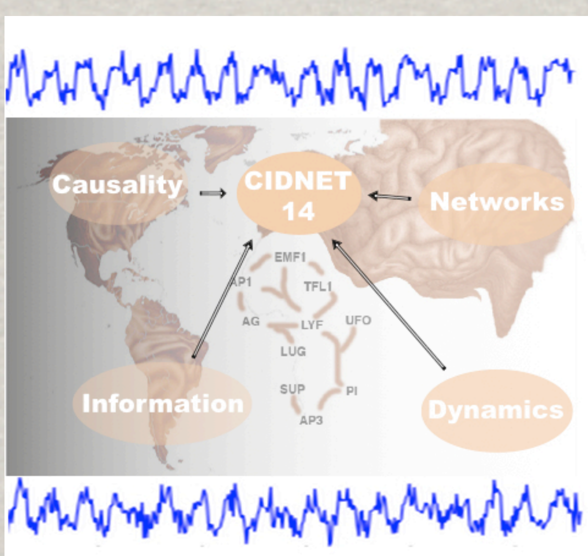
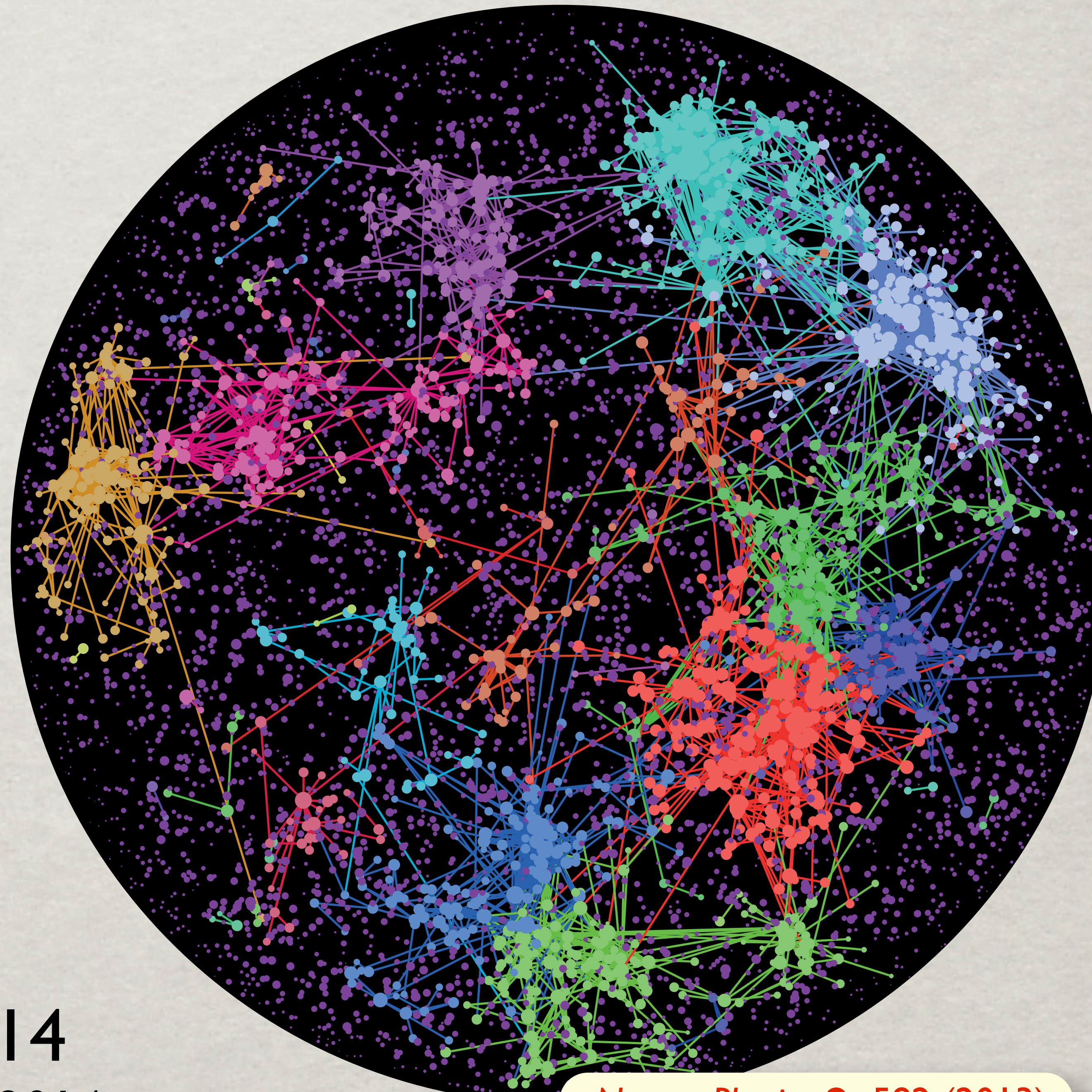
NOISE FOCUSING: THE EMERGENCE OF COHERENT ACTIVITY IN NEURONAL CULTURES

Jaume Casademunt
J. G. Orlandi
J. Soriano
S. Teller
Universitat de Barcelona

E. Álvarez-Lacalle
Universitat Politècnica de Catalunya

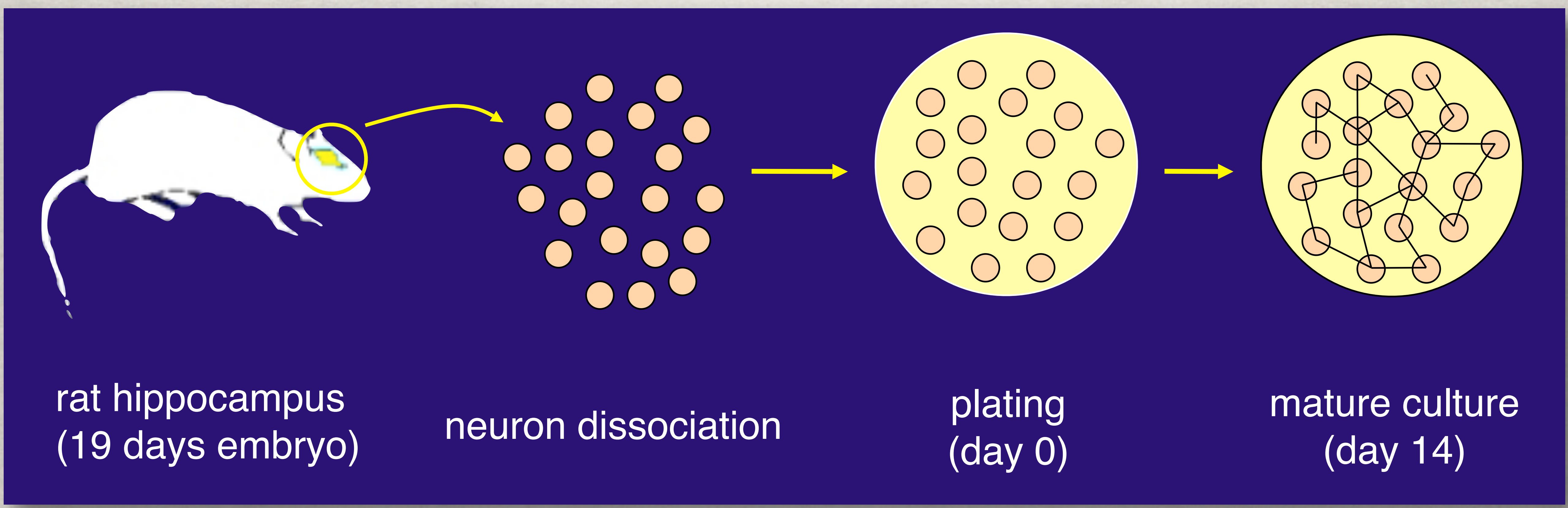


CIDNET14
Dresden, June 2014

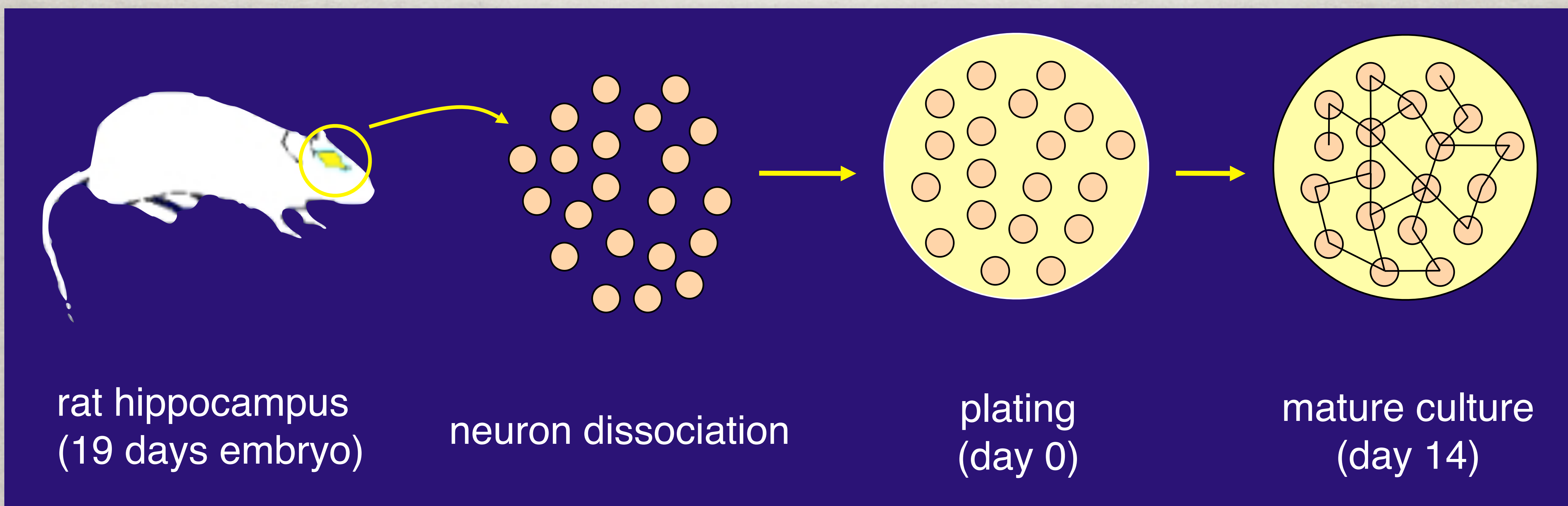


Nature Physics **9,** 582 (2013)

