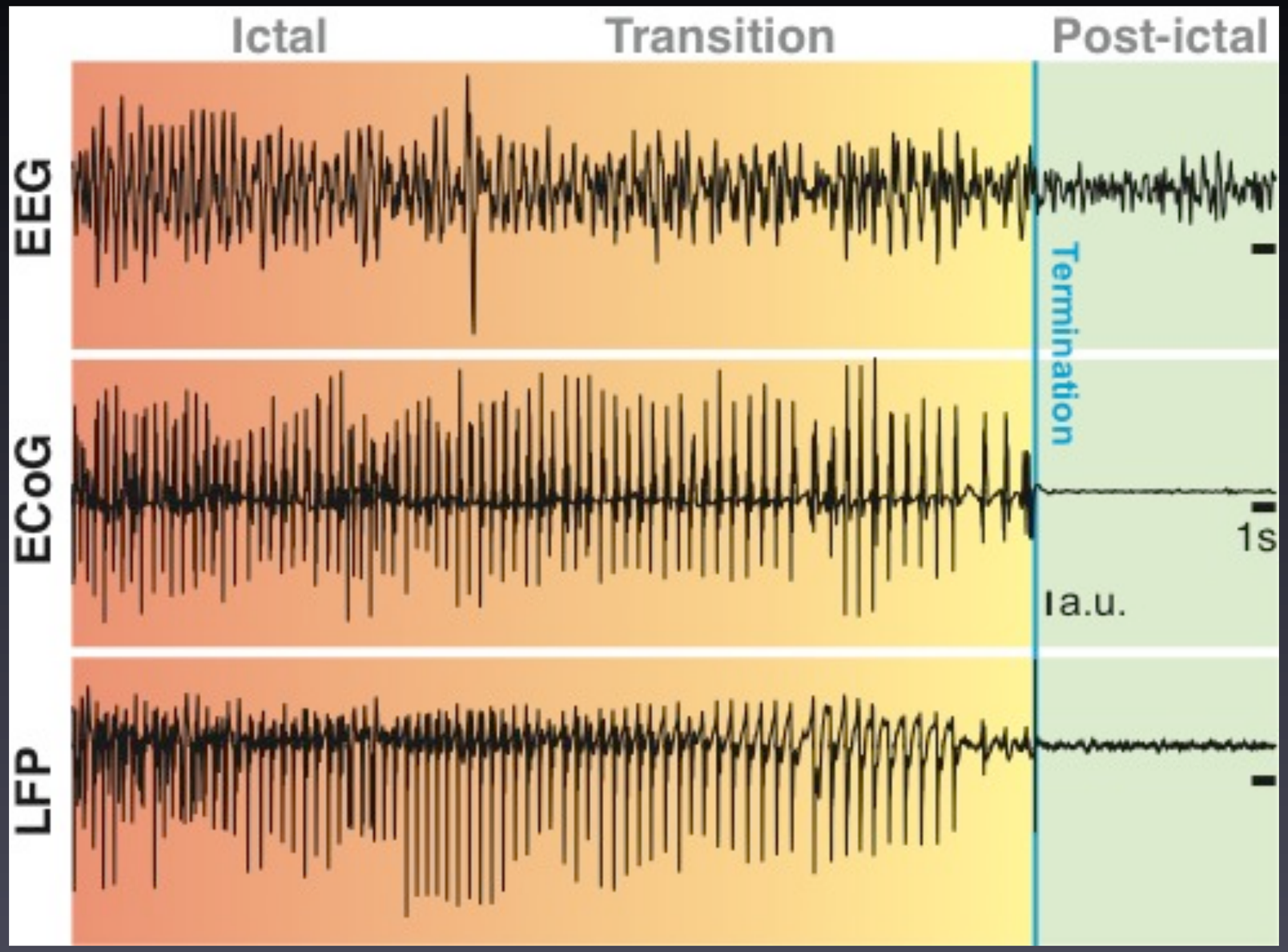
Multi-scale seizure dynamics



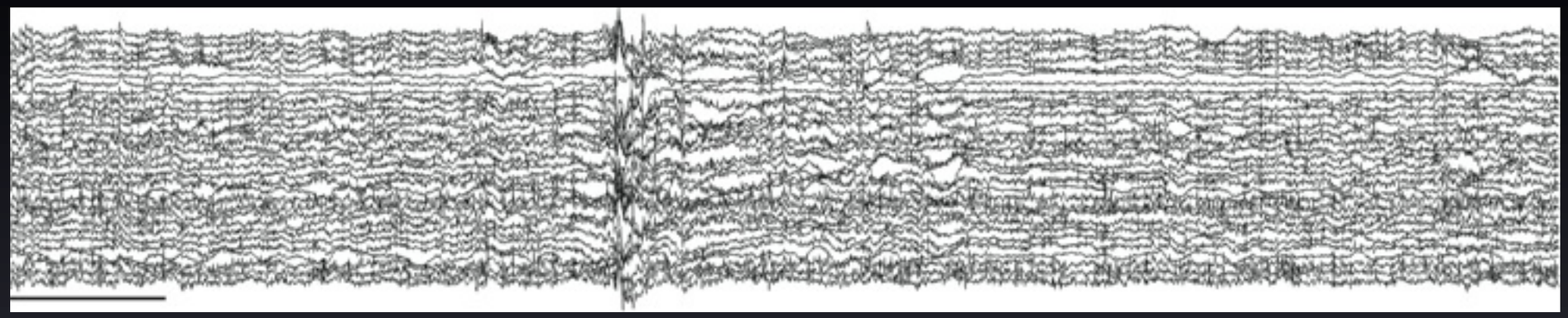
Mark Kramer, Uri Eden, Eric Kolaczyk, Kyle Lepage
Boston University

Wilson Truccolo
Brown University

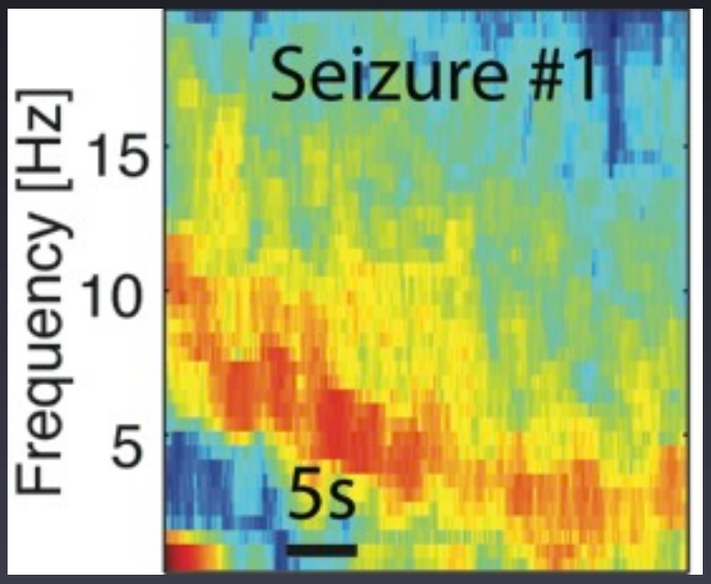
Sydney Cash, Catherine Chu, Emad Eskandar
MGH