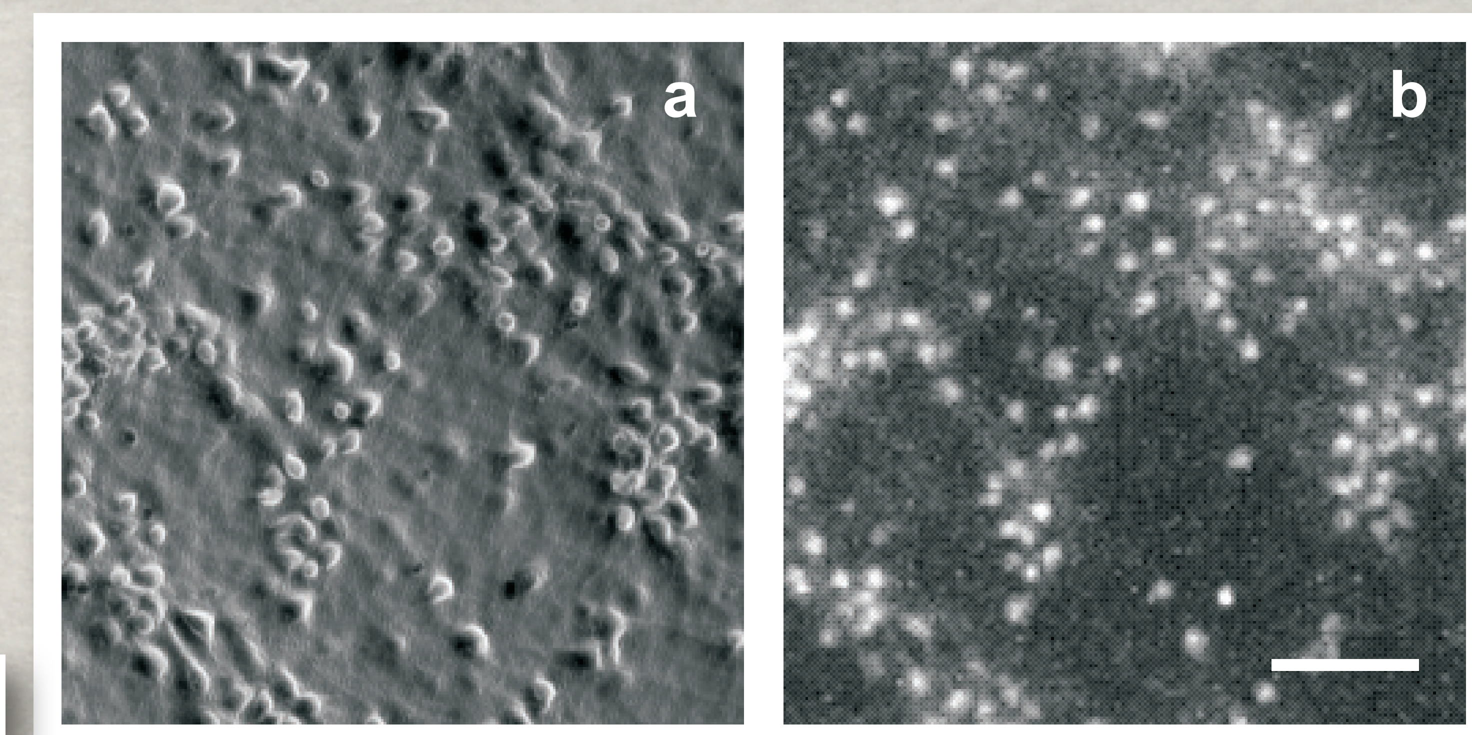
NEURONAL CULTURES AS MODEL SYSTEMS



NEURONAL CULTURES AS MODEL SYSTEMS



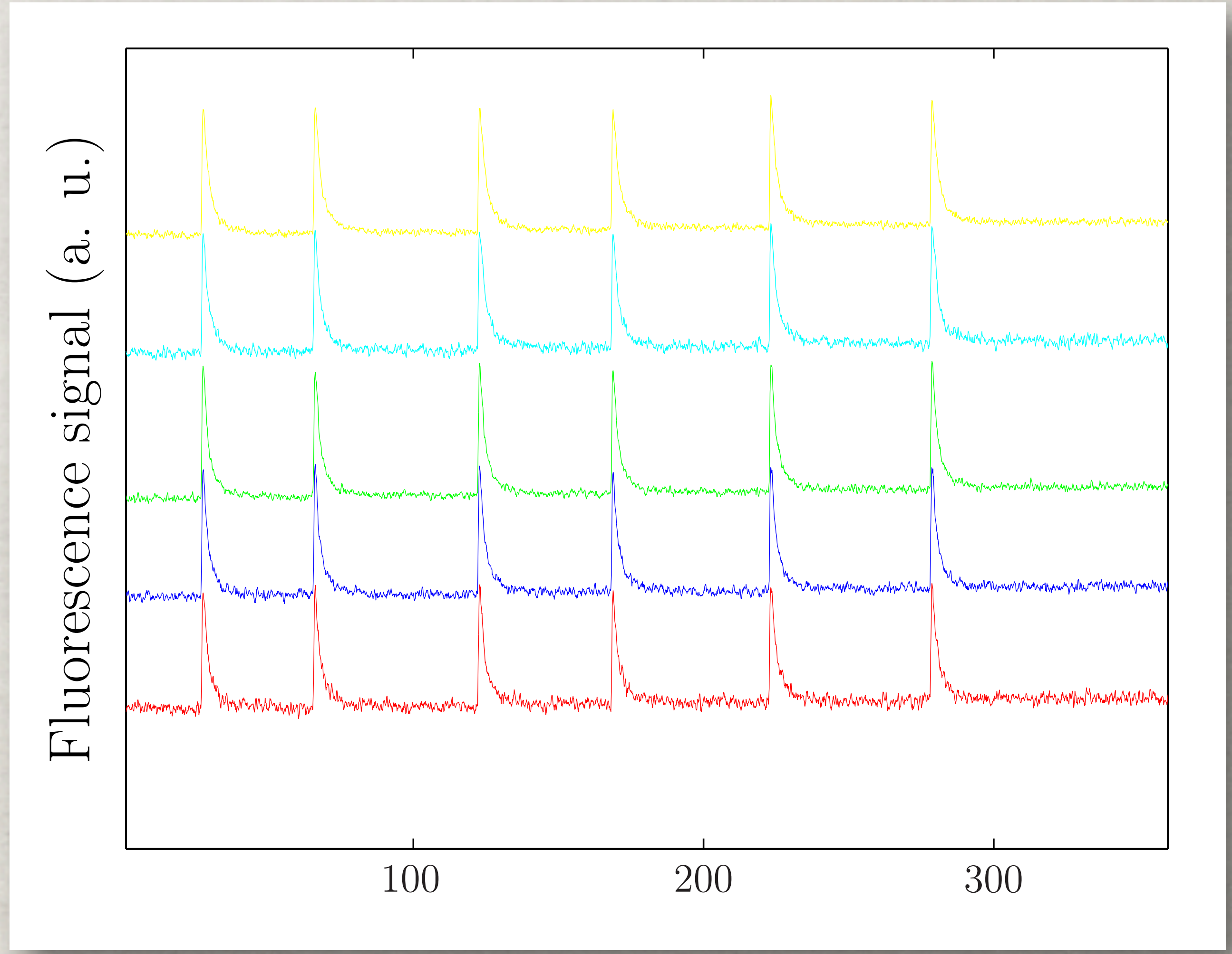
Bright field



Fluorescence

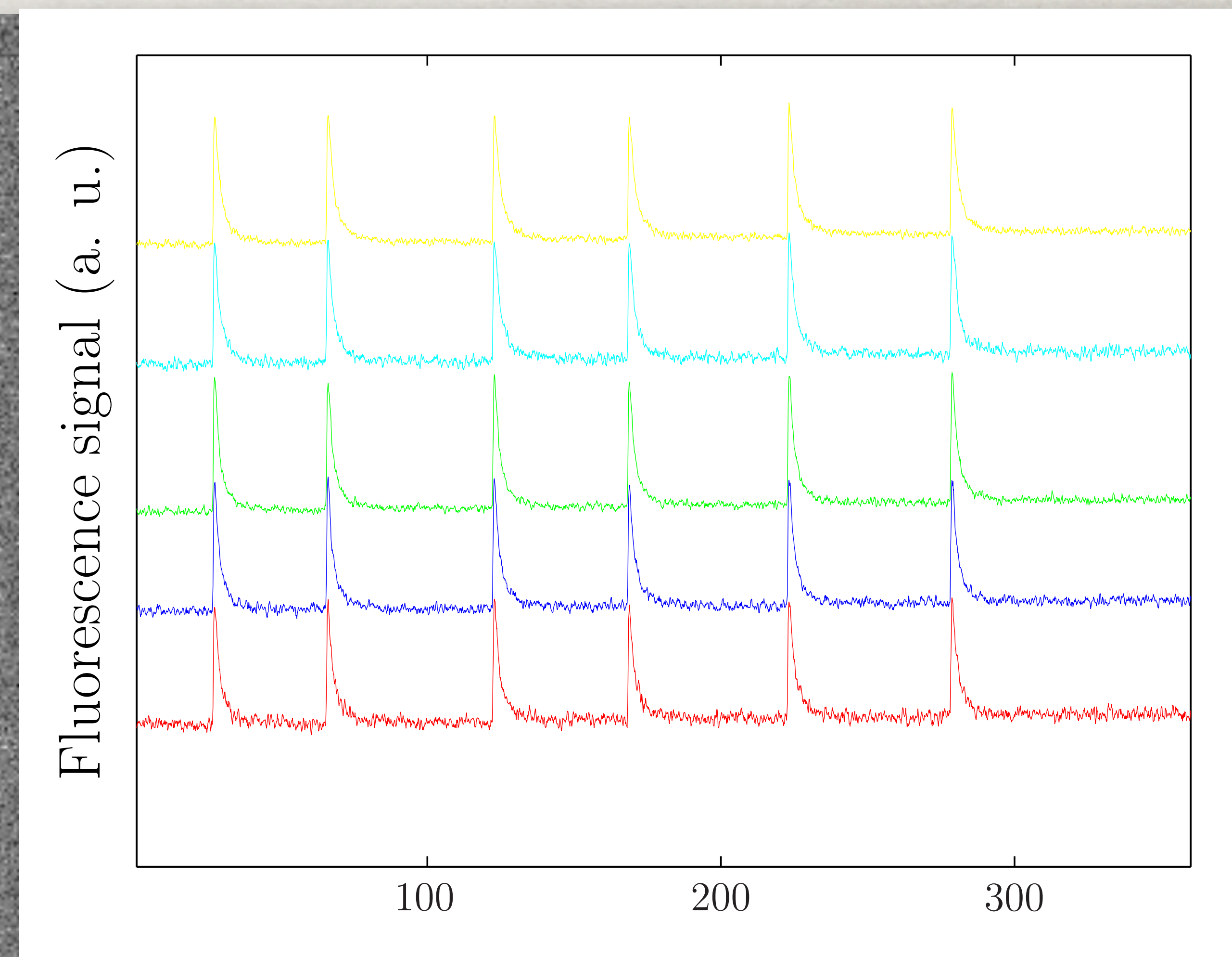
EMERGENCE OF COHERENT BEHAVIOUR

The phenomenon:
Noisy incoherent firing turns into a global highly periodic bursting



EMERGENCE OF COHERENT BEHAVIOUR

The phenomenon:
Noisy incoherent firing turns into a global highly periodic bursting



What is the nature of this periodic pulsation?

A FIRST BASIC QUESTION

What is the nature of this periodic pulsation?

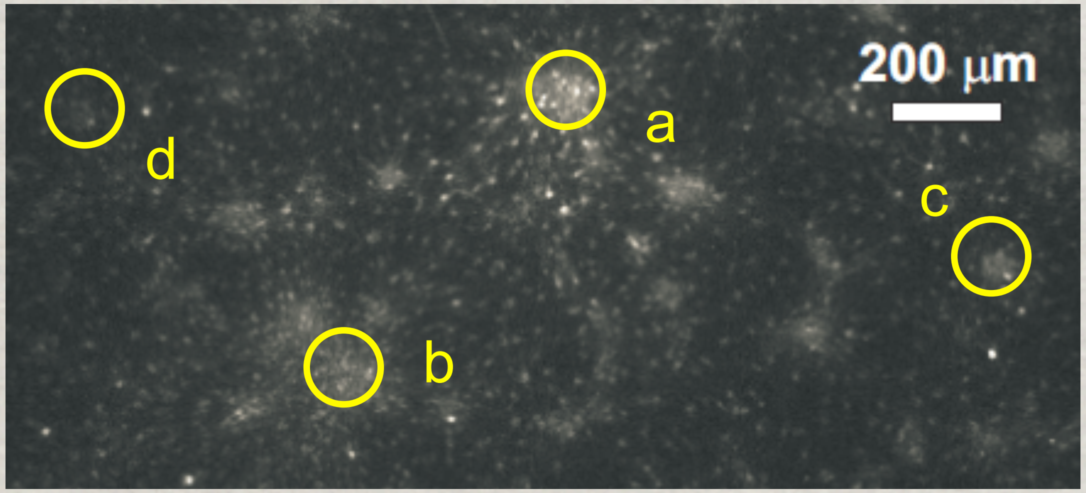
Synchronization? Wave propagation?

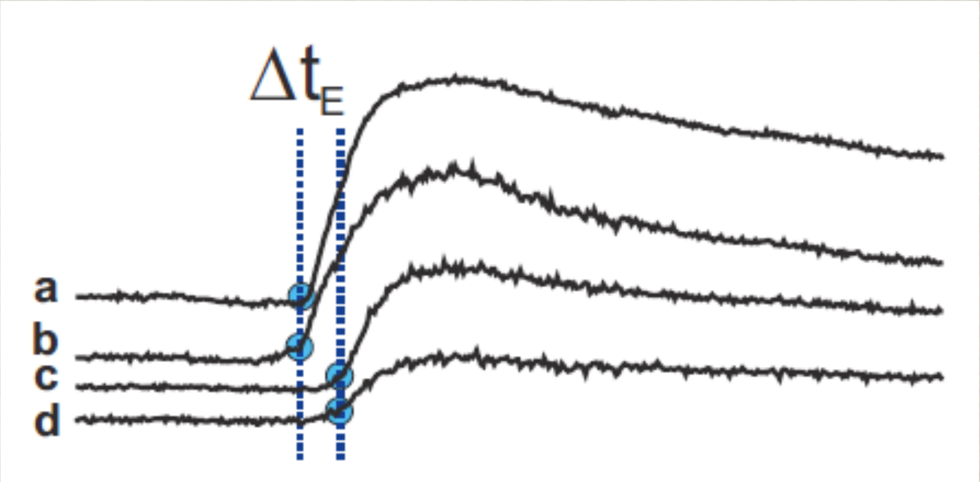
Are there pacemakers?

Are there leader neurons?

Is it self-organized? What mechanism?

RESOLVING A WAVE

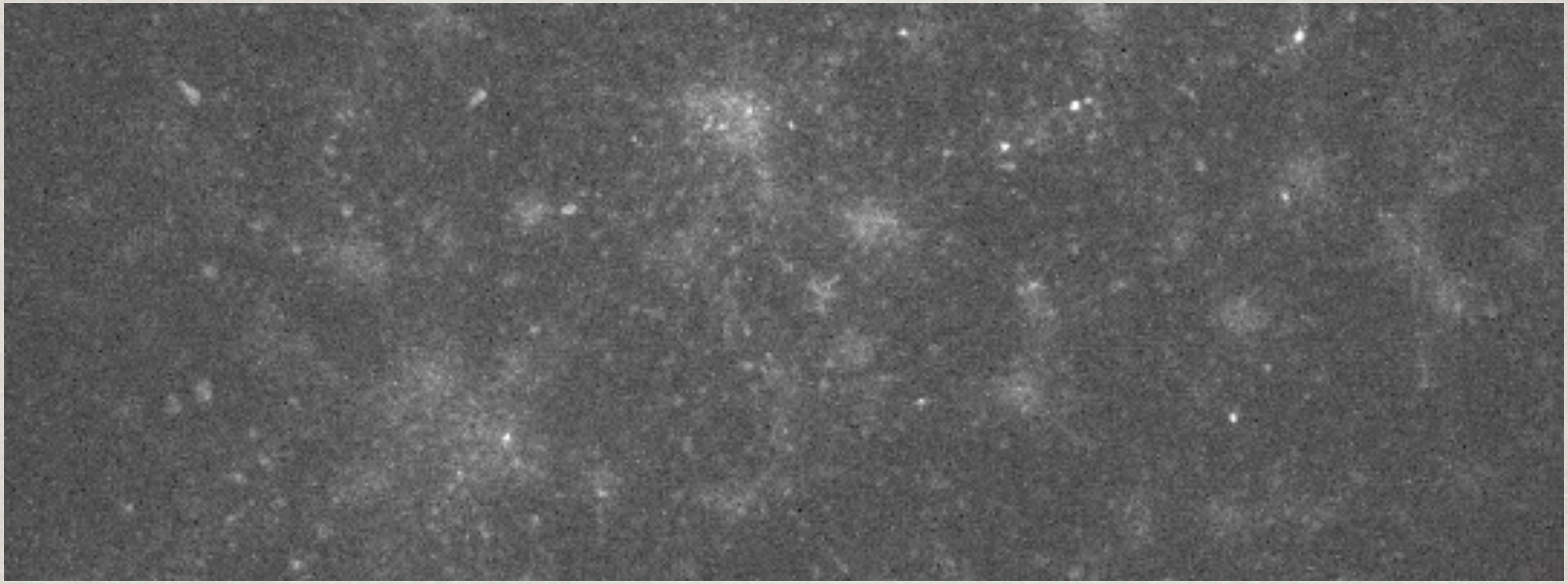


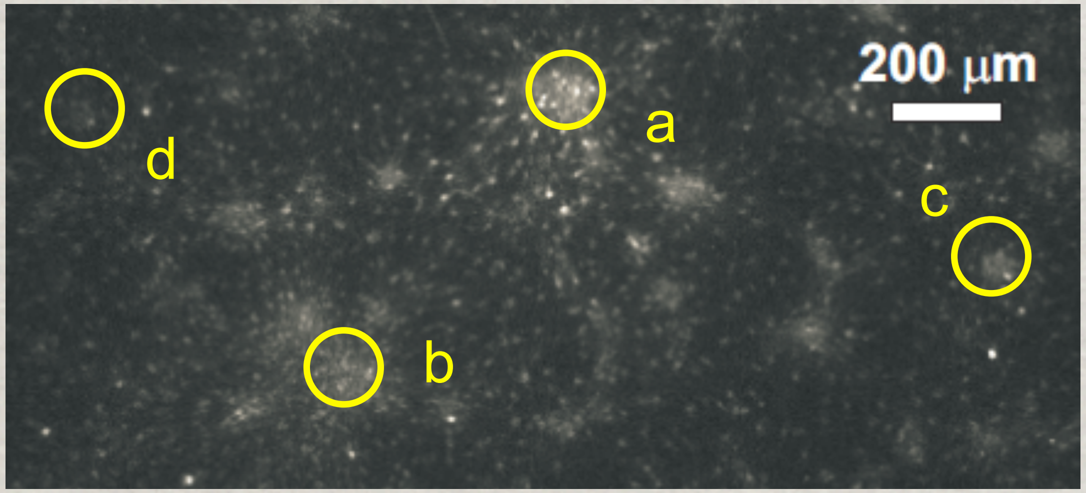


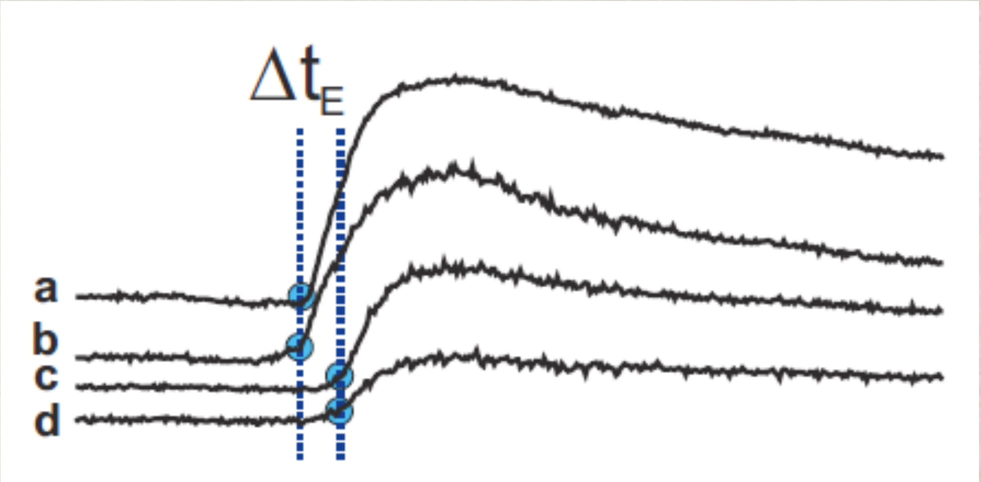
200 frames/s
4 µm/pixel

High-speed Calcium imaging allows to resolve waves

RESOLVING A WAVE



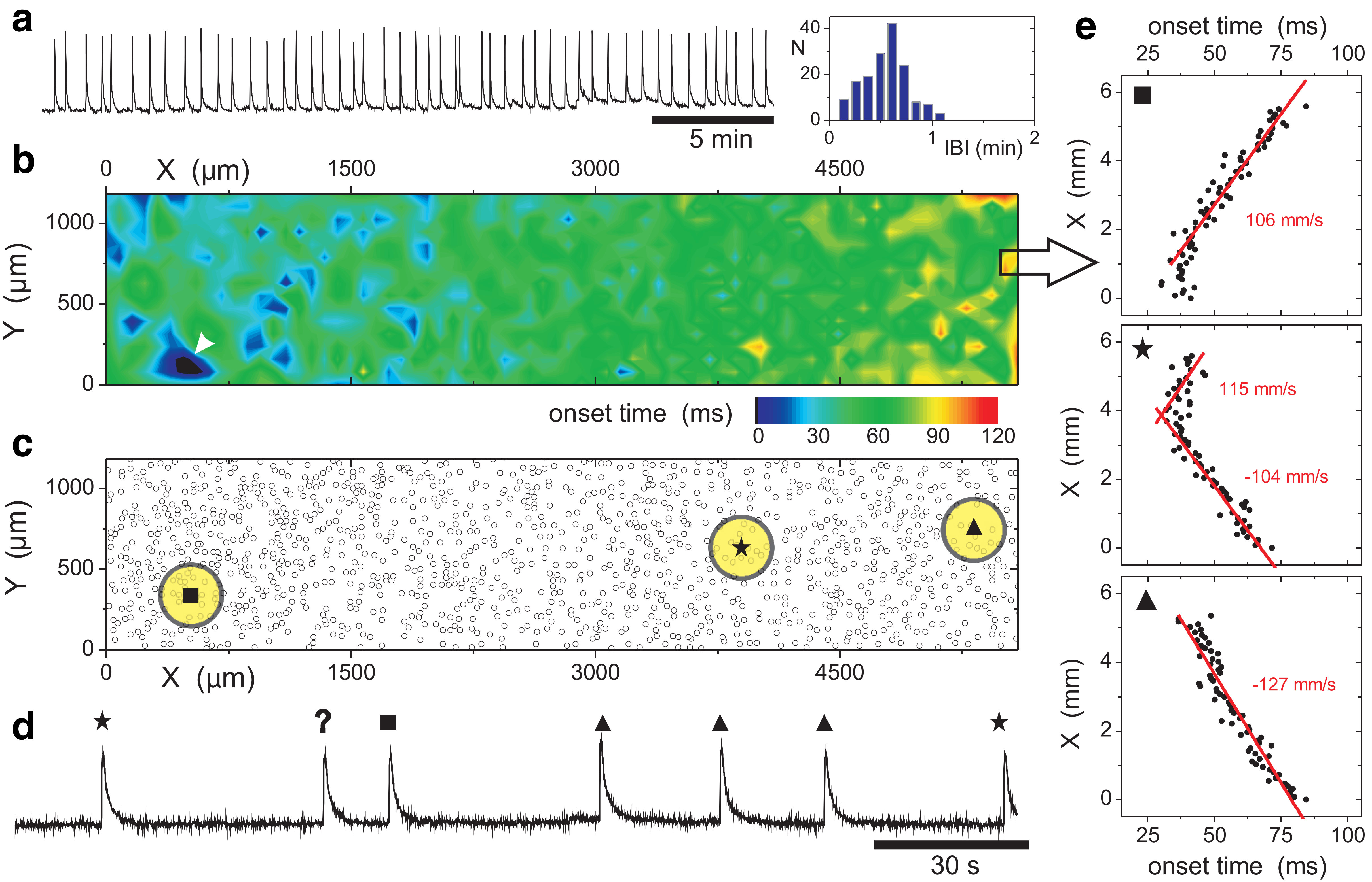




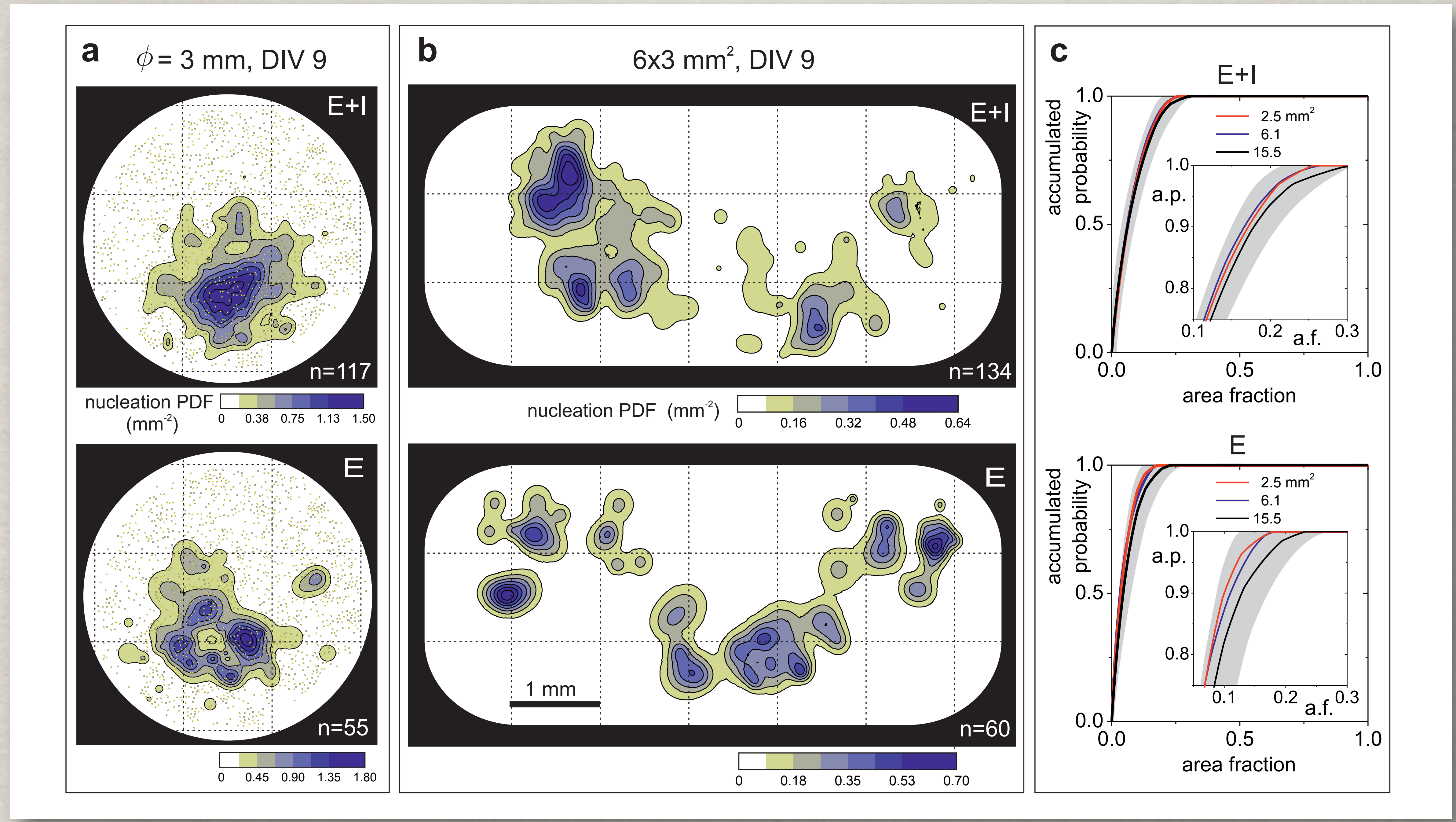
200 frames/s
4 μm/pixel

High-speed Calcium imaging allows to resolve waves

WAVE INITIATION AND PROPAGATION



LOCALIZATION OF WAVE NUCLEATION PROBABILITY



The distribution of wave-initiation points is very sharply peaked, defining specific ‘nucleation sites’.

The time sequence of nucleation events is completely random: the phenomenon is noise-driven !

THE PUZZLE

Why are the nucleation sites so sharply selected out of a fairly homogeneous network?

How can it be periodic but initiated randomly from a set of spots?

THE PUZZLE

Why are the nucleation sites so sharply selected out of a fairly homogeneous network?

How can it be periodic but initiated randomly from a set of spots?

The nucleation must be extremely fast, comparable to the spontaneous firing rate of an isolated neuron (0.1 - 1 Hz) !!

THE PUZZLE

Why are the nucleation sites so sharply selected out of a fairly homogeneous network?

How can it be periodic but initiated randomly from a set of spots?

The nucleation must be extremely fast, comparable to the spontaneous firing rate of an isolated neuron (0.1 - 1 Hz) !!

We need to explain highly inhomogeneous effective noise and fast nucleation, i.e. strong spatio-temporal localization:

THE PUZZLE

Why are the nucleation sites so sharply selected out of a fairly homogeneous network?

How can it be periodic but initiated randomly from a set of spots?

The nucleation must be extremely fast, comparable to the spontaneous firing rate of an isolated neuron (0.1 - 1 Hz) !!

We need to explain highly inhomogeneous effective noise and fast nucleation, i.e. strong spatio-temporal localization:

NOISE FOCUSING

THE MODEL *IN SILICO*

Constructing the network:

- We place identical neurons randomly and mimic the axon growth to establish connections
- The degree distribution is Gaussian
- There are metric correlations (high clustering)

THE MODEL *IN SILICO*

Constructing the network:

- We place identical neurons randomly and mimic the axon growth to establish connections
- The degree distribution is Gaussian
- There are metric correlations (high clustering)

Modeling the dynamics: integrate-and-fire with internal shot noise

Canonical Model

$$
\begin{aligned}
C\dot{v} &= k(v - v_r)(v - v_t) - u + I \\
\dot{u} &= a(b(v - v_r) - u)
\end{aligned}
$$