Outline

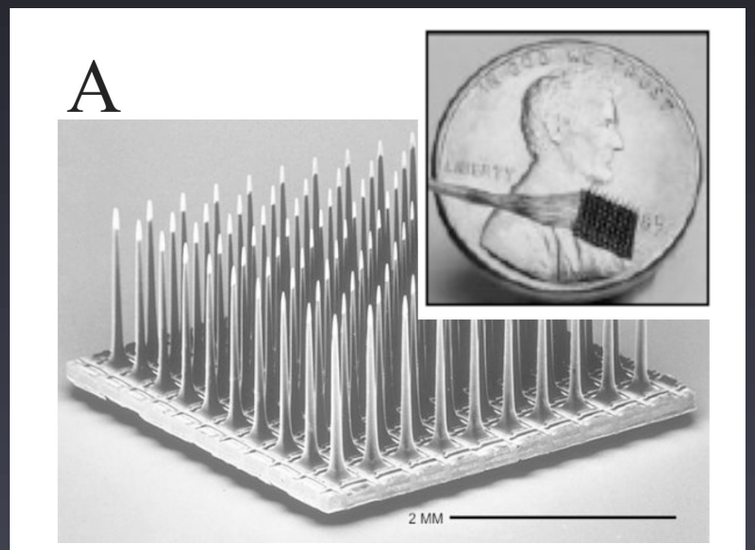
- Data



- Temporal scales

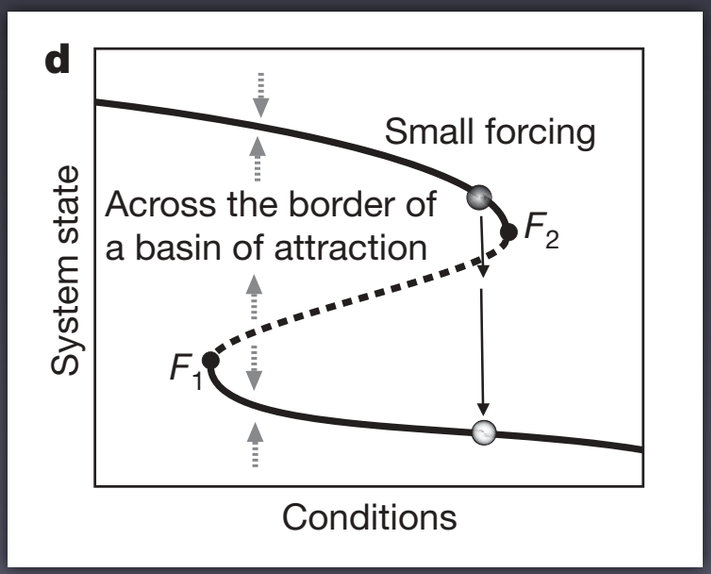


- Spatial scales

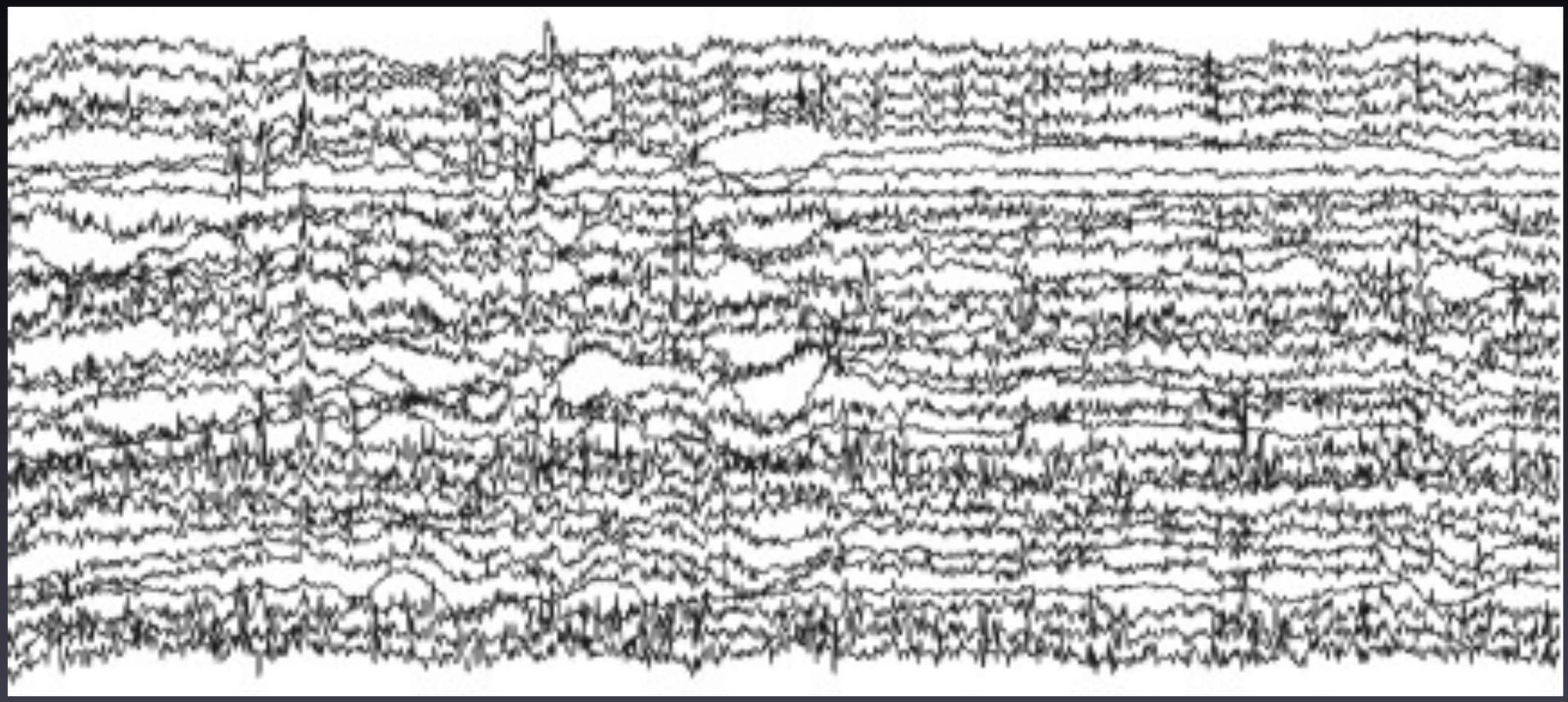


- Why do seizures stop?
  or fail to stop?

- Illustrate richness of data …



Macroscale Data: Invasive EEG or ECoG



Multivariate, high density

~ 100 electrodes (surface & depth)

Sampling 500 Hz

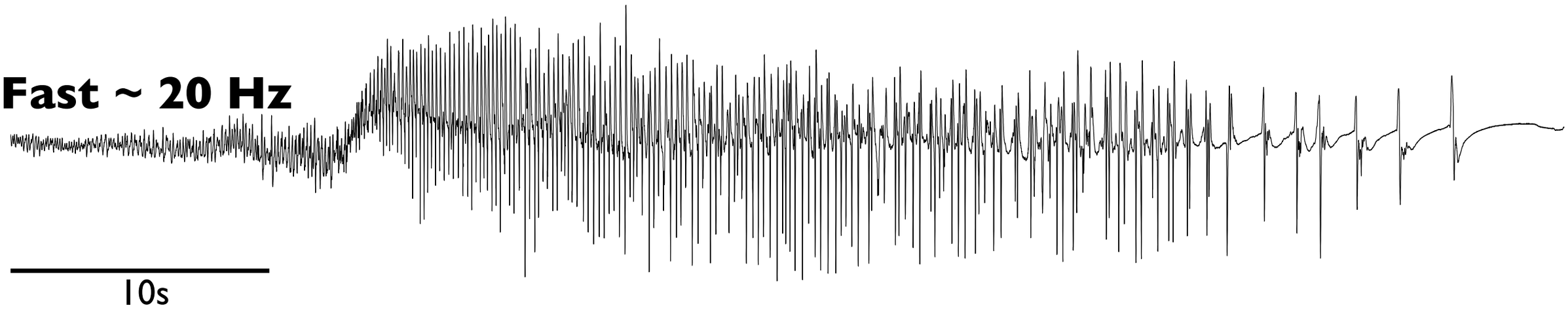
Purpose: localize seizure focus.

Q: How to characterize these data?

Temporal scales: rhythms

One electrode

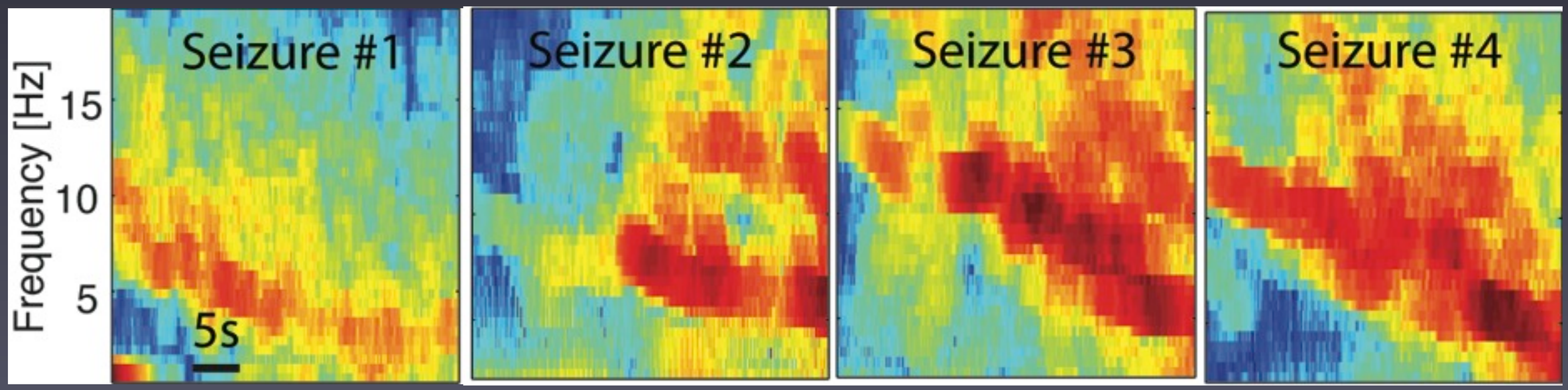
Brain chirp [Schiff et al, 2000]



Intermediate ~ 10 Hz

Slow ~ 2 Hz

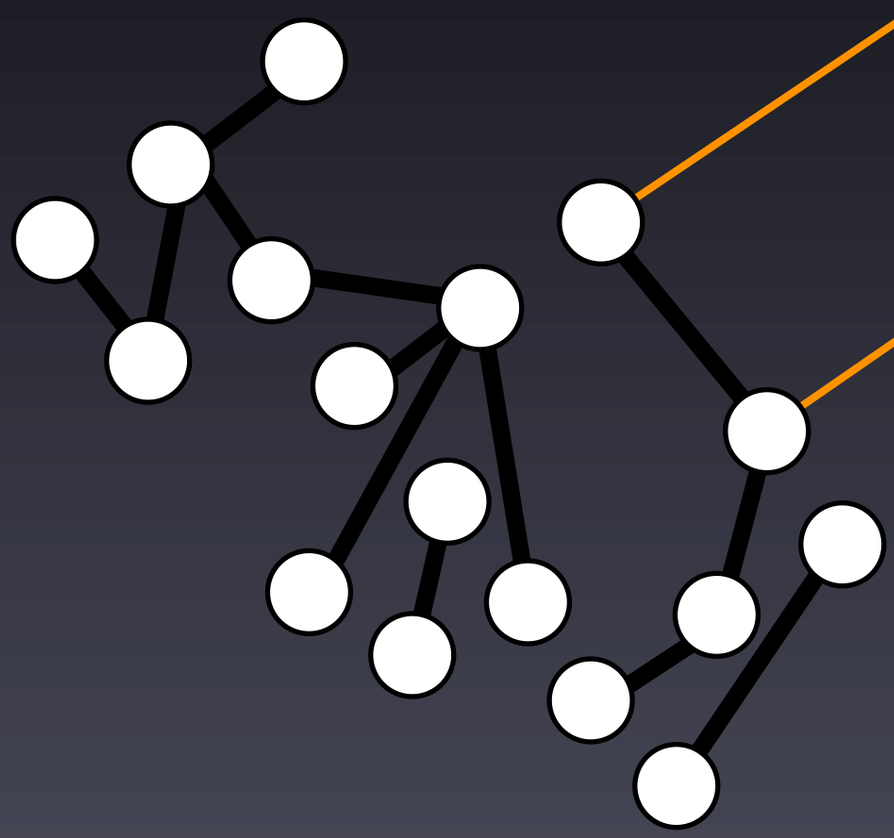
Quantify: Time-frequency spectra

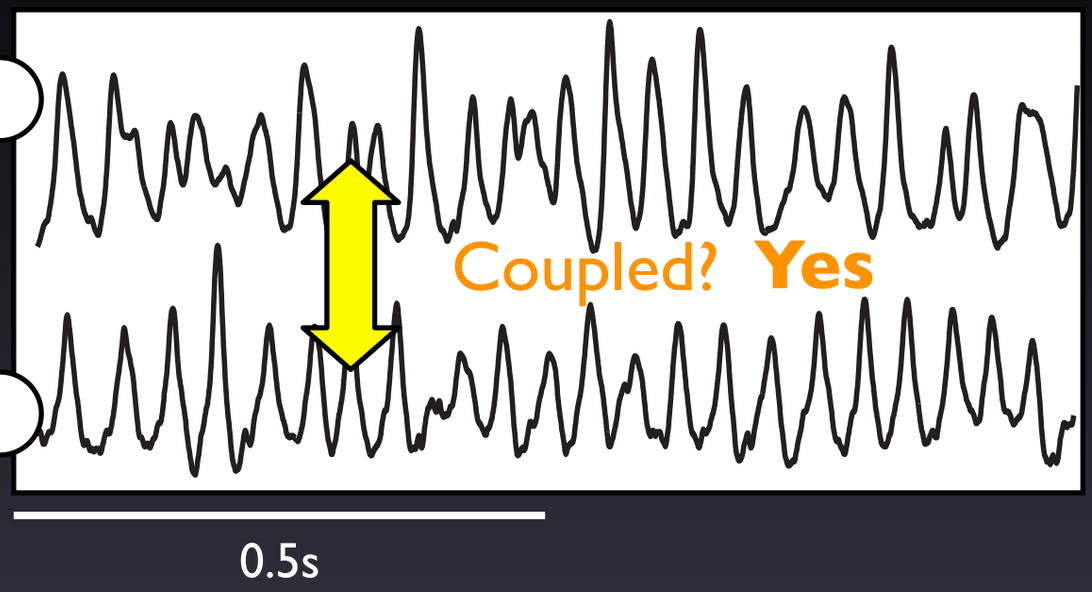


H: Rhythms slow during seizure.

Spatial scales: coupling

Multiple electrodes





Long history

[Brazier, 1972 & 1973; Gotman, 1981 & 1983; . . .]