$$
\text{if } v \geq v_p \Rightarrow \quad v = c,\ u = u + d
$$

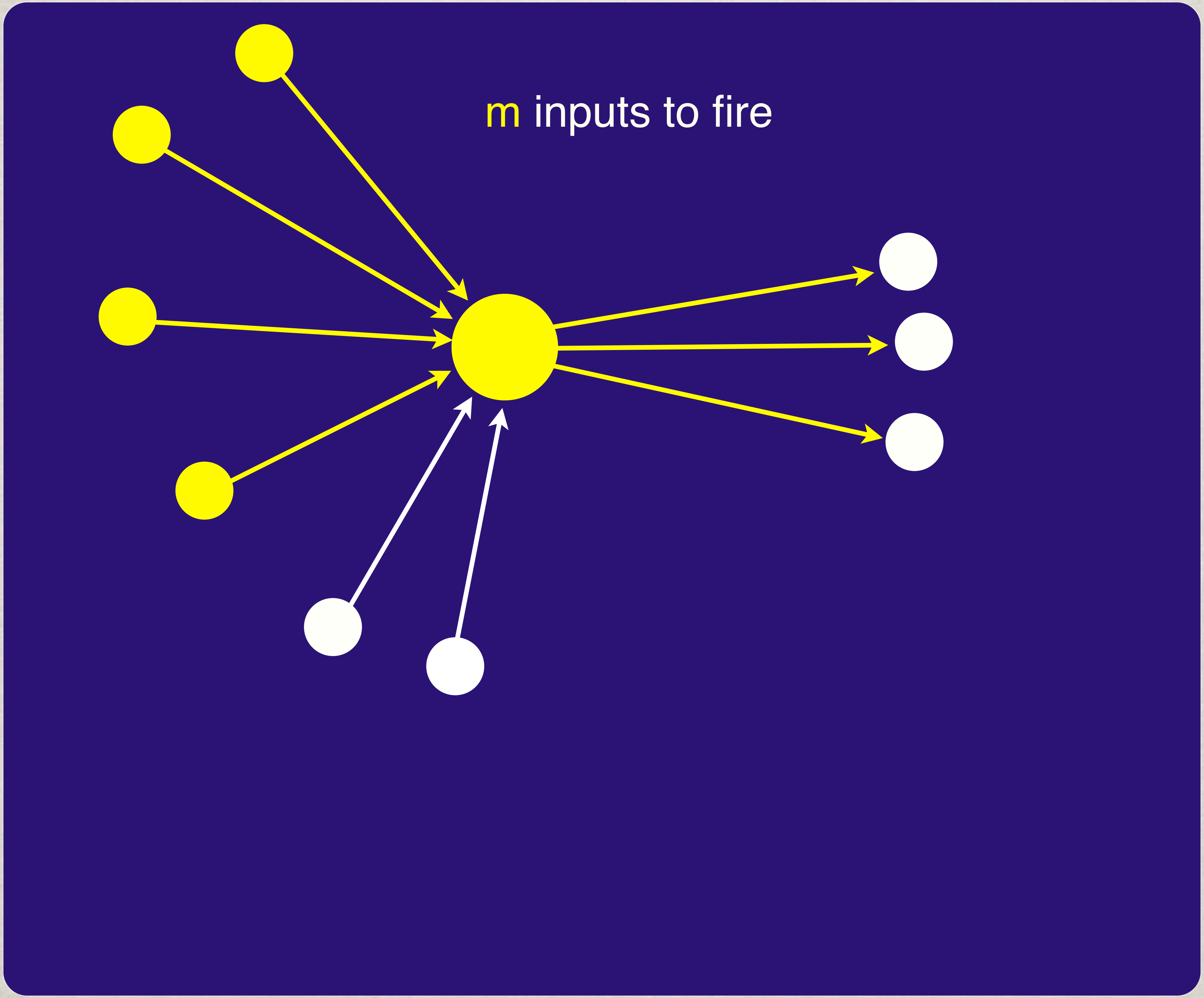
Soma: 2 equations + reset

$$
I_s = gD(t_0)\exp\left(-\frac{t - t_0}{\tau_s}\right)\theta(t - t_0)
$$

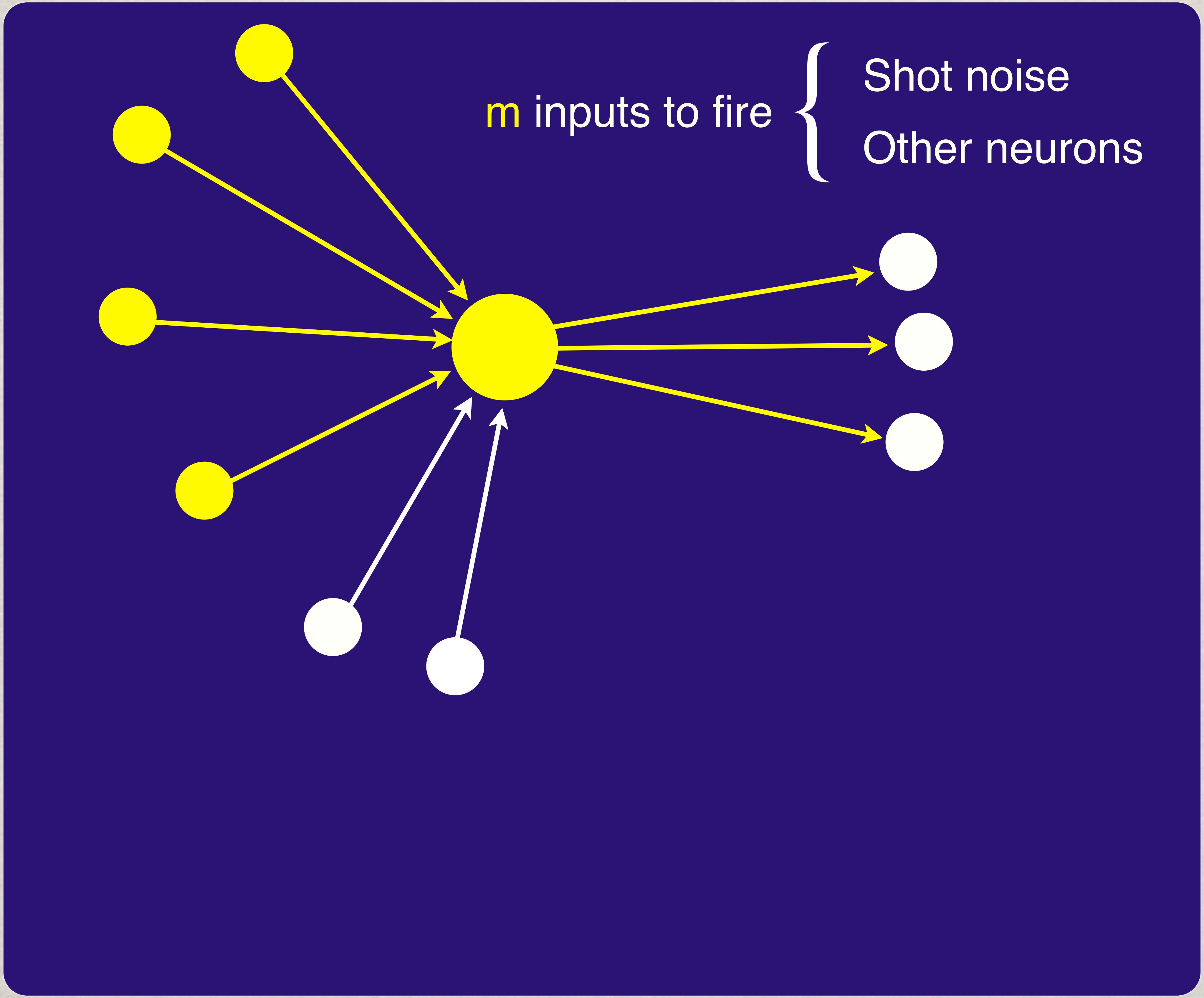
$$
\dot{D} = \frac{1}{\tau_D}(1 - D) \qquad \text{at } t_m \Rightarrow D = \beta D
$$