Many options for coupling measure

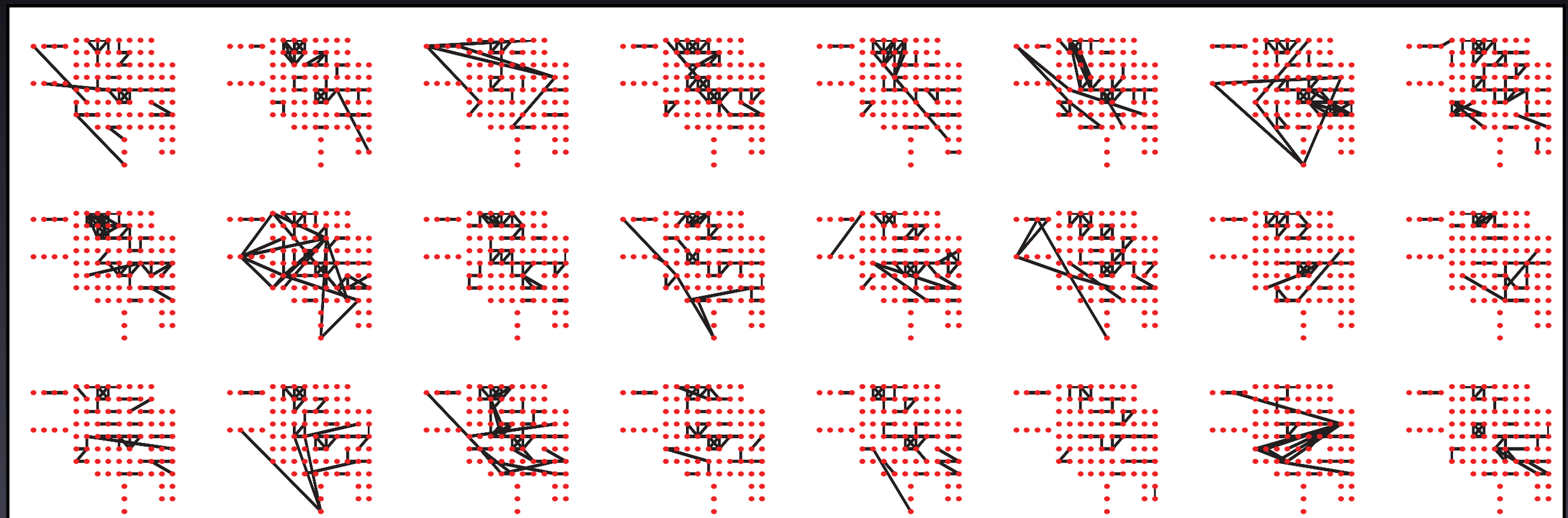
[Pereda et al, 2005]

Repeat for all electrode pairs: We employ cross correlation

Functional network: node, edge

Results

Networks evolving in time



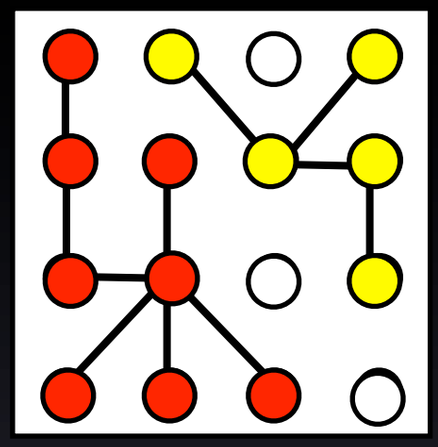
Data overload. Succinct measures to characterize network evolution.

One example . . .

Components

Groups of electrodes connected by edges

Red is biggest

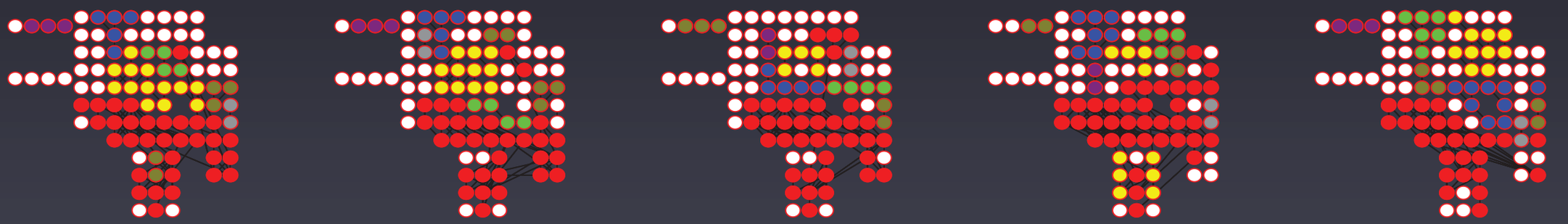


One dominant component

Onset

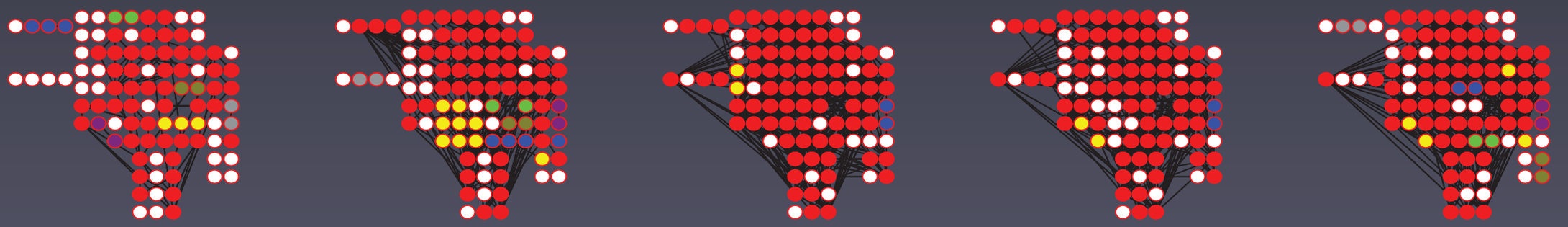
Dominant component **fractures**

Middle



One dominant component

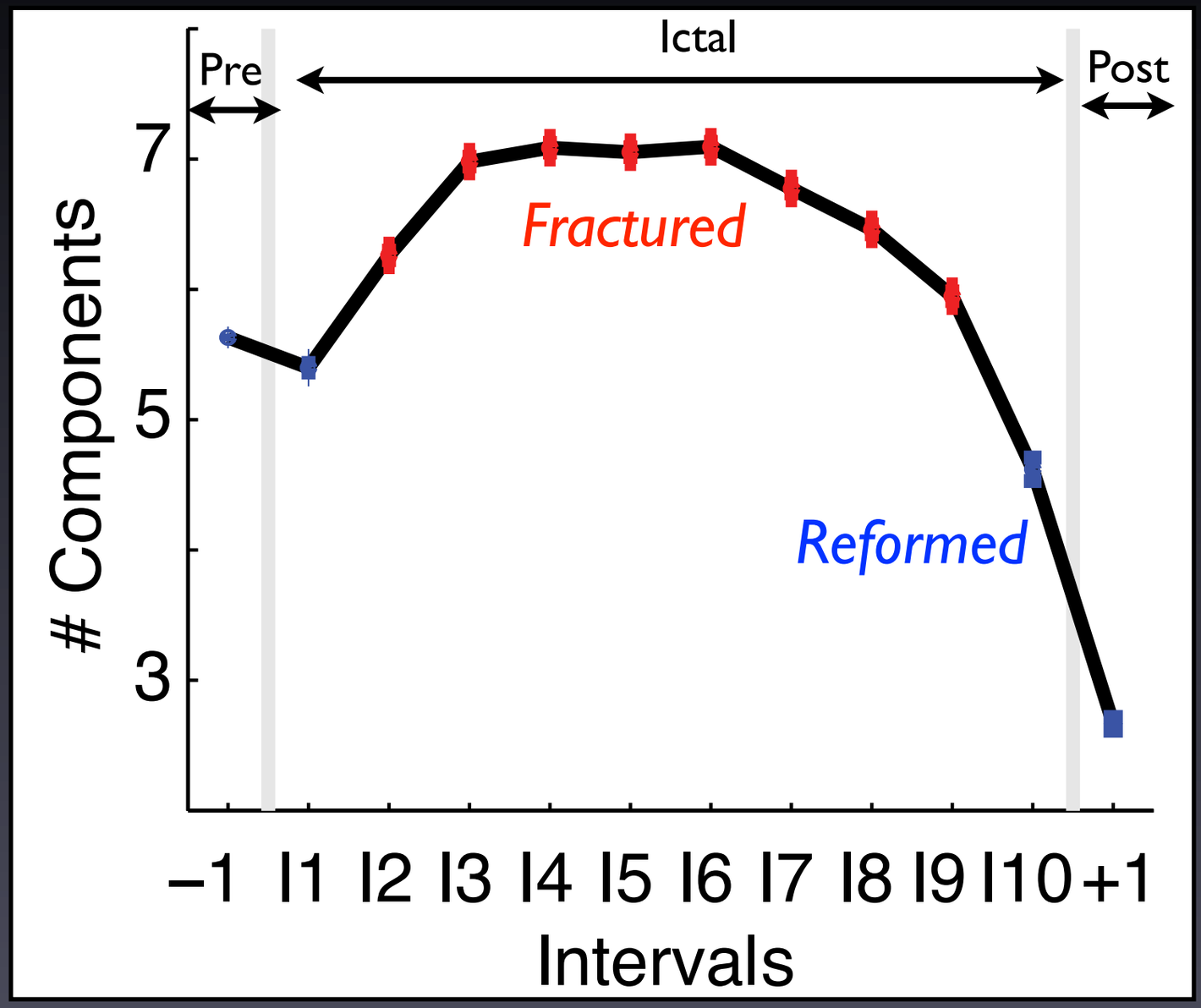
End



A fracturing and reforming of the seizure topology . . .

Population Results

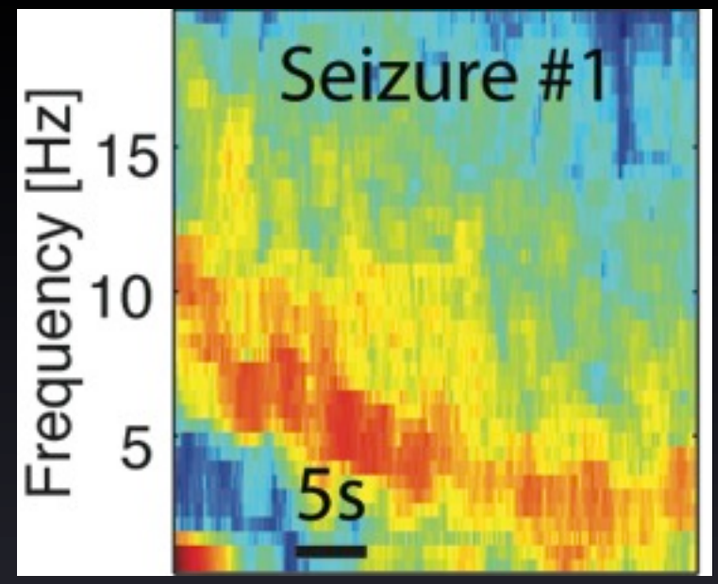
11 subjects, 48 seizures



Components ↑

H: Networks fracture then reform during the seizure.