Synapse: 2 equations + reset

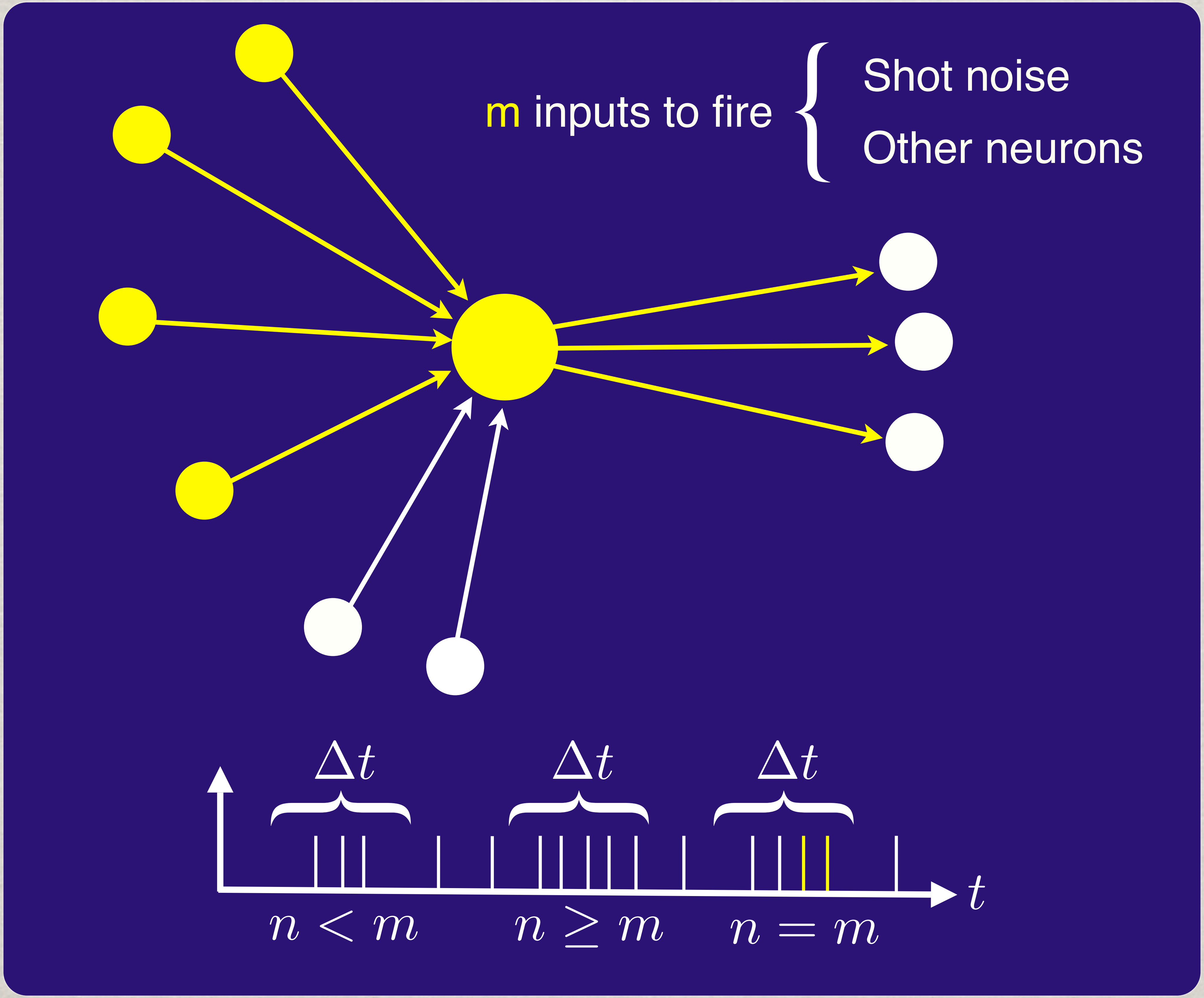
NOISY INTEGRATE-AND-FIRE DYNAMICS: SUB-QUORUM FIRING



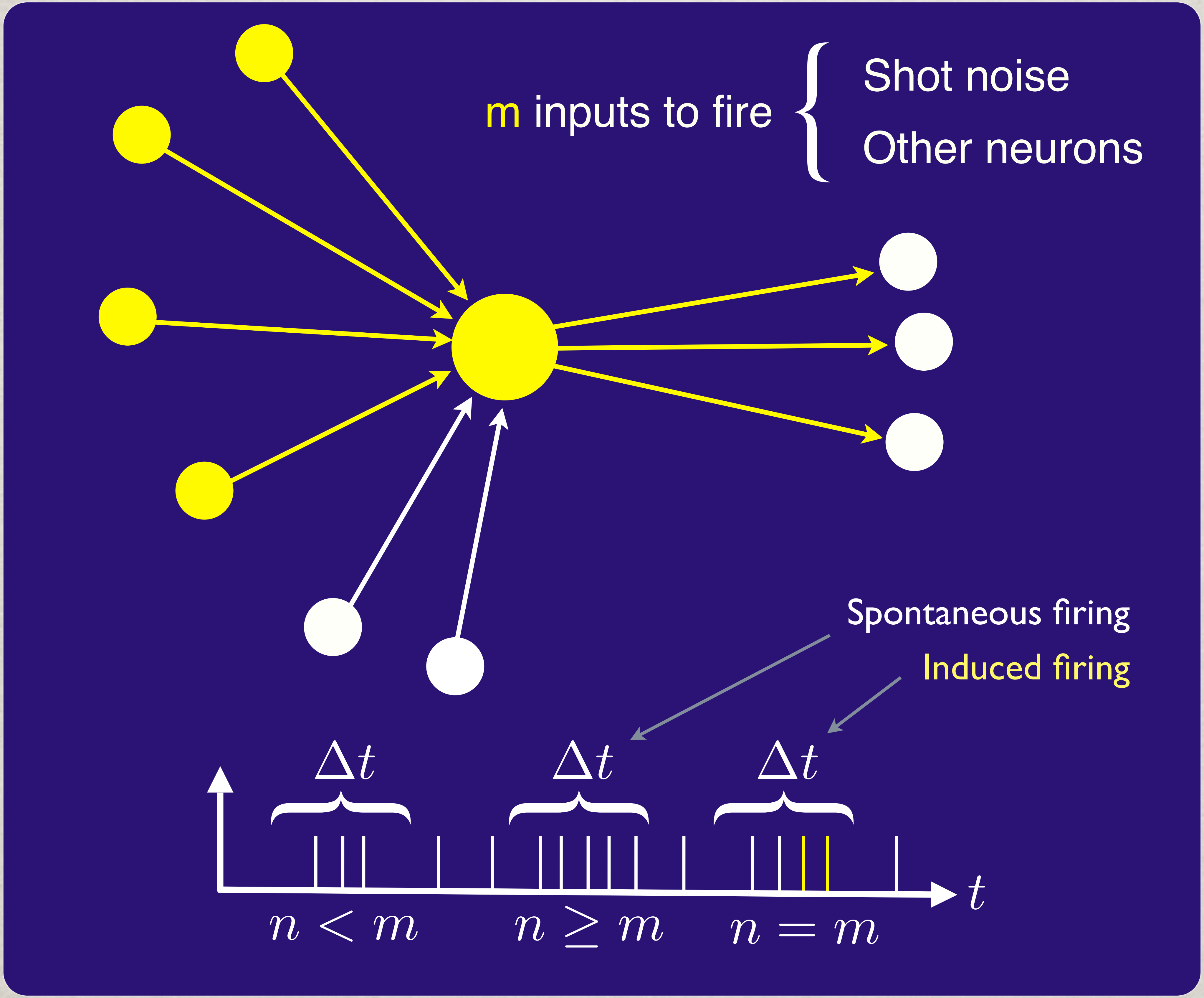
NOISY INTEGRATE-AND-FIRE DYNAMICS: SUB-QUORUM FIRING



NOISY INTEGRATE-AND-FIRE DYNAMICS: SUB-QUORUM FIRING



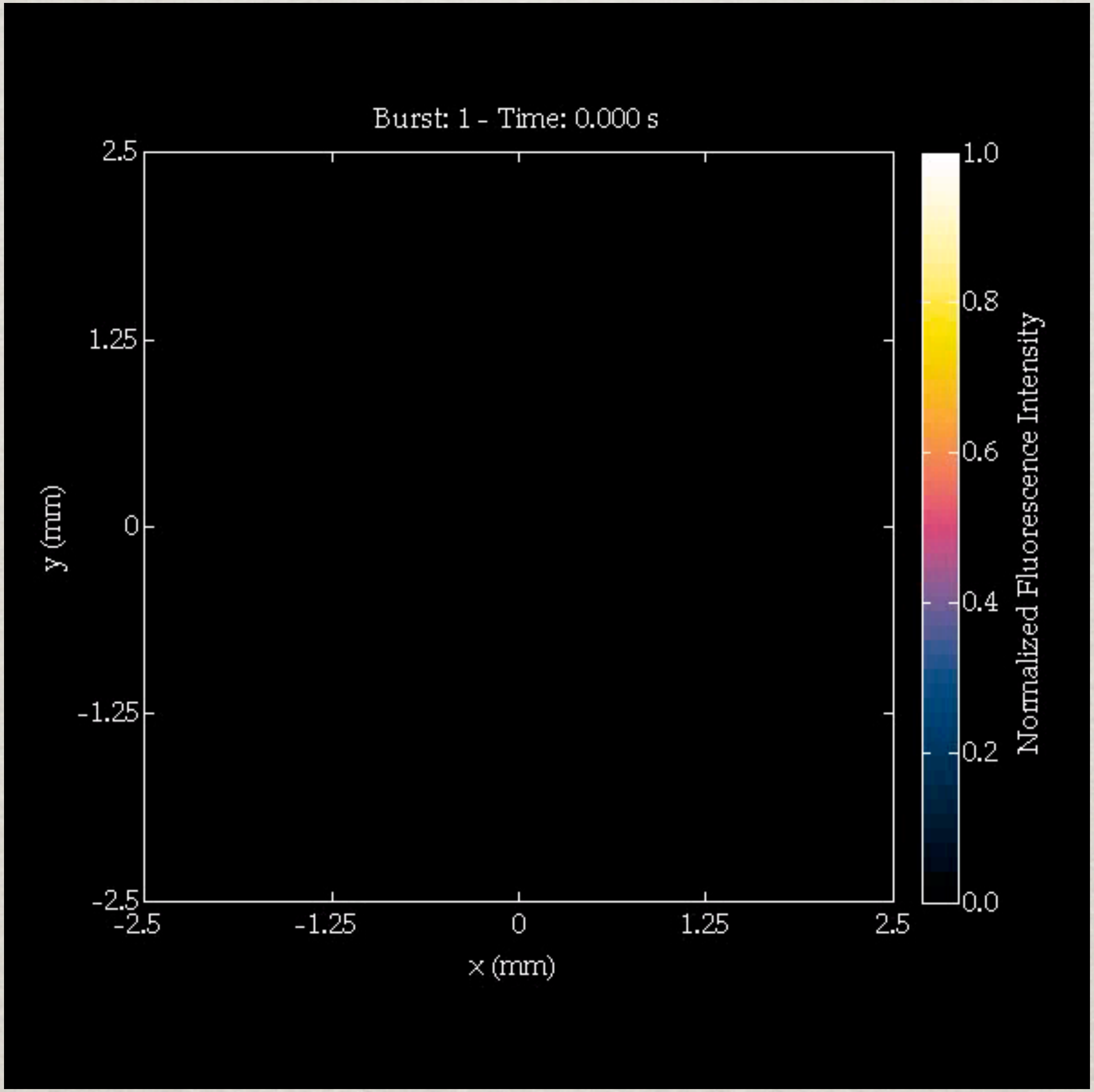
NOISY INTEGRATE-AND-FIRE DYNAMICS: SUB-QUORUM FIRING



BACKGROUND ACTIVITY

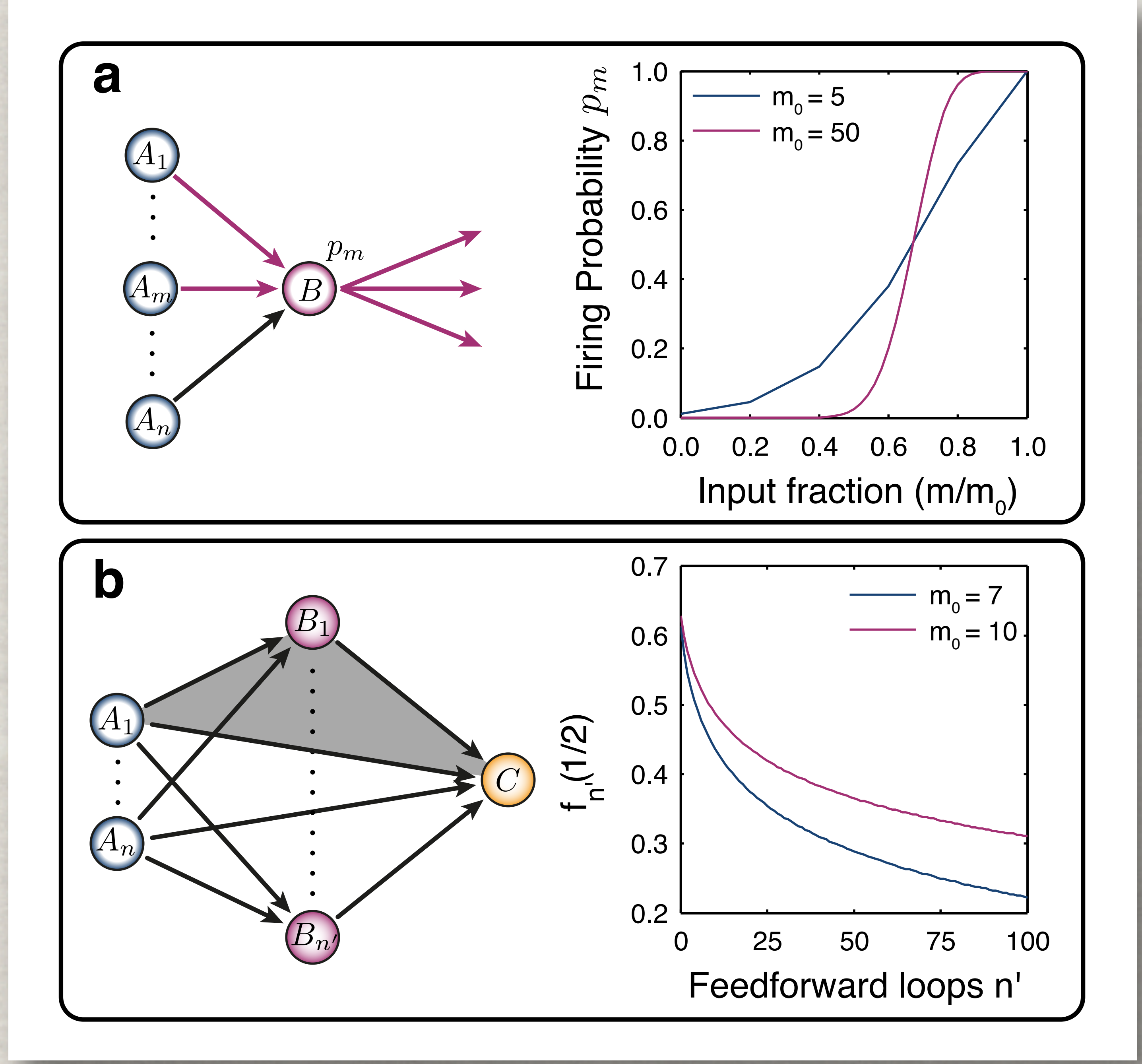
Simulation of identical neurons reproduces all results

BACKGROUND ACTIVITY



Simulation of identical neurons reproduces all results

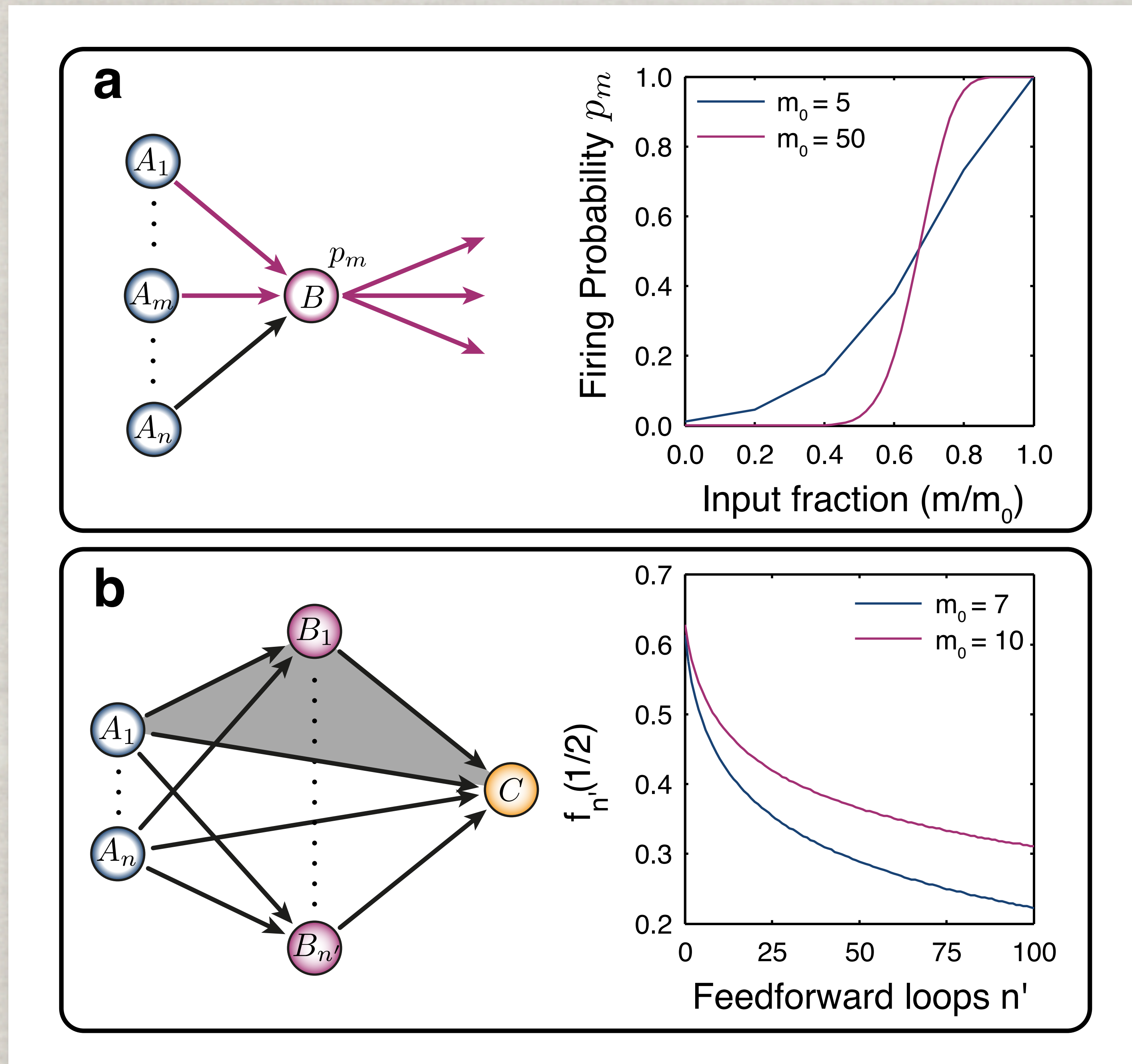
MECHANISMS OF NOISE AMPLIFICATION



Dynamical noise amplification

Topological noise amplification

MECHANISMS OF NOISE AMPLIFICATION

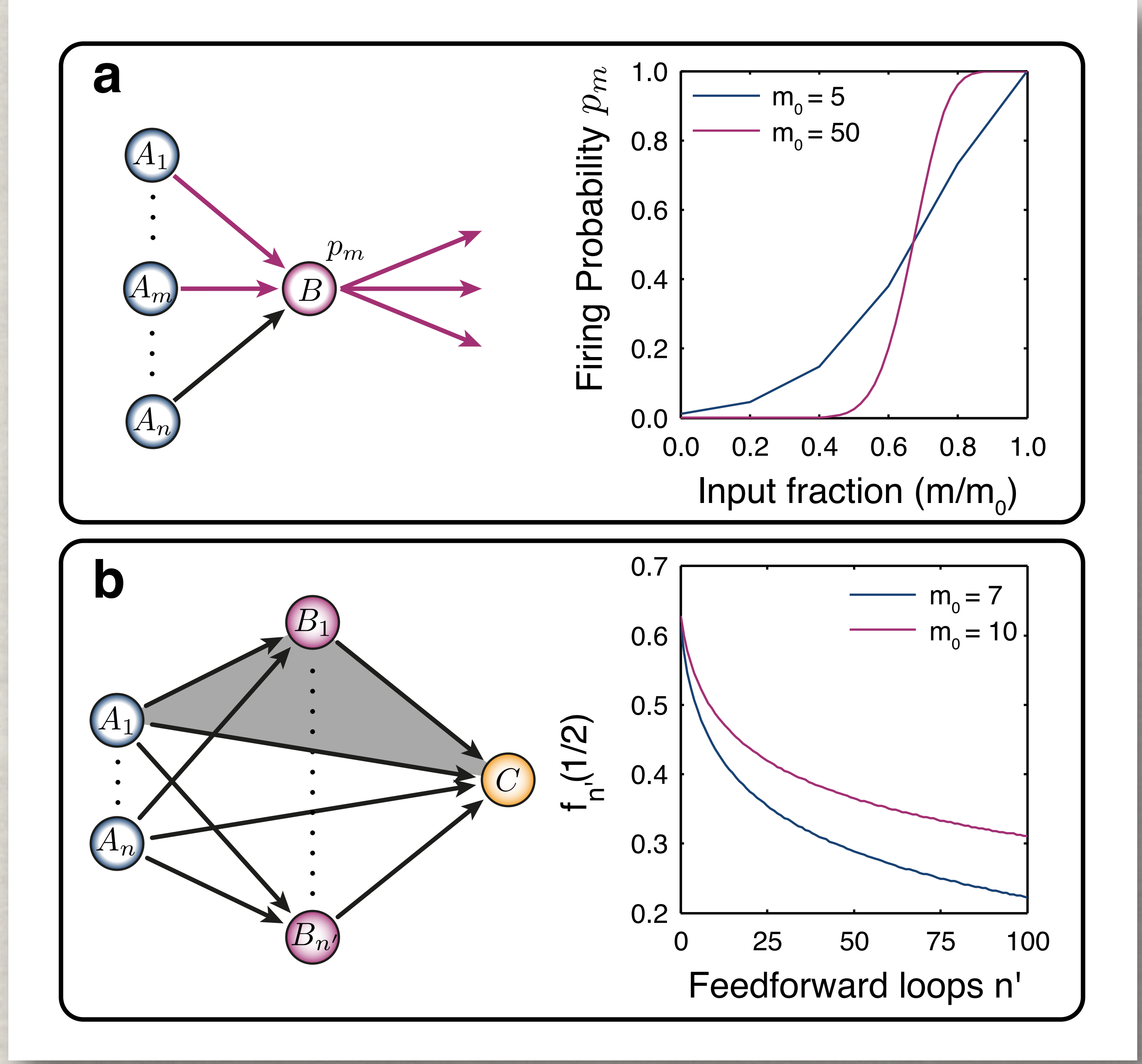


Dynamical noise amplification

Topological noise amplification

These mechanisms are strongly enhanced by metric connectivity correlations

MECHANISMS OF NOISE AMPLIFICATION



Dynamical noise amplification

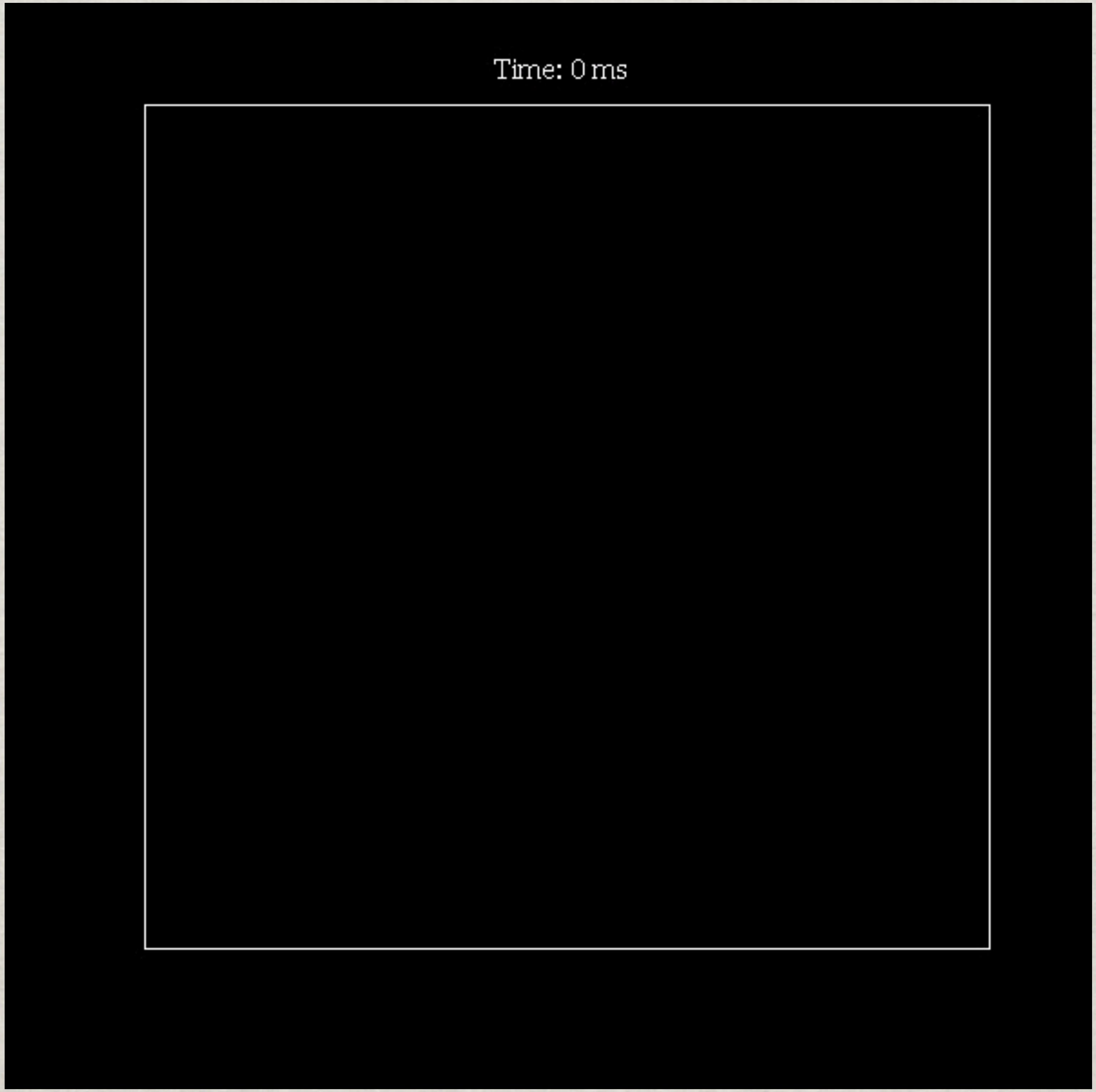
Topological noise amplification

These mechanisms are strongly enhanced by metric connectivity correlations

Noise amplification and propagation introduces strong dynamical correlations: AVALANCHES

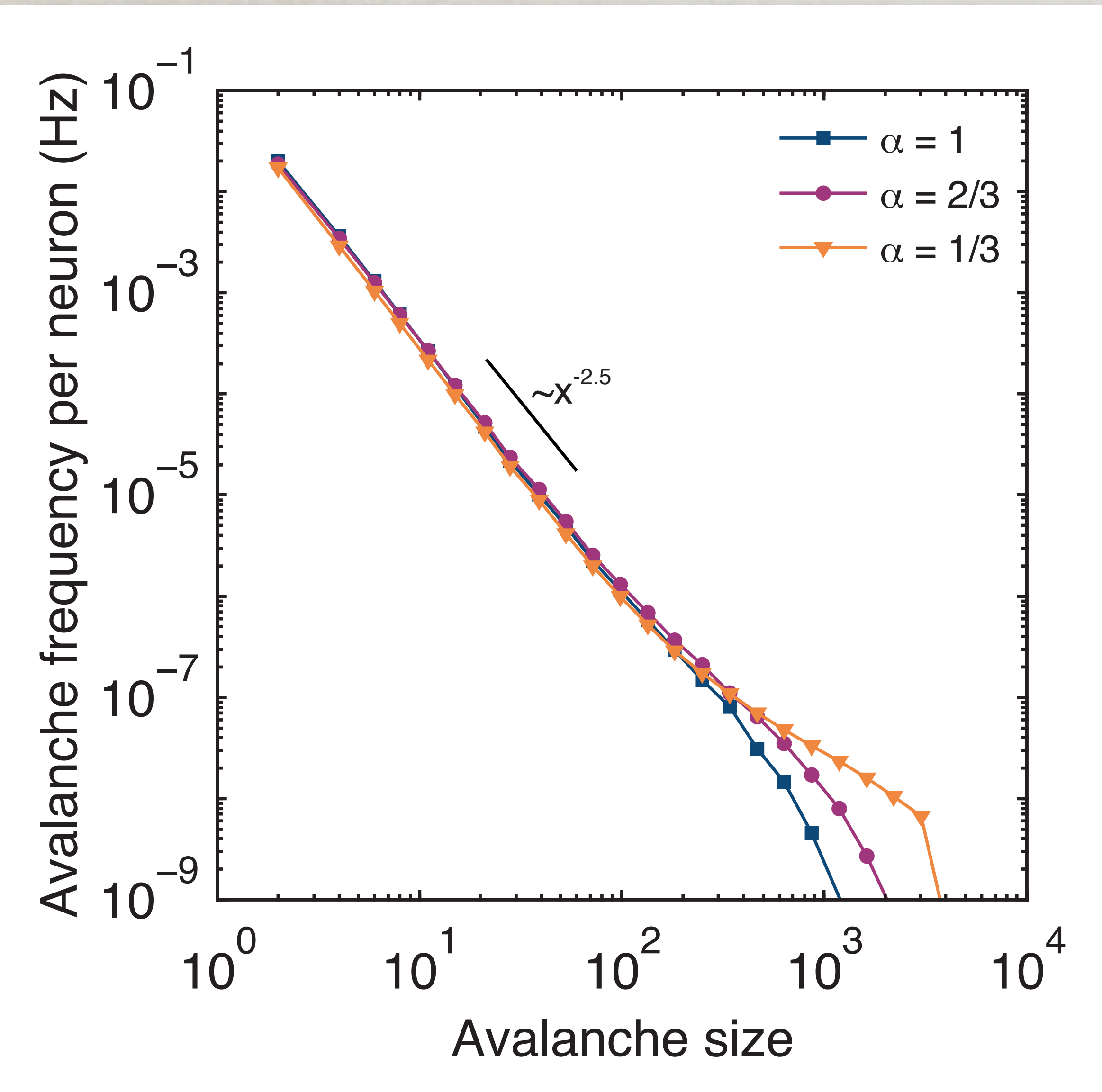
CAUSAL LINKS BETWEEN FIRINGS: BACKGROUND AVALANCHES

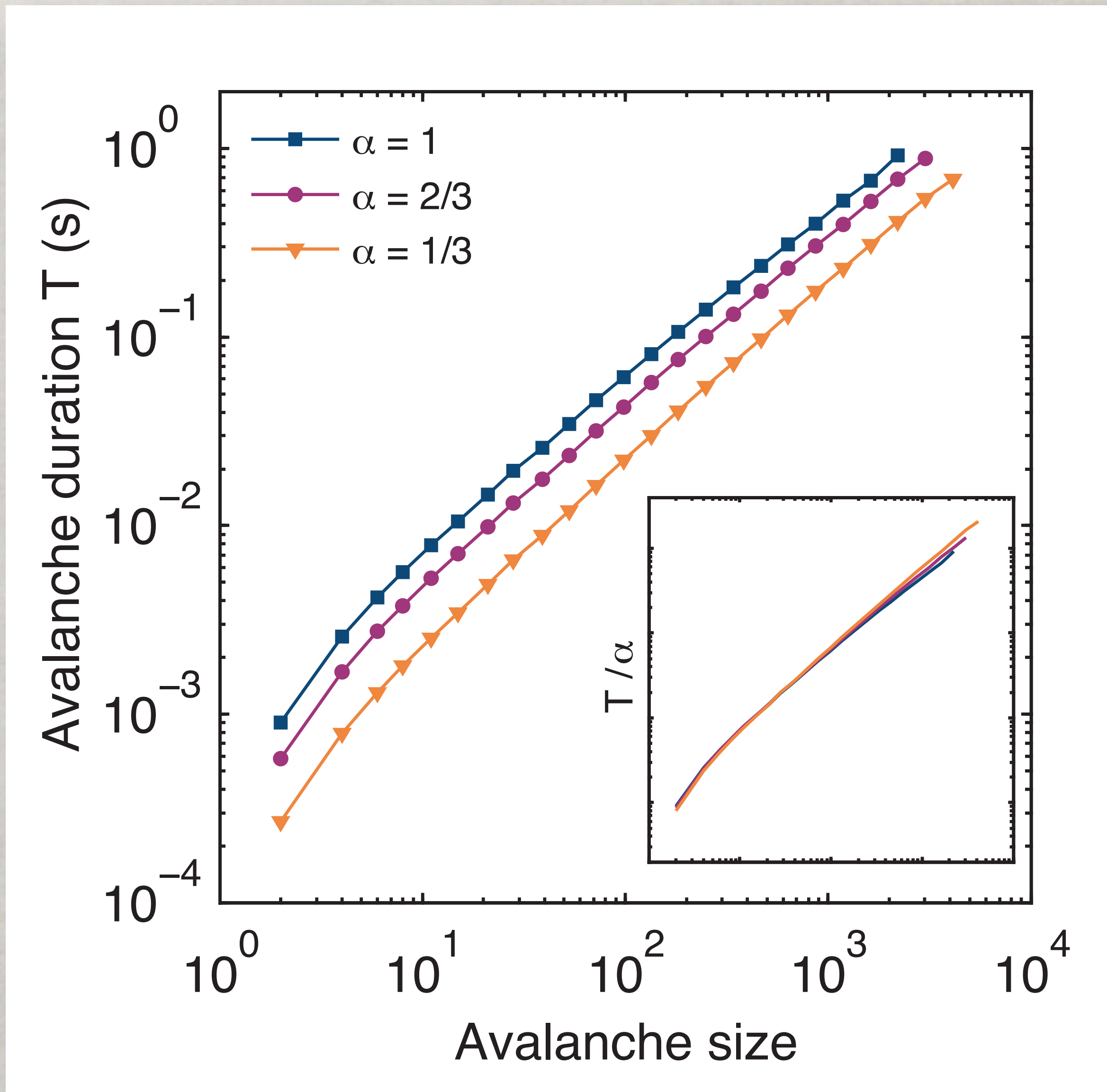
We can extract all causal relationships between firings (reconstruct individual avalanches)



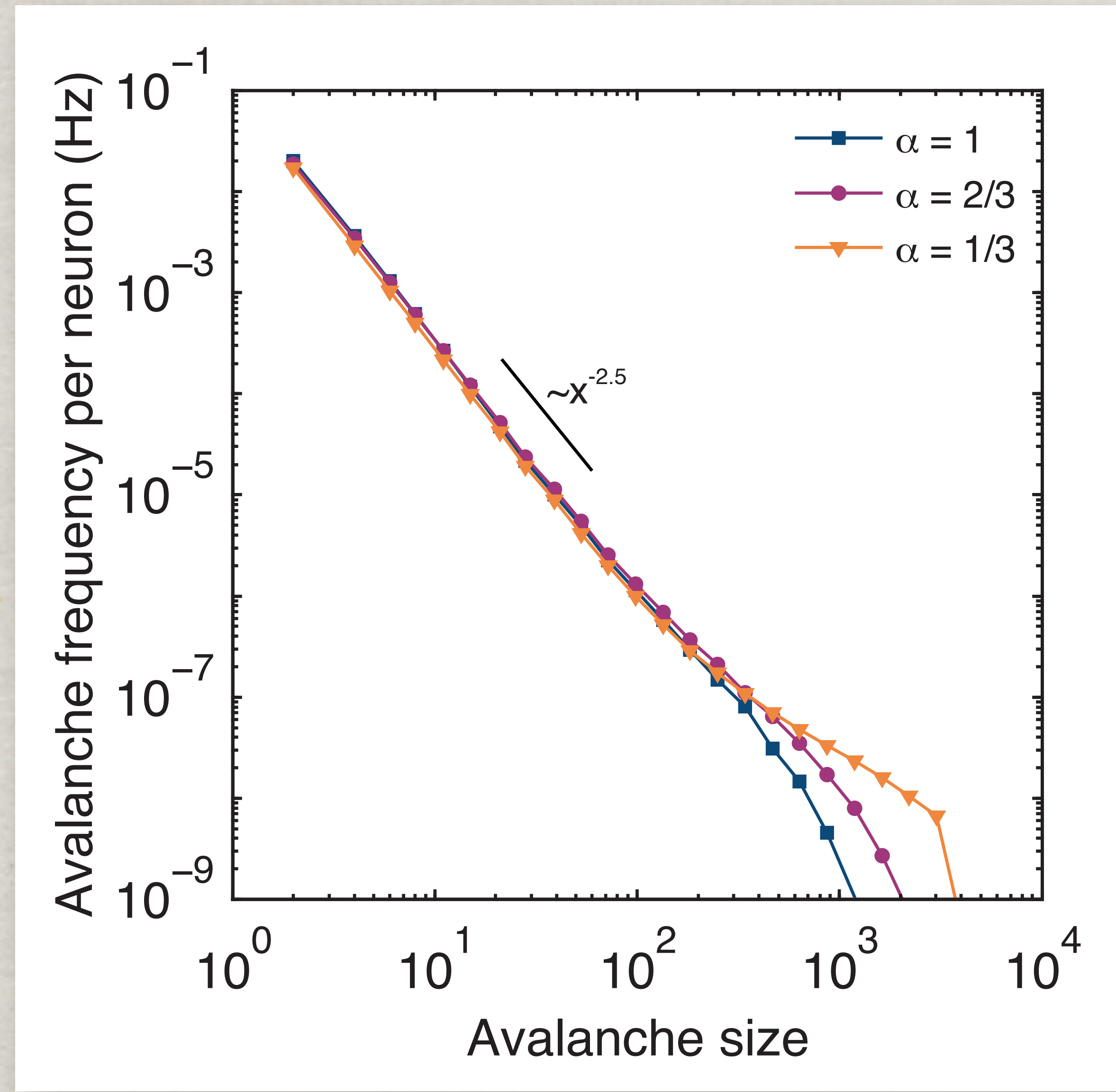
We can extract all causal relationships between firings (reconstruct individual avalanches)