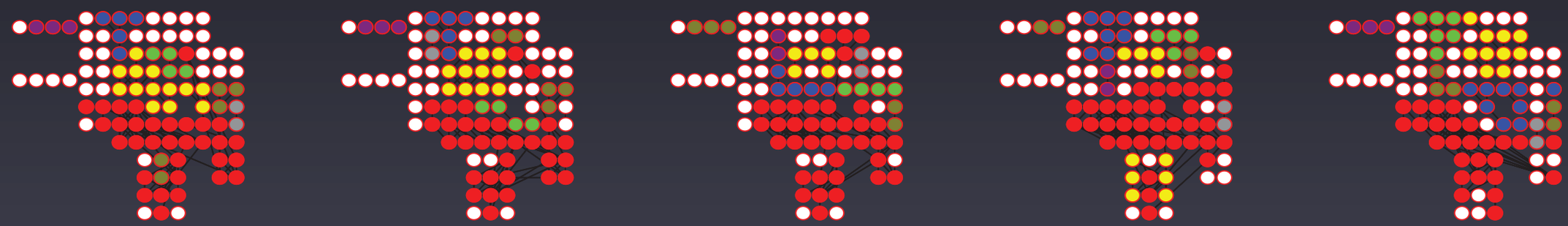
Summary



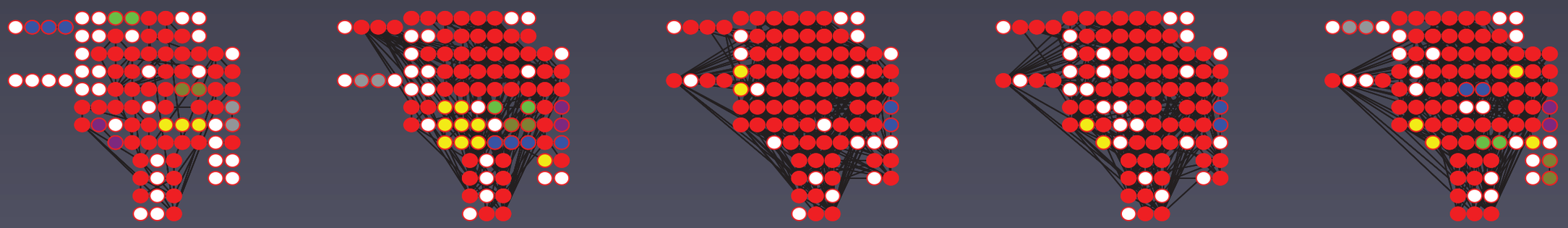
- So far: Macroscale data

Rhythms **slow** during seizure (ictal chirp)

Brain regions **fracture** during seizure

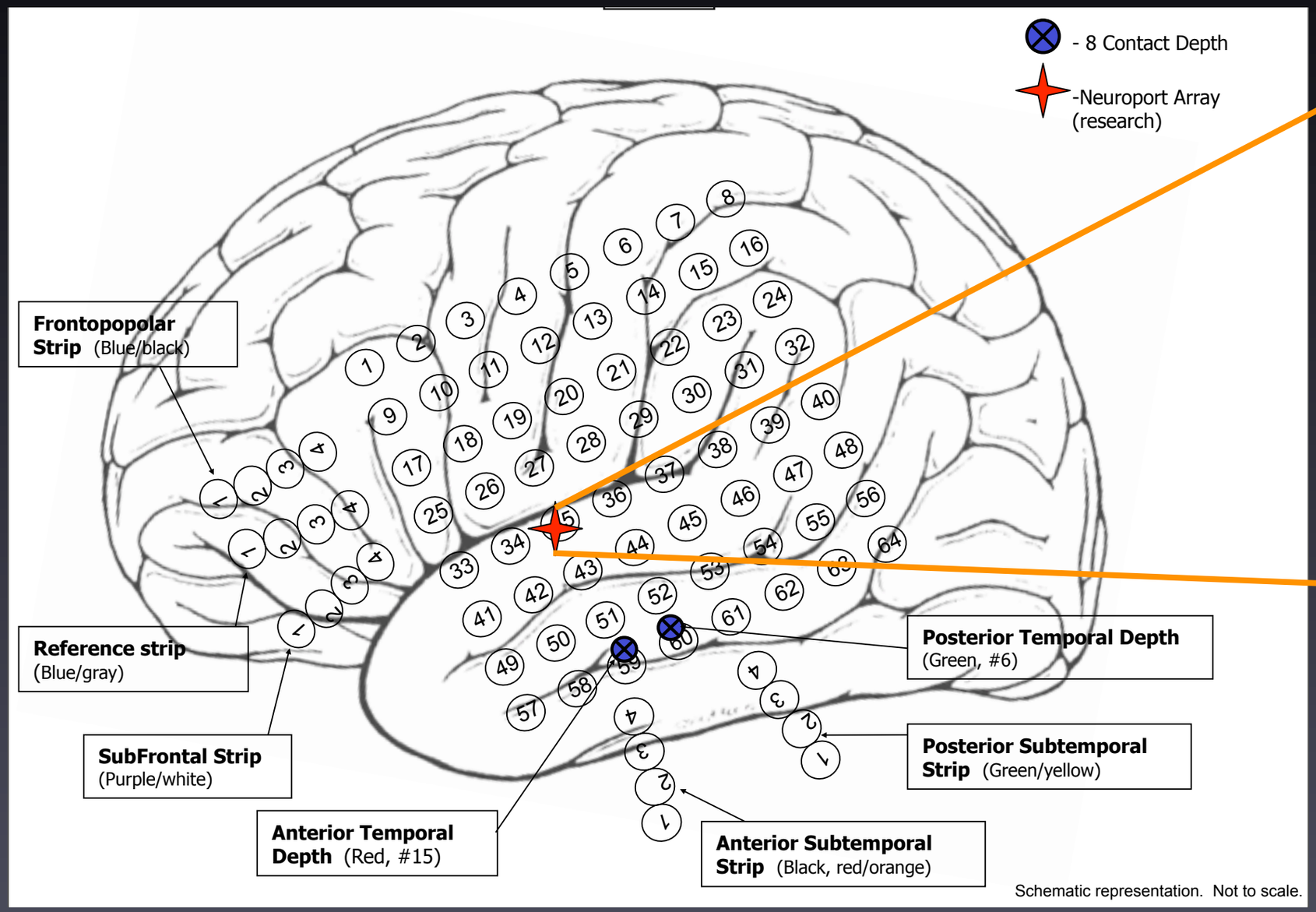


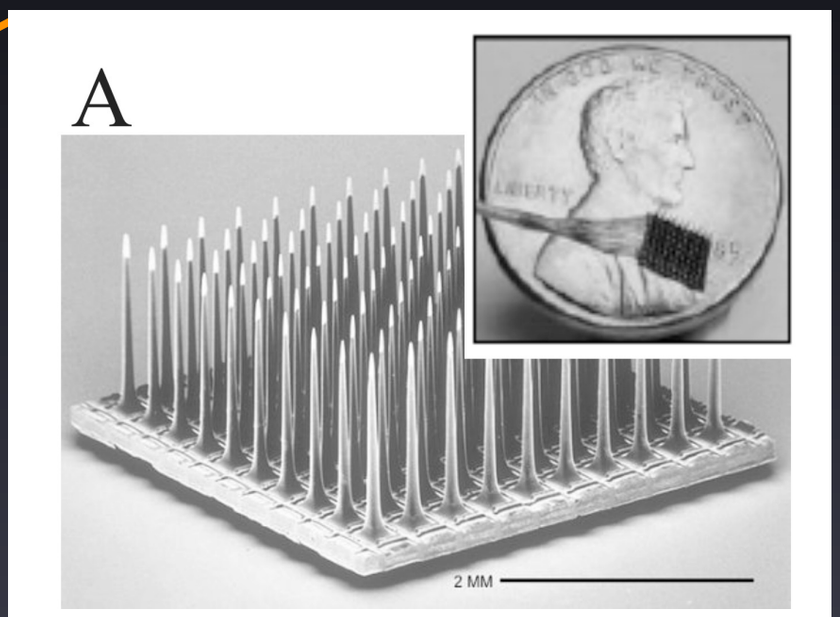
Brain regions **coalesce** at termination



Now, consider a smaller spatial scale . . .

Microscale Data: Local field potential, LFP





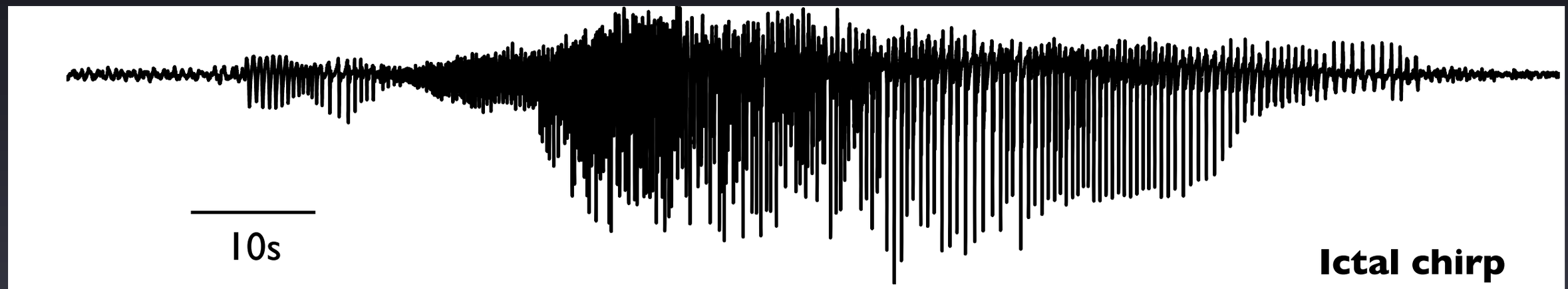
Microelectrode array

Records voltage from small neural populations

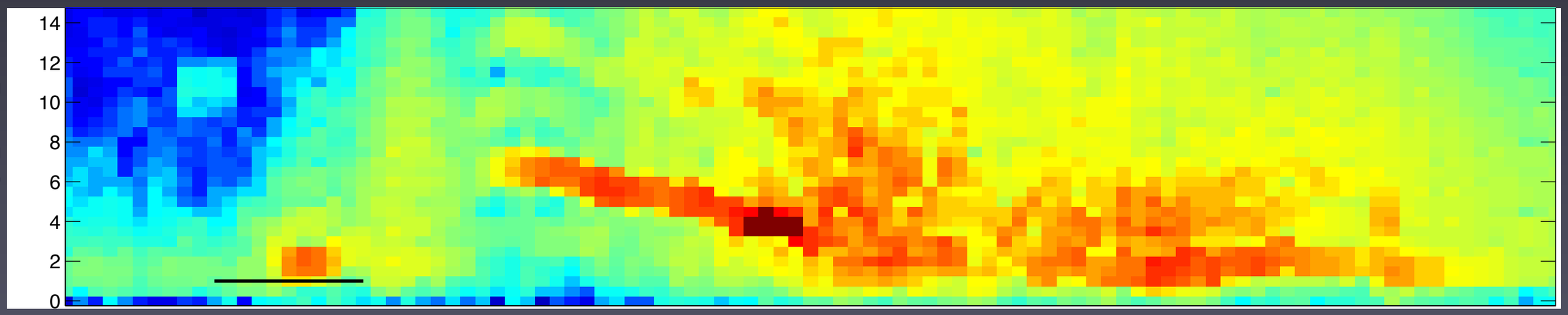
Consider the LFP data . . .