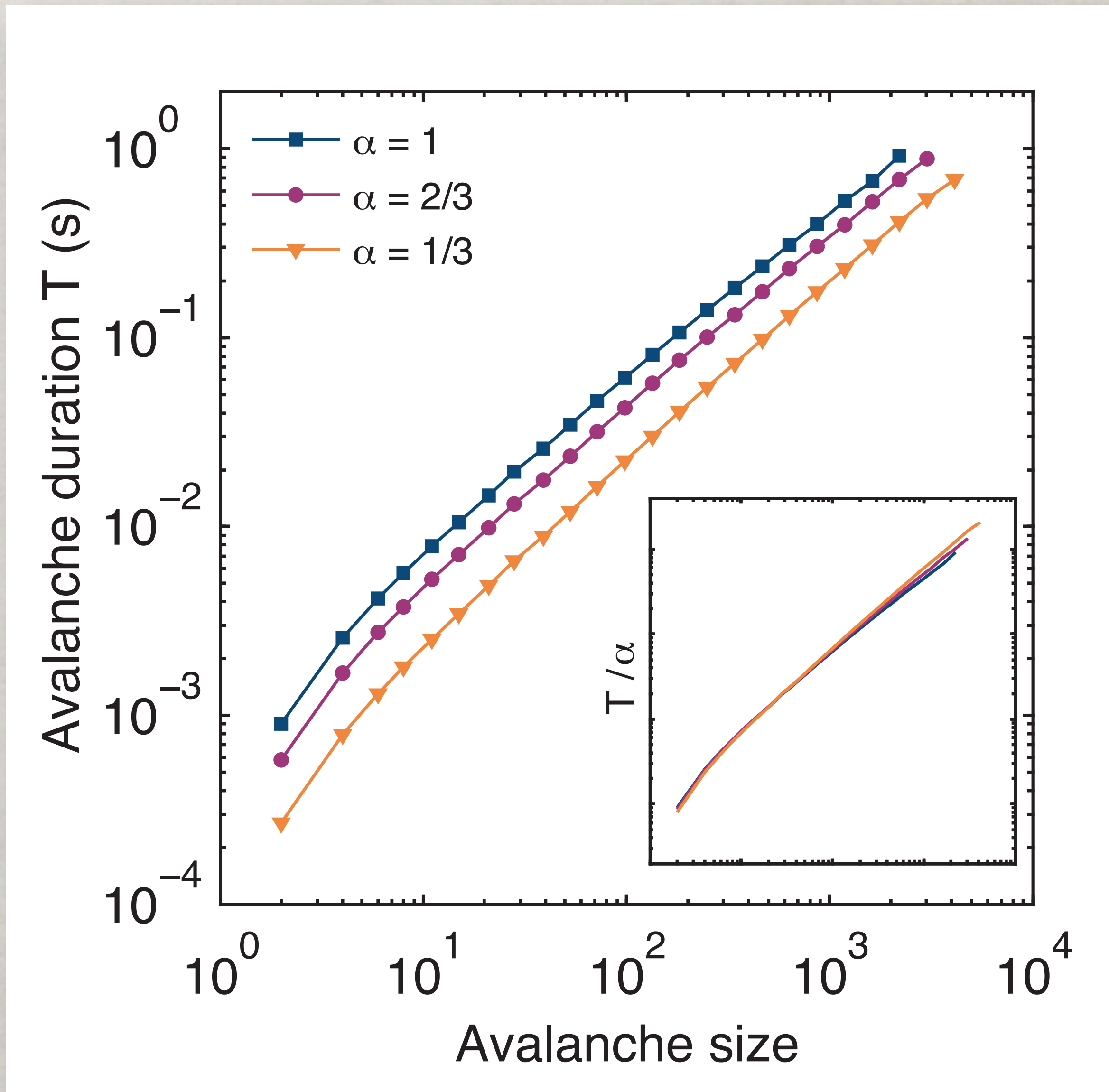
POWER-LAW SCALING OF BACKGROUND AVALANCHES





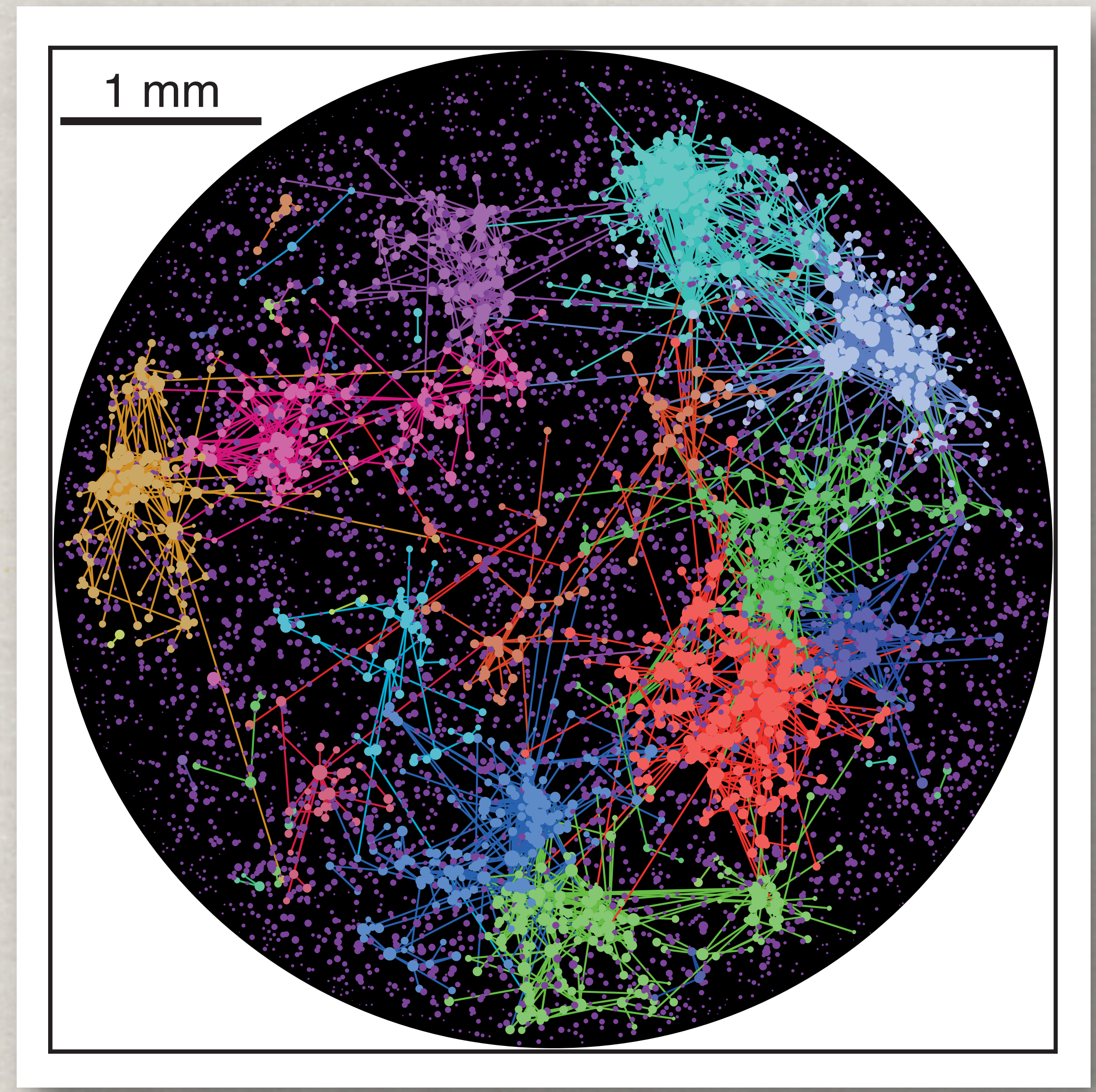
POWER-LAW SCALING OF BACKGROUND AVALANCHES

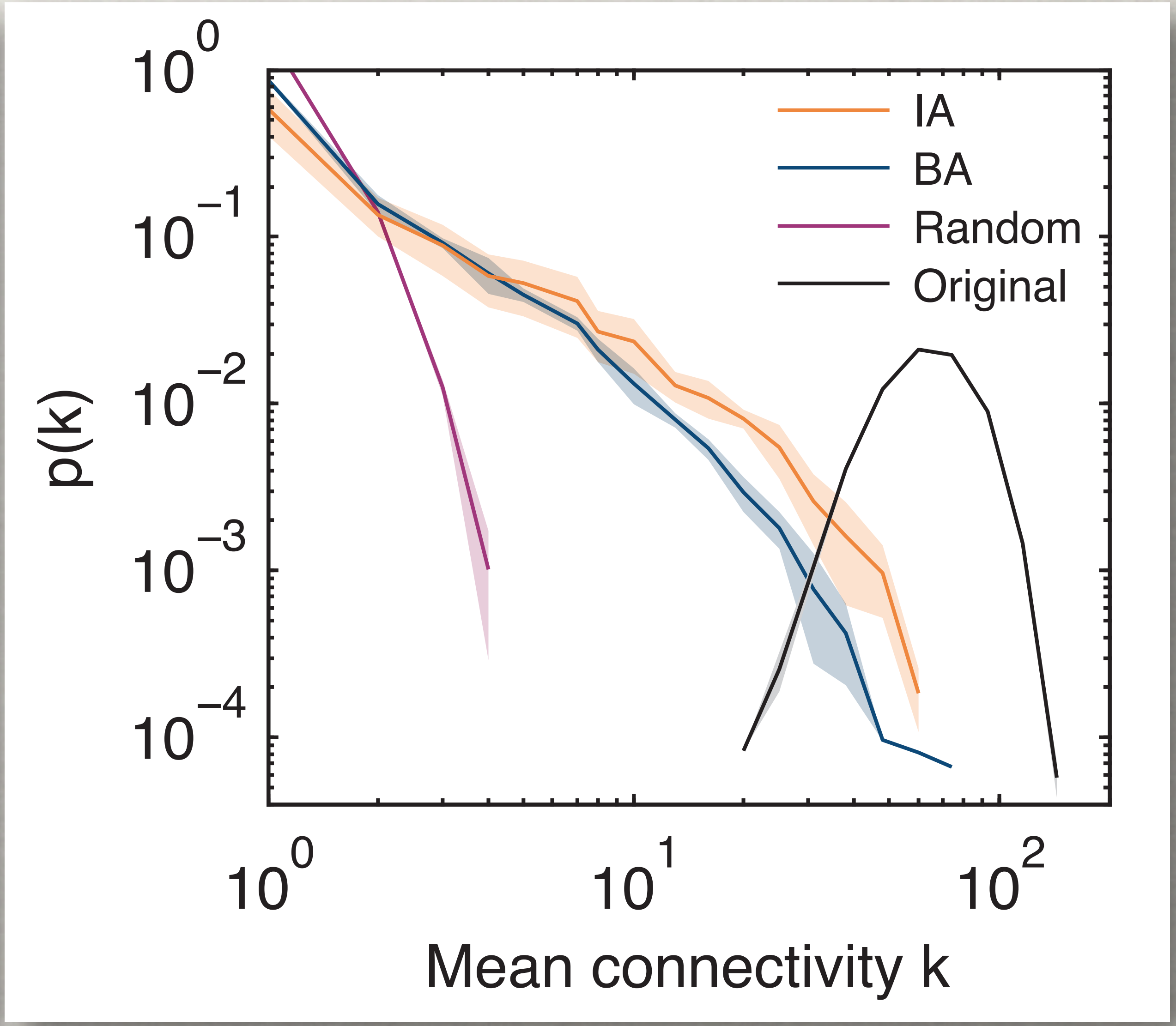




‘Universal’ exponent -5/2:
avalanches can be mapped to percolation clusters of a Cayley tree near criticality

"FUNCTIONAL" NETWORK





Time-averaging unveils a hidden functional network: hierarchically structured and inhomogeneous. A dynamically generated scale-free network !

IGNITION AVALANCHES AND NUCLEATION RATE

Nucleation condition: simultaneous activation of the critical percolation fraction in a region of critical size (N_c neurons)

This defines an 'Ignition Avalanche' (IA)

IGNITION AVALANCHES AND NUCLEATION RATE

Nucleation condition: simultaneous activation of the critical percolation fraction in a region of critical size (N_c neurons)

This defines an 'Ignition Avalanche' (IA)

Region contributing to an IA: $N > N_c$

Spontaneous firing rate of a single neuron: ω_0

Probability that a spontaneous firing generates an IA: $\mathcal{P}_{IA}$

IGNITION AVALANCHES AND NUCLEATION RATE

Nucleation condition: simultaneous activation of the critical percolation fraction in a region of critical size (N_c neurons)

This defines an 'Ignition Avalanche' (IA)

Region contributing to an IA: $N > N_c$

Spontaneous firing rate of a single neuron: ω_0

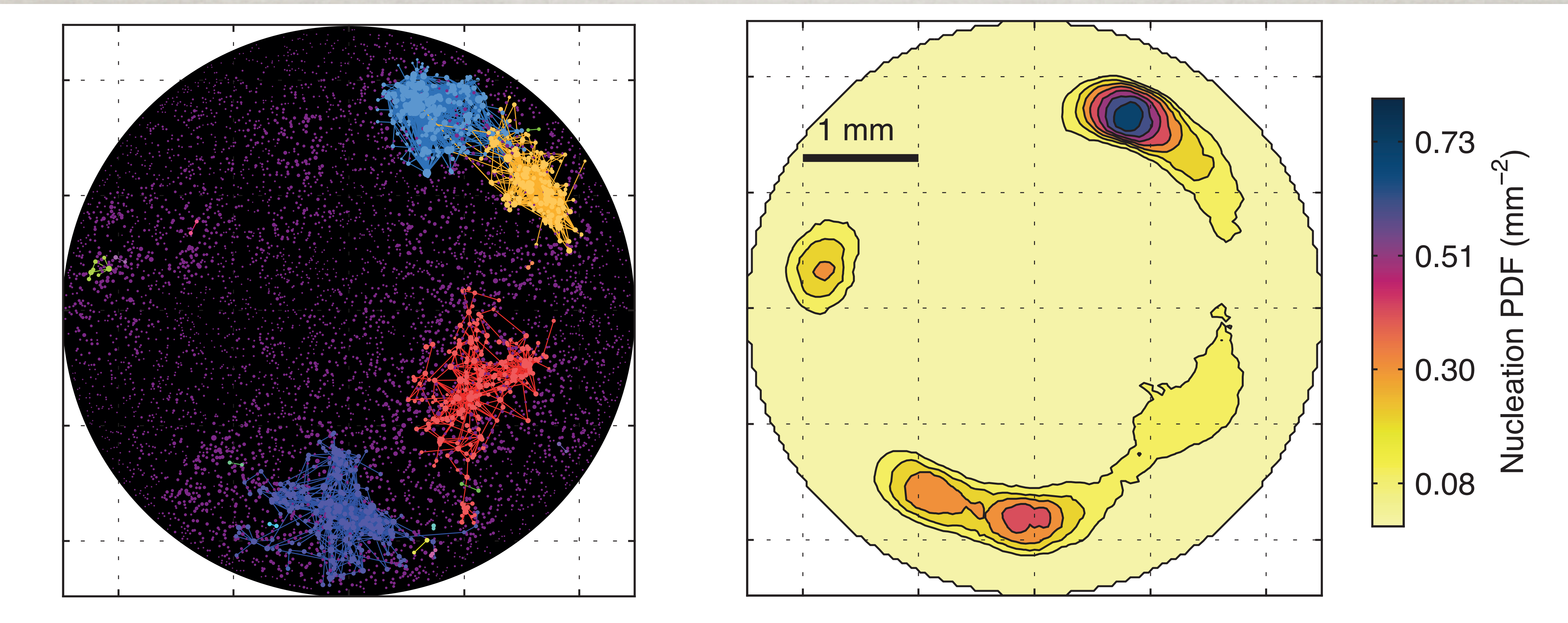
Probability that a spontaneous firing generates an IA: $\mathcal{P}_{IA}$

Nucleation rate: $N\omega_0\mathcal{P}_{IA}$

with $$N\mathcal{P}_{IA} \sim 0.1 - 1$$

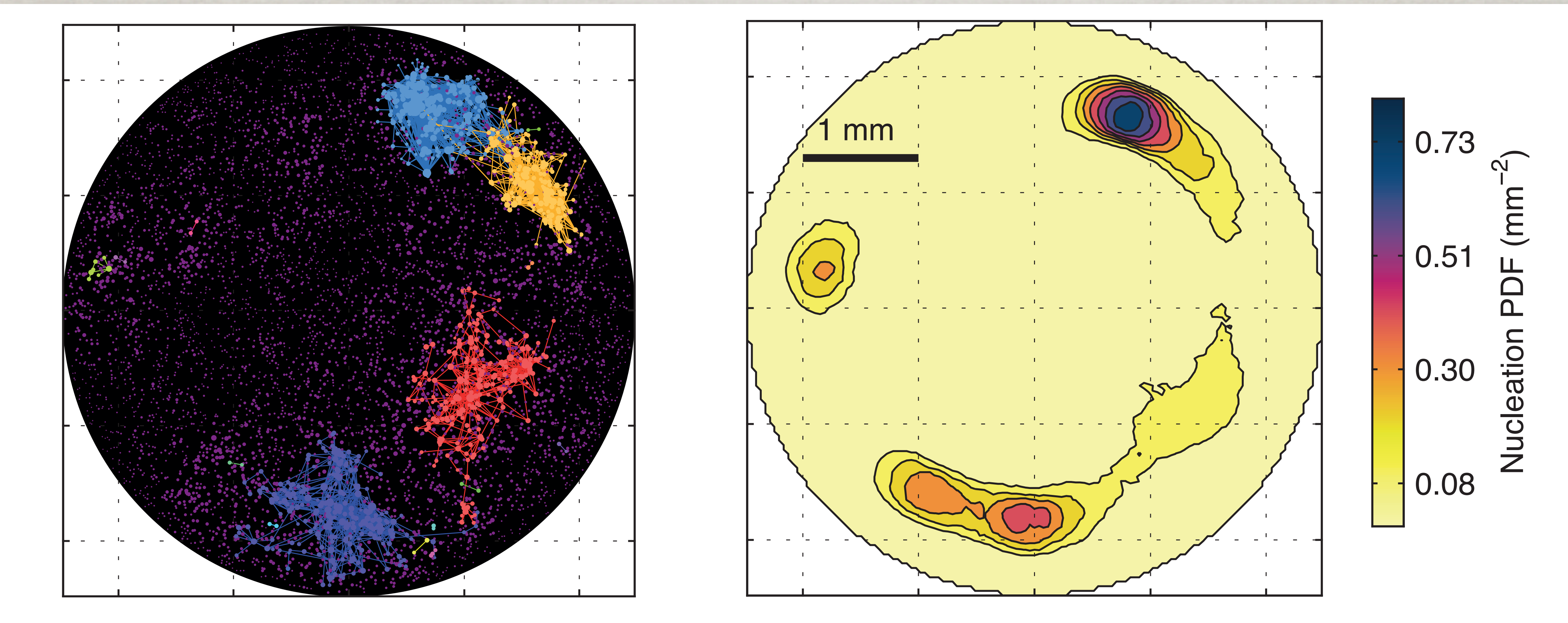
The nucleation time scale is explained by the statistics of avalanches

STATISTICS AND STRUCTURE OF IGNITION AVALANCHES



The Ignition functional network does not quite overlap with the nucleation map (yet)