Temporal scales: LFP rhythms

Ex: one microelectrode

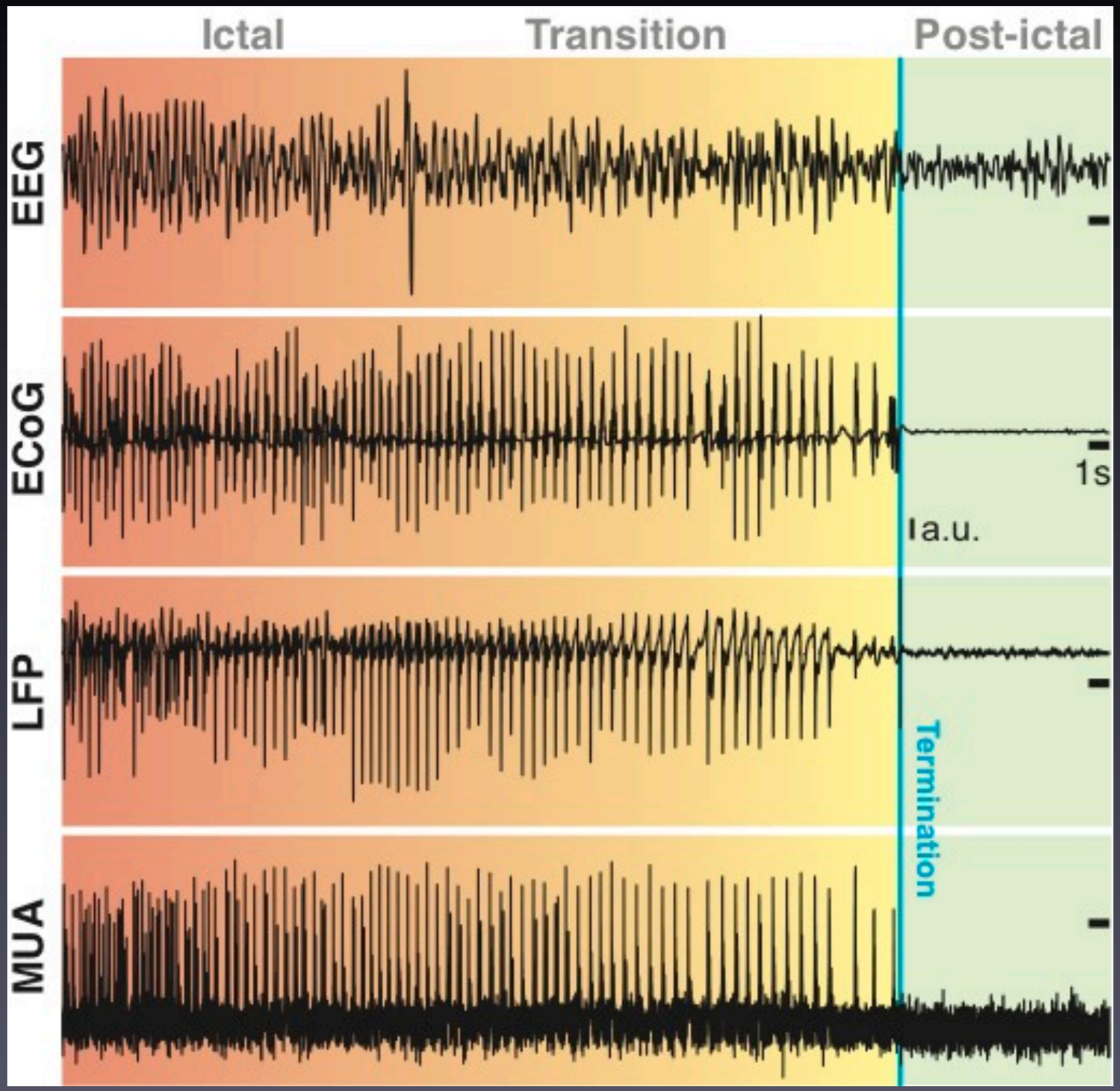


Time-frequency spectrum



H: Rhythms slow at microscale during seizure.

Ex: dynamics across scales

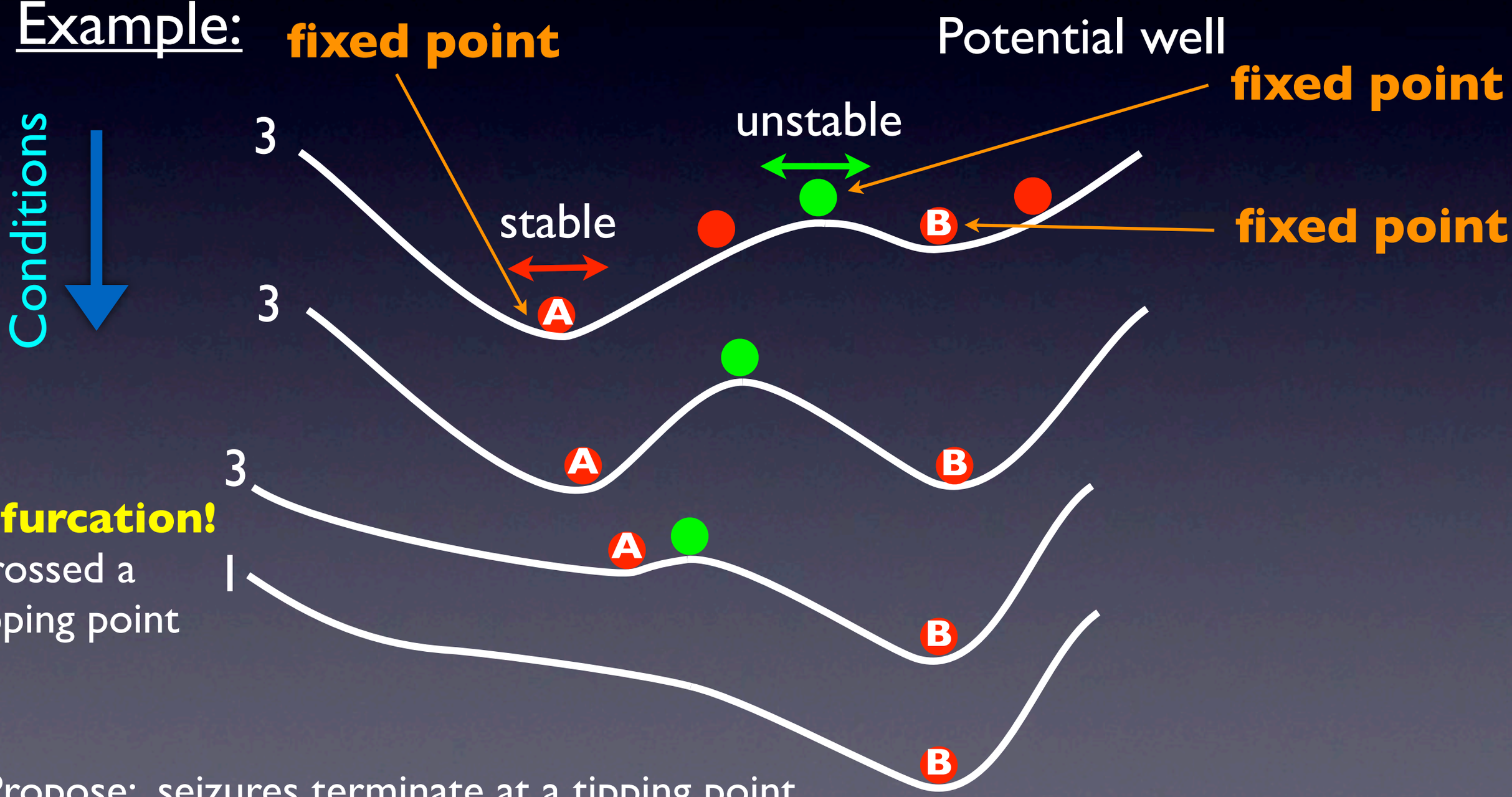


What's happening <u>dynamically</u> at the end of the seizure?

Tipping point

- An <u>abrupt transition</u> at which the system shifts from one state to another (a.k.a, catastrophic shift, critical transition, . . .)

<u>Example:</u>



bifurcation!
Crossed a tipping point

<u>Propose</u>: seizures terminate at a tipping point . . .

Warning signs (I)

Tipping points can be preceded by dynamical signatures:

- **Critical slowing down**

  Near the transition, the system becomes increasingly slow in recovering from perturbations.

Potential well

Far from transition:

Kick - quickly return

Near transition:

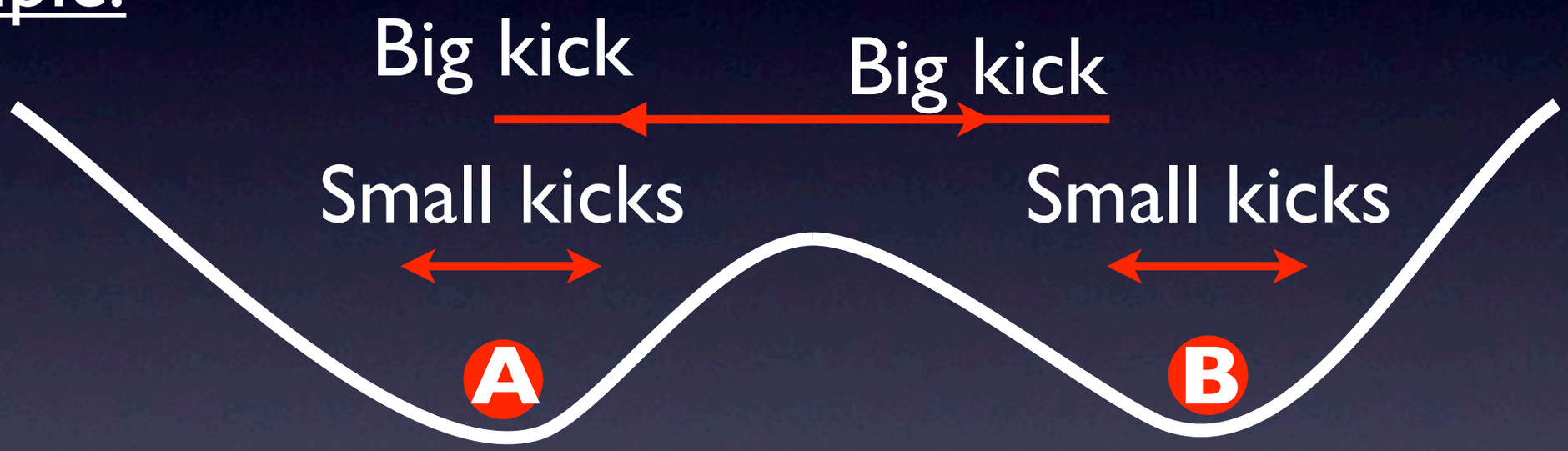
Kick - slowly return

- Slower fluctuations & increased autocorrelations

Warning signs (2)

- **Flickering**
  The system moves back and forth between two alternative attractors just before the tipping point.

Example:



Position:

B ——— ——— “Flicker” between two states

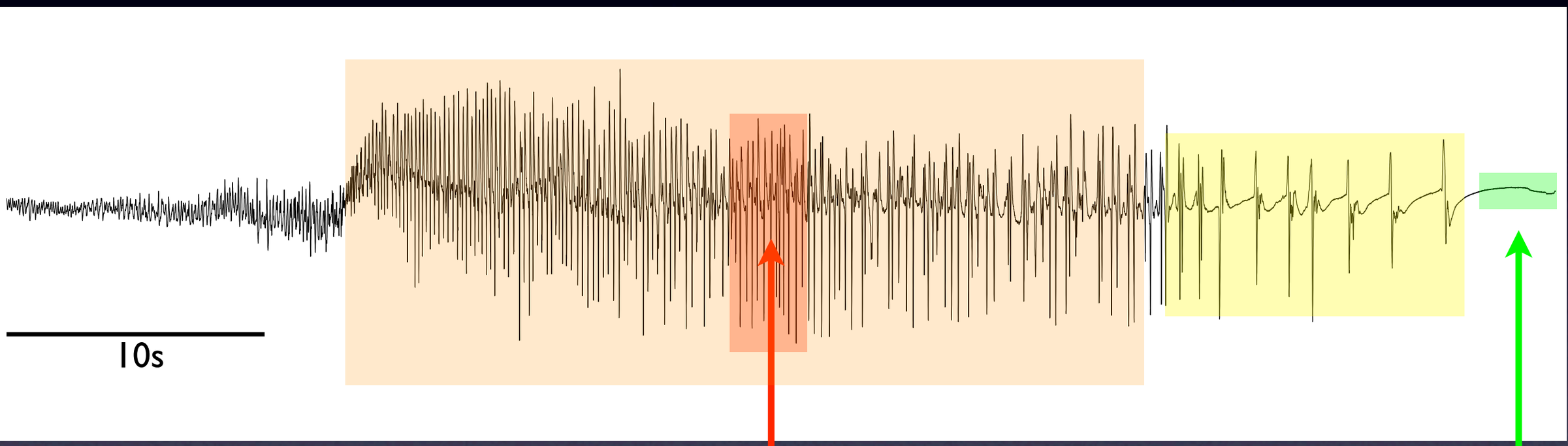
A ——— ———

“time”

Ex: ECoG data

Dynamical signatures of tipping point?

Visual inspection:



1. Critical slowing down?

Ictal chirp

Autocorrelation?

"Seizure state"

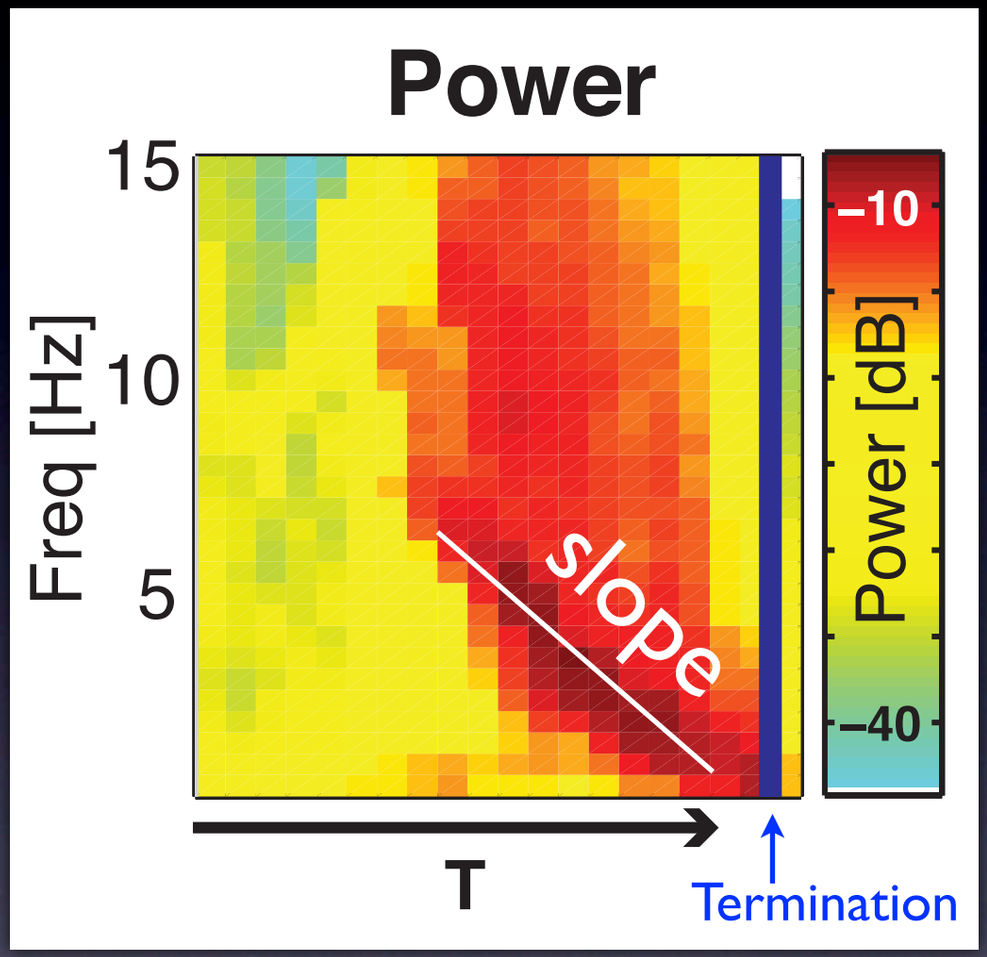
2. Flickering?

"Post-seizure state"

Consider quantitative analysis …

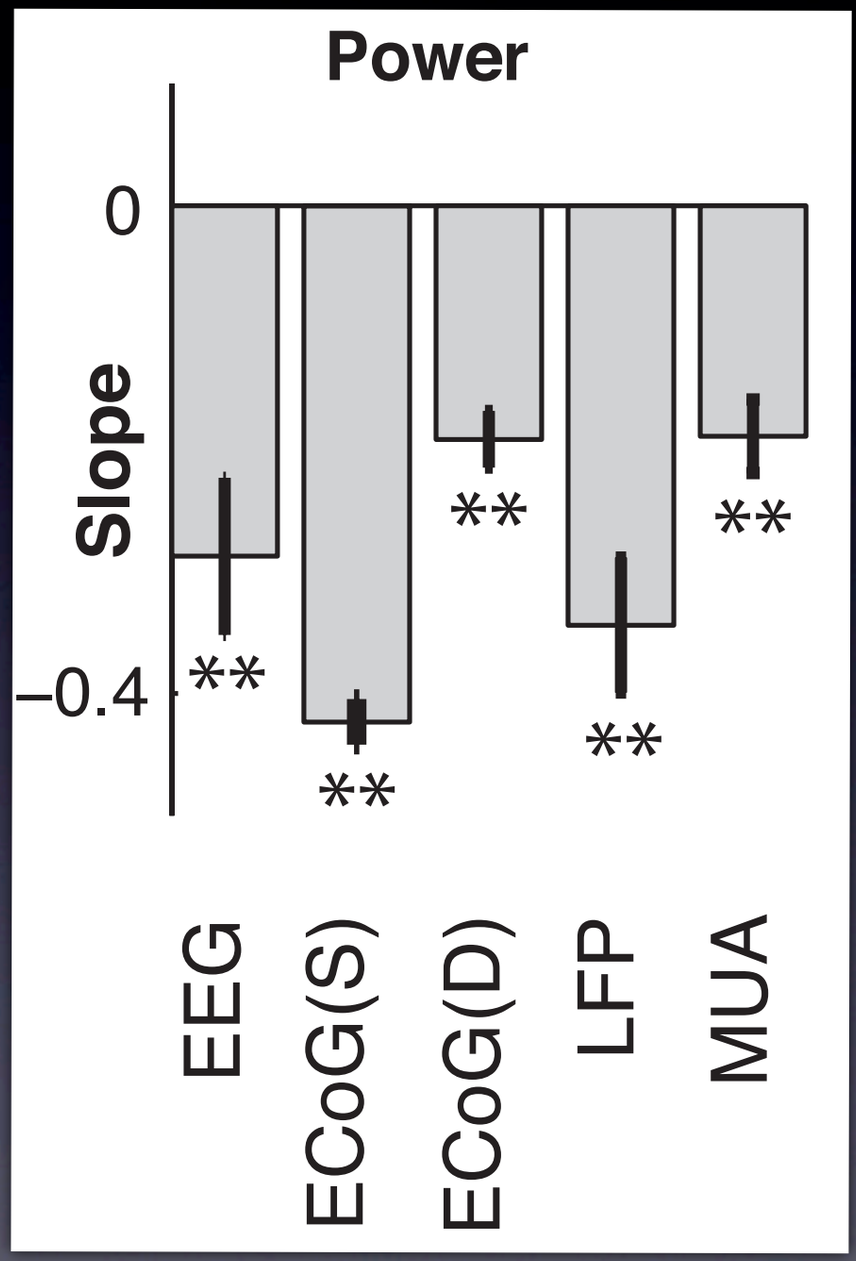
Critical Slowing Down

"Ictal chirp"



Average all electrodes

Repeat for spatial scales



Slope **negative**

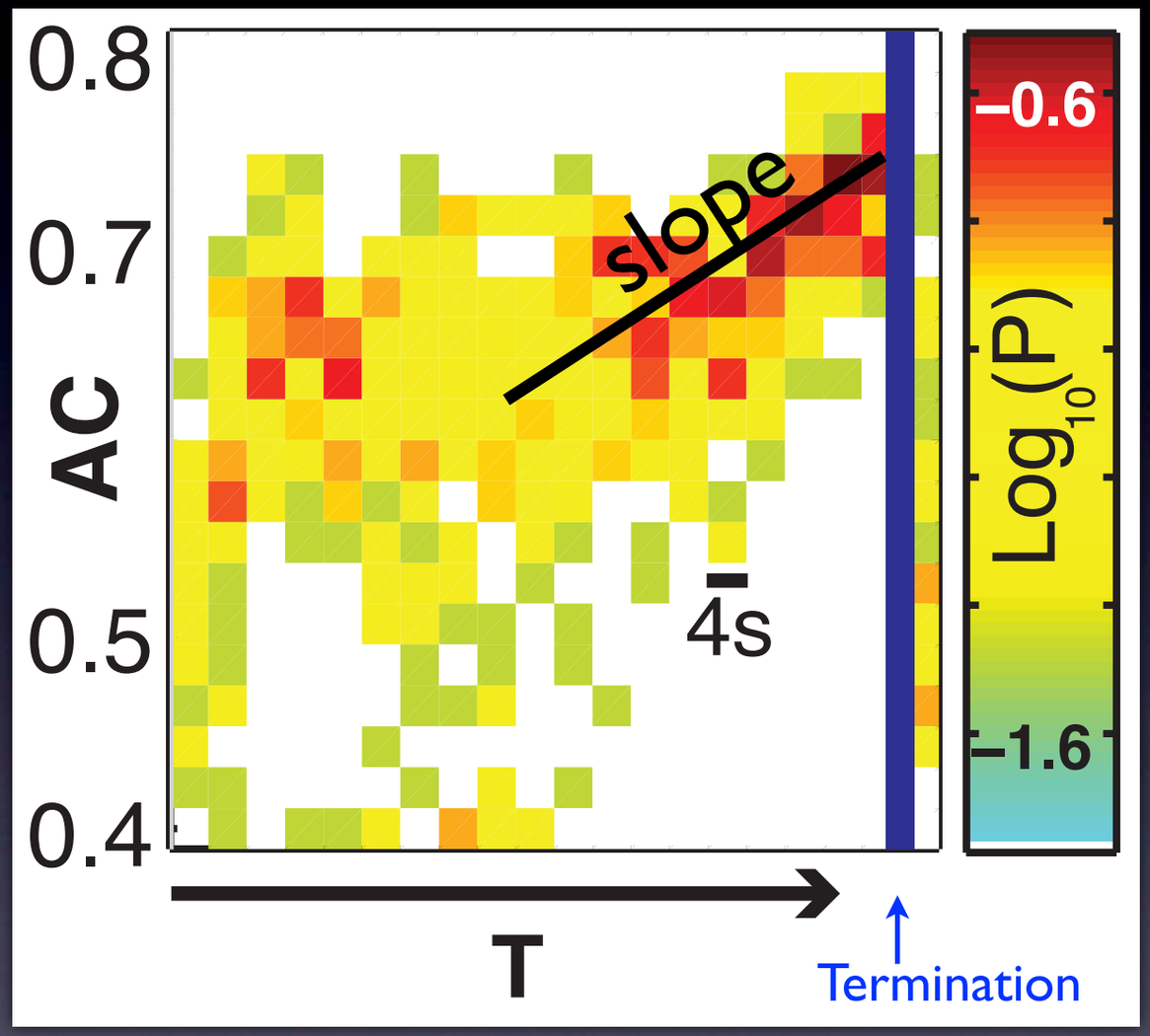
Fit the freq of dominant power vs time.

Slope **negative**: rhythms slow

H: Dominant rhythms slow in approach to termination

Critical Slowing Down

Autocorrelation (10 ms)

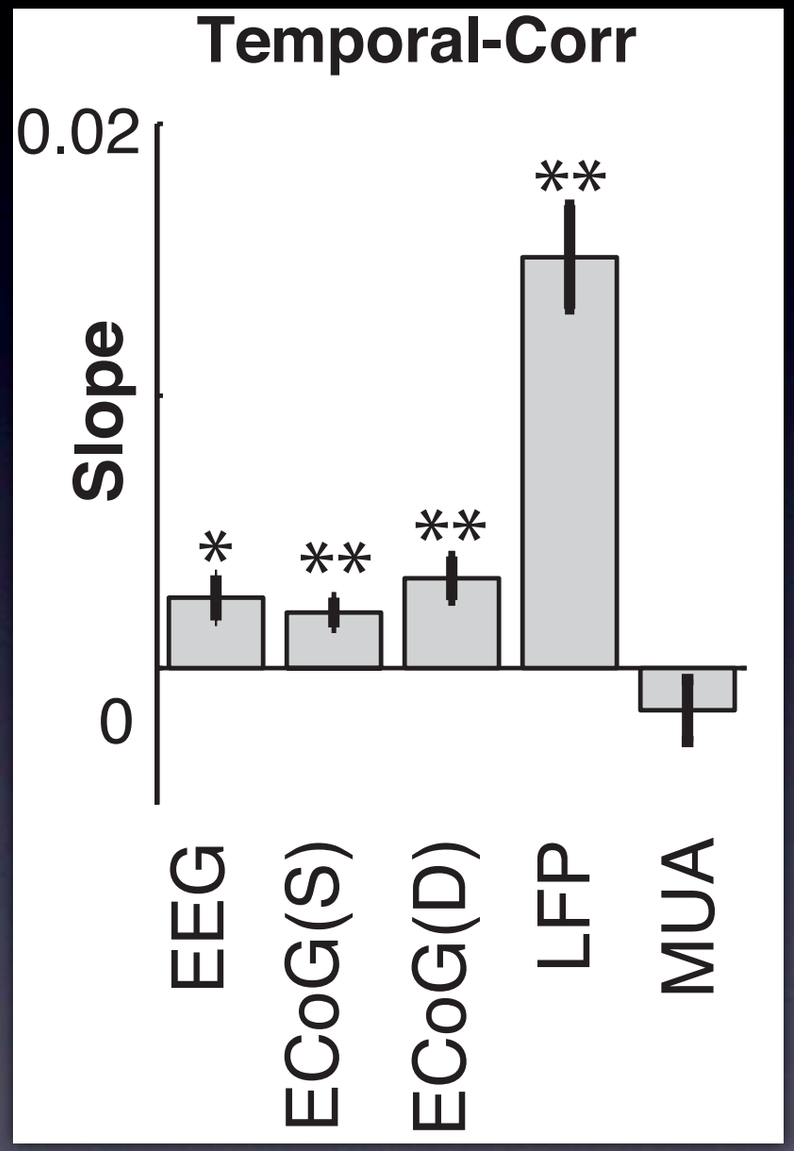


Distribution from all electrodes

Fit the mean AC vs time.

Slope **positive**: AC increases

Repeat for spatial scales

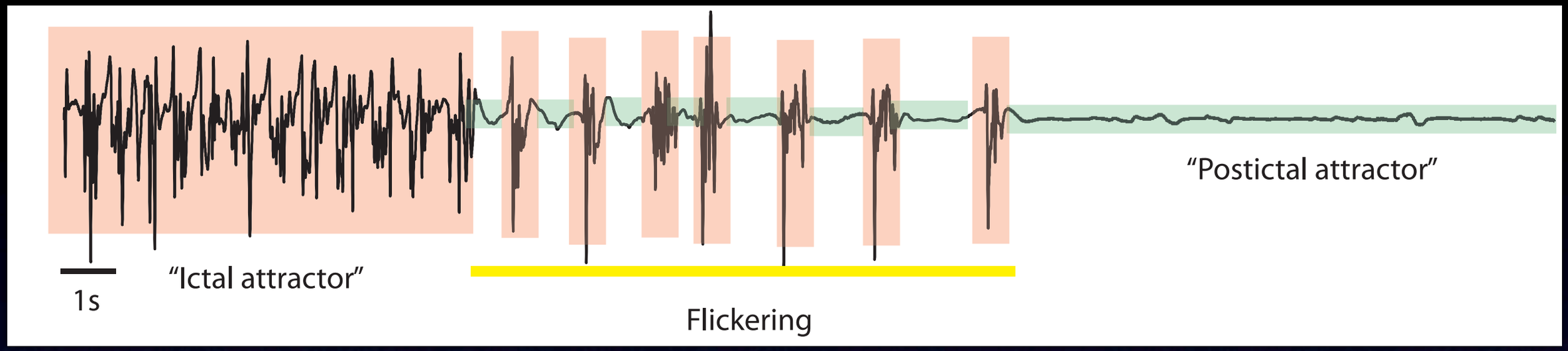


Field: slope **positive**

Unit: slope **~ 0**

H: Field autocorrelations increase in approach to termination

2. Flickering



Define states:

ictal = high variance

post-ictal = low variance

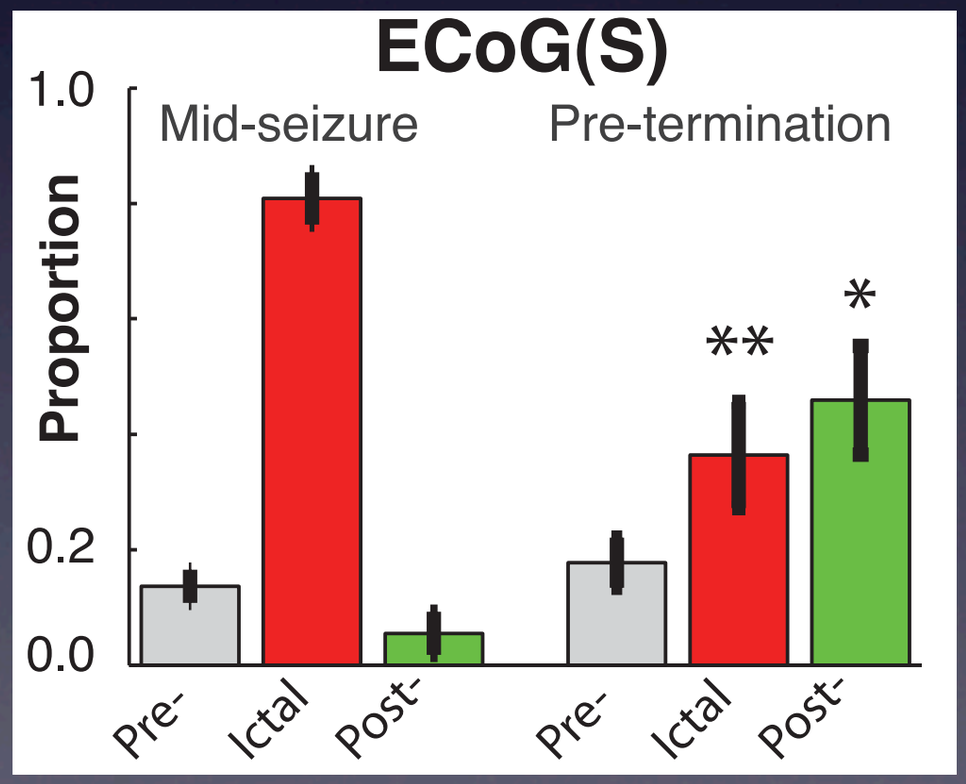
pre-ictal = med variance

<u>mid-seizure</u>: var = ictal state

<u>pre-termination</u>: 1) ictal ↓

2) post-ictal ↑

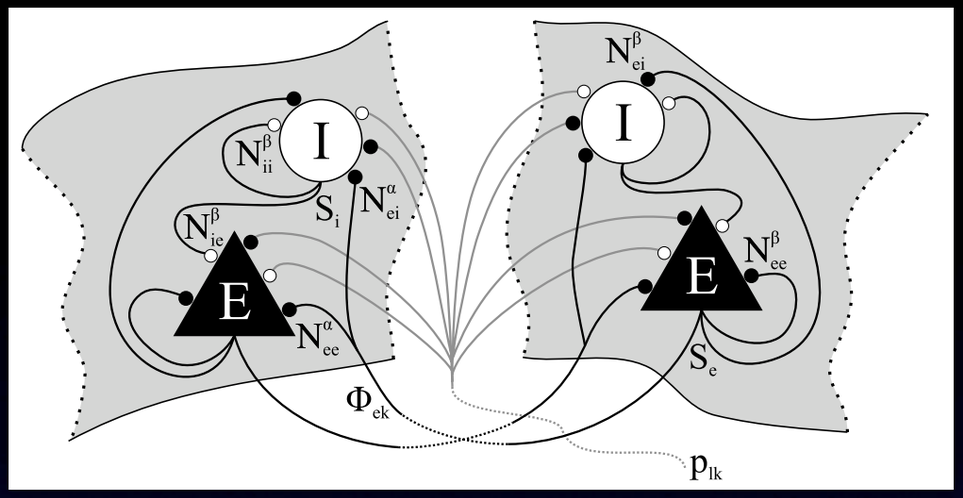
Classify var in two intervals:



Consistent with flickering - both states appear

Model

A "simple" biophysical model of seizure termination



Mean-field model of population activity, (not "spikes" of individual neurons).

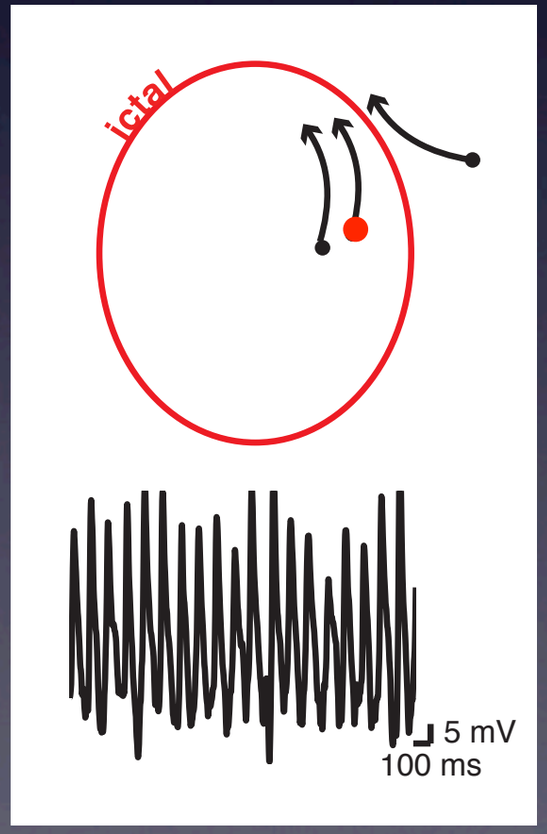
[Liley et al, Network, 2002]

Analyze model dynamics:

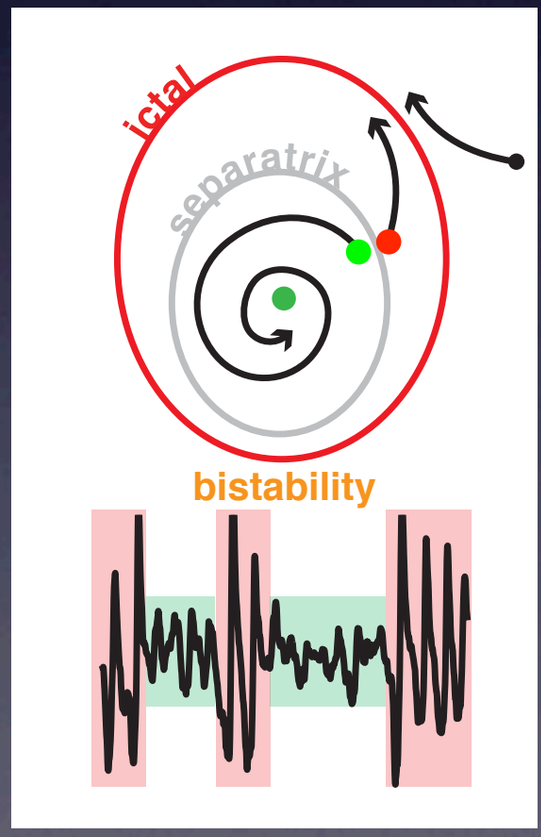
Conditions

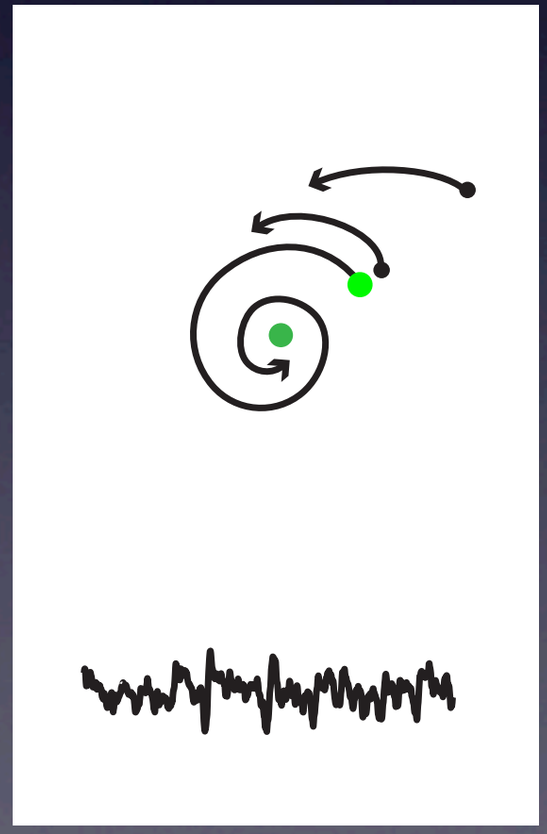
Seizure attractor — **Both!** — **Post-seizure attractor**

"ring" is stable



Large amplitude rhythms, high var





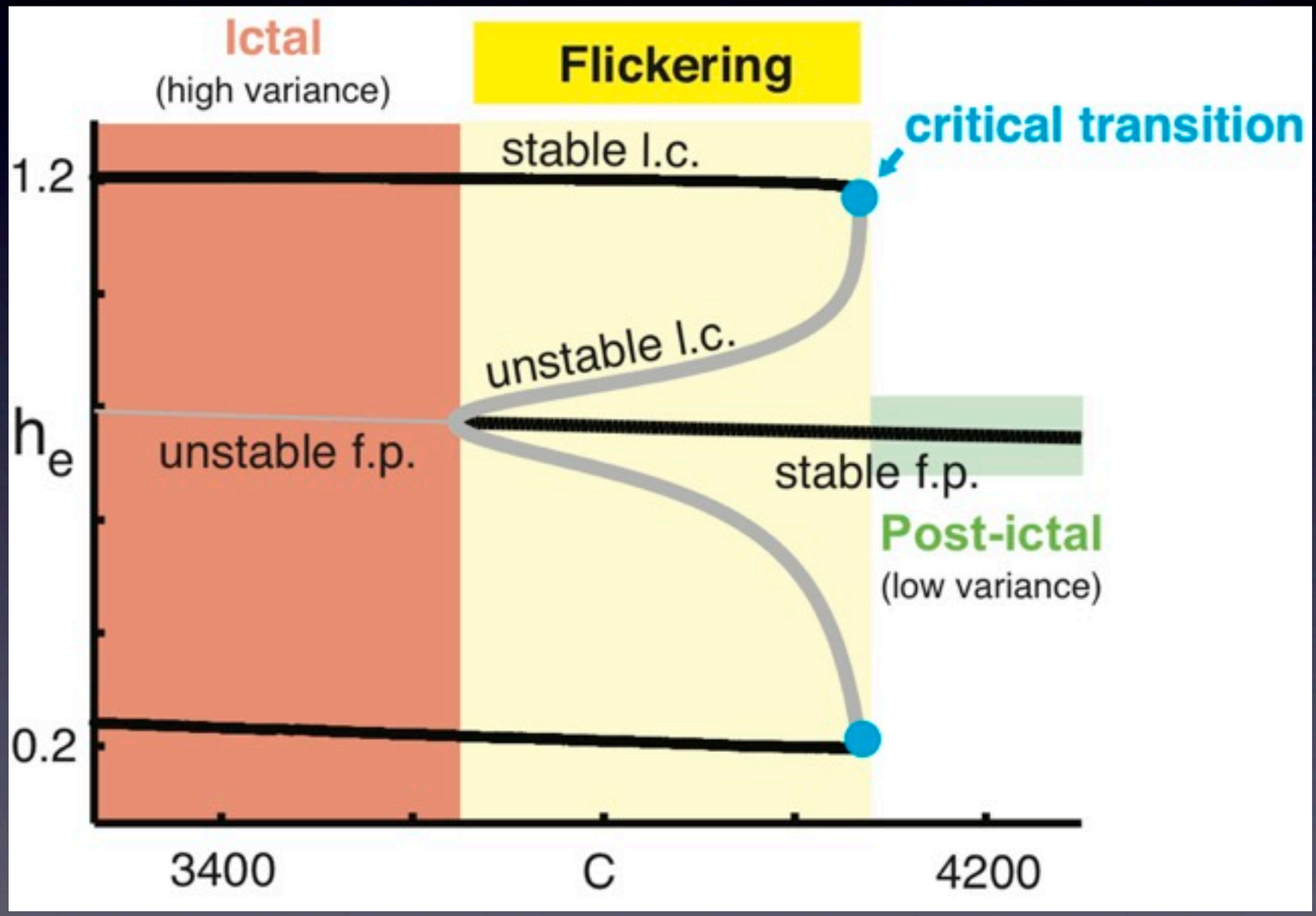
"point" is stable

Small amplitude rhythms, low var

Flickering between two attractors

Model (details)

Bifurcation diagram (single "cortical column")



Saddle node of limit cycles

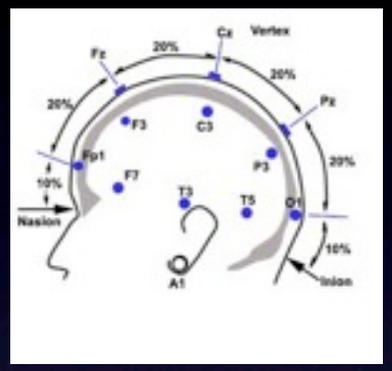
Mimics behavior of clinical data . . .

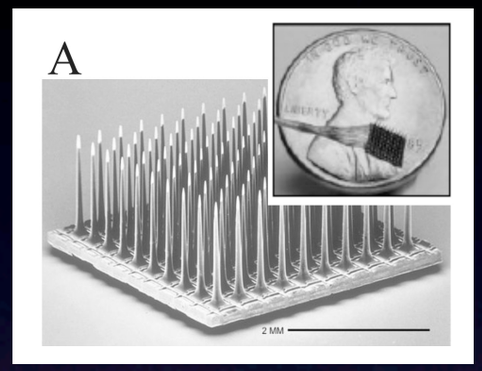
- Critical slowing
- Flickering

Dynamical mechanisms of seizure termination . . .

Conclusions

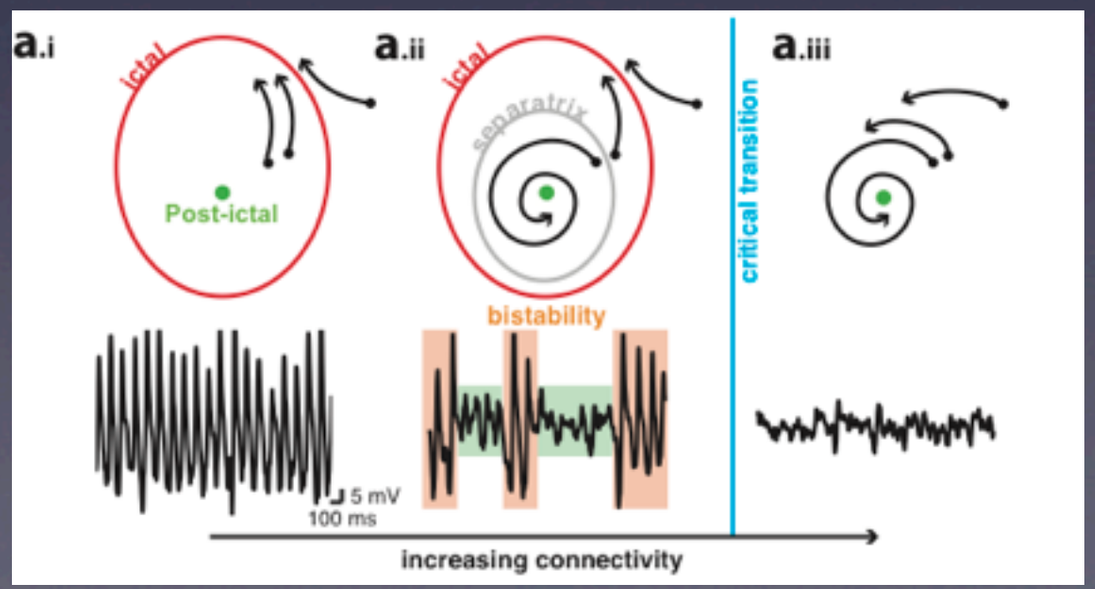
- Seizures across spatial and temporal scales





- Time: ictal chirp

- Space: fracturing & coalescence
- Termination: tipping point.
- Status: failure to cross tipping point.



Thanks

The patient volunteers

Burroughs Wellcome Fund

NIH R01NS072023

BU: Uri Eden, Eric Kolaczyk, Kyle Lepage

Brown: Wilson Truccolo

MGH: Sydney Cash, Catherine Chu, Emad Eskandar

http://makramer.info