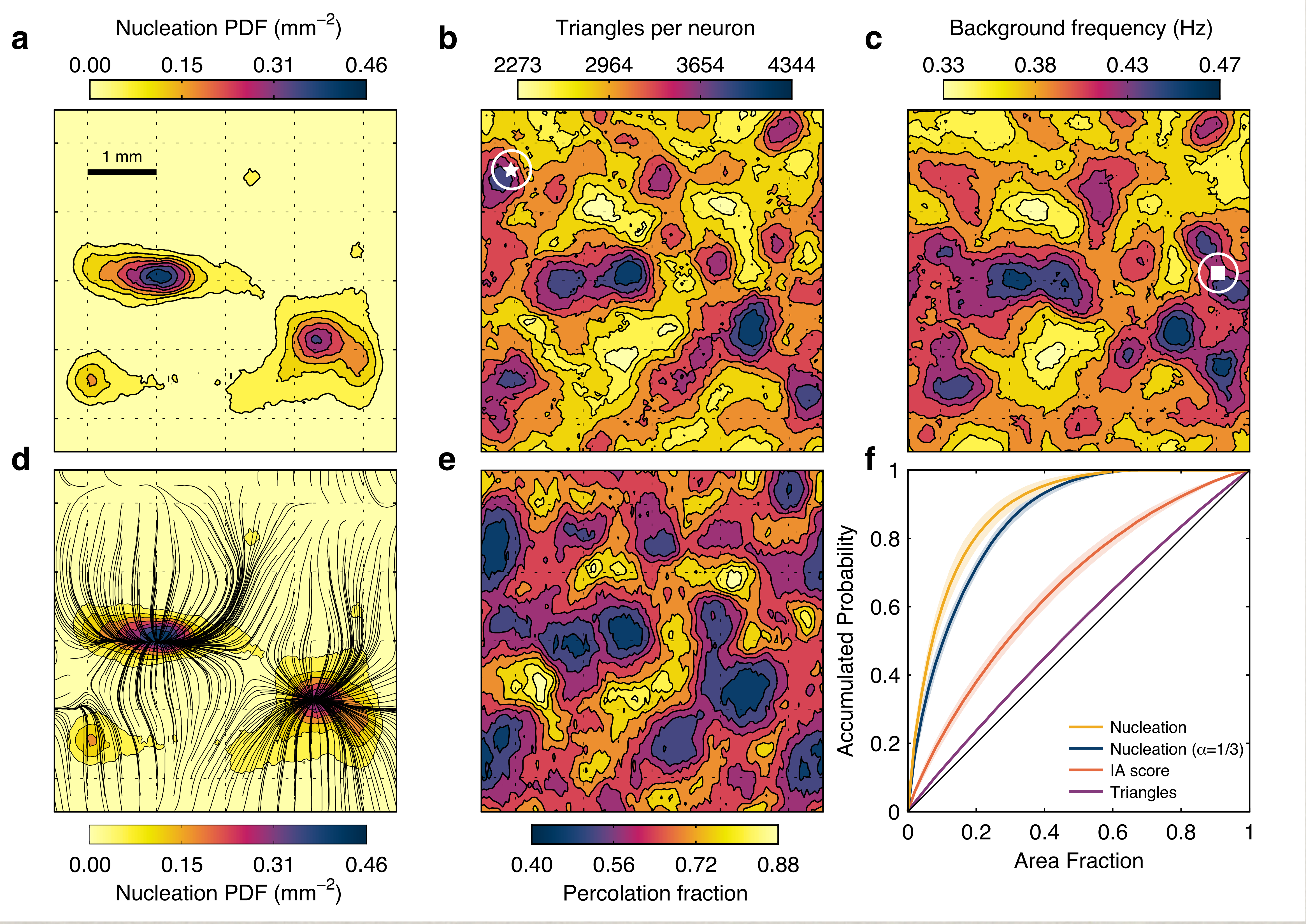
STATISTICS AND STRUCTURE OF IGNITION AVALANCHES



The Ignition functional network does not quite overlap with the nucleation map (yet)

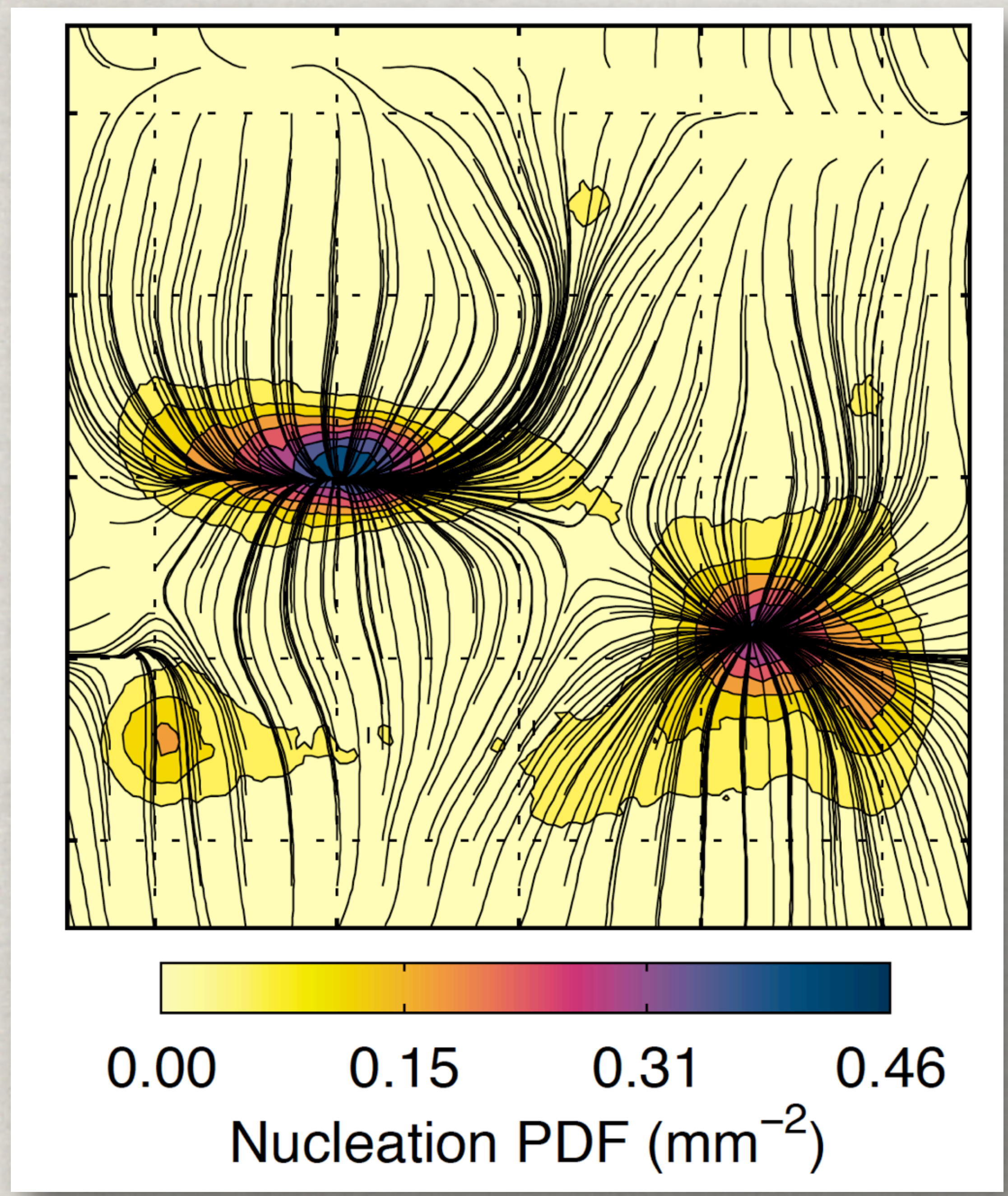
Spatio-temporal correlations still missing !

NOISE FOCUSING



AVERAGED NOISE FLOW AND SELECTION OF NUCLEATION SITES

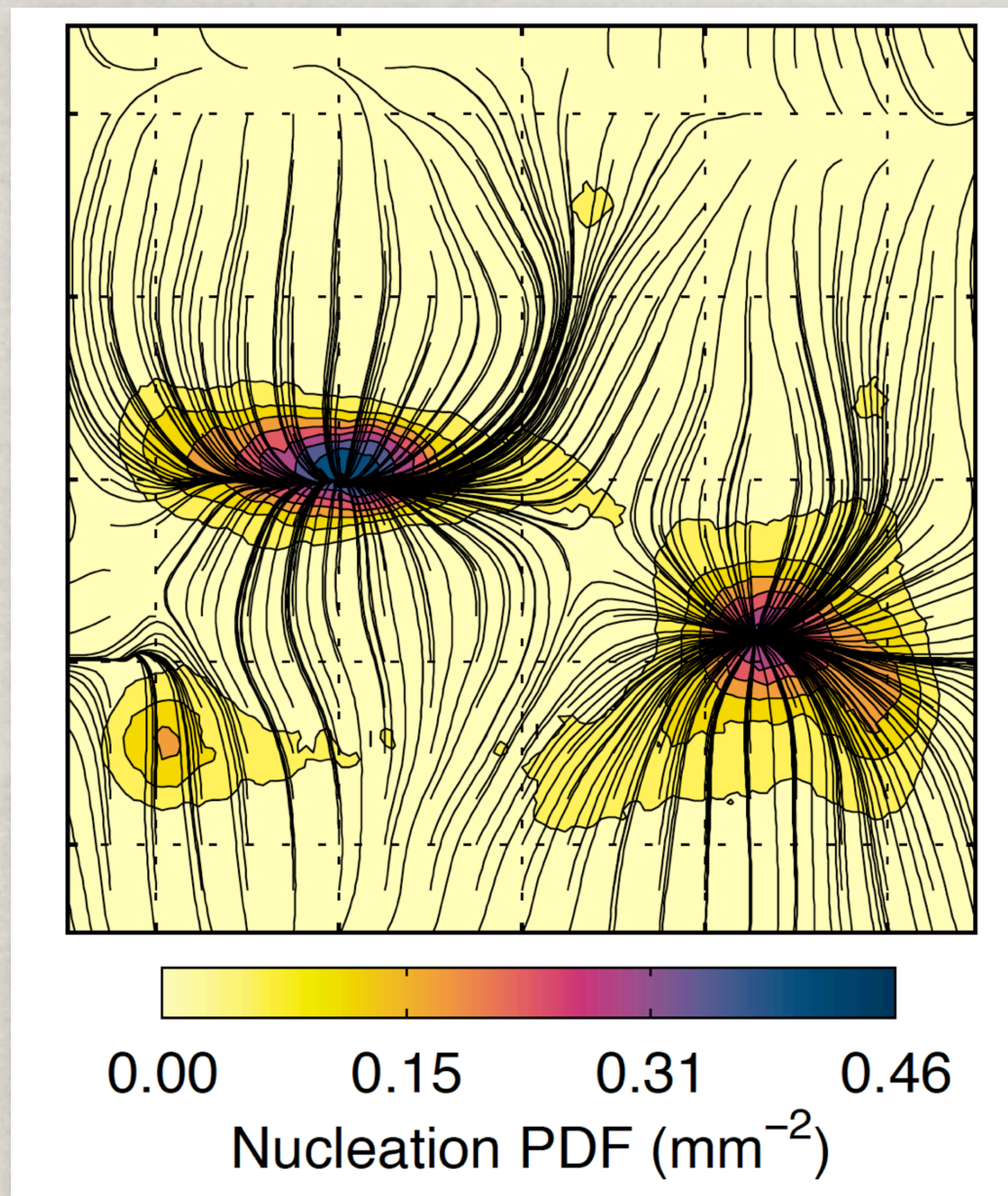
Average noise flow of IAs



What makes one region a nucleation site?

AVERAGED NOISE FLOW AND SELECTION OF NUCLEATION SITES

Average noise flow of IAs

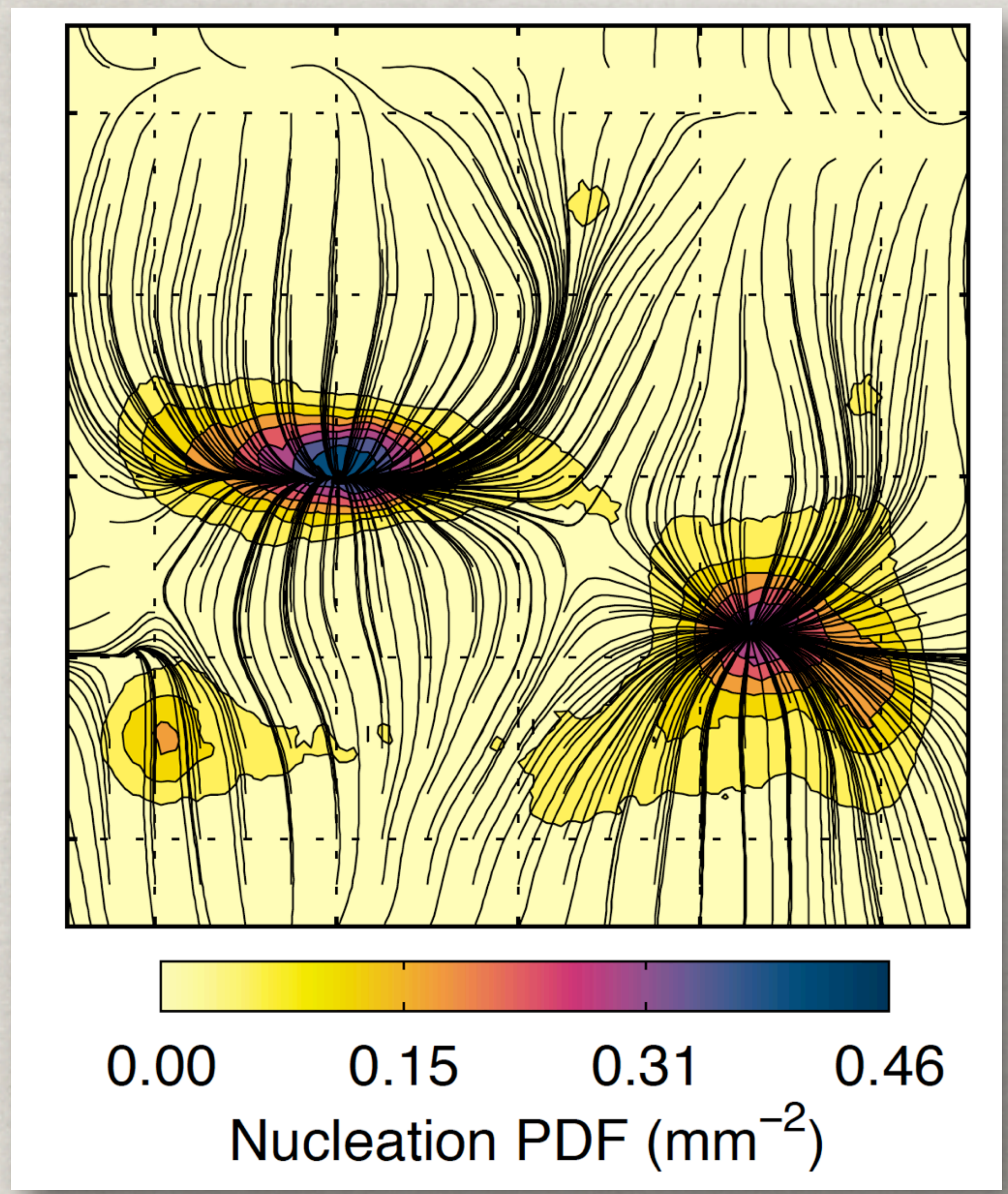


What makes one region a nucleation site?

Not a local statistical property of the network

AVERAGED NOISE FLOW AND SELECTION OF NUCLEATION SITES

Average noise flow of IAs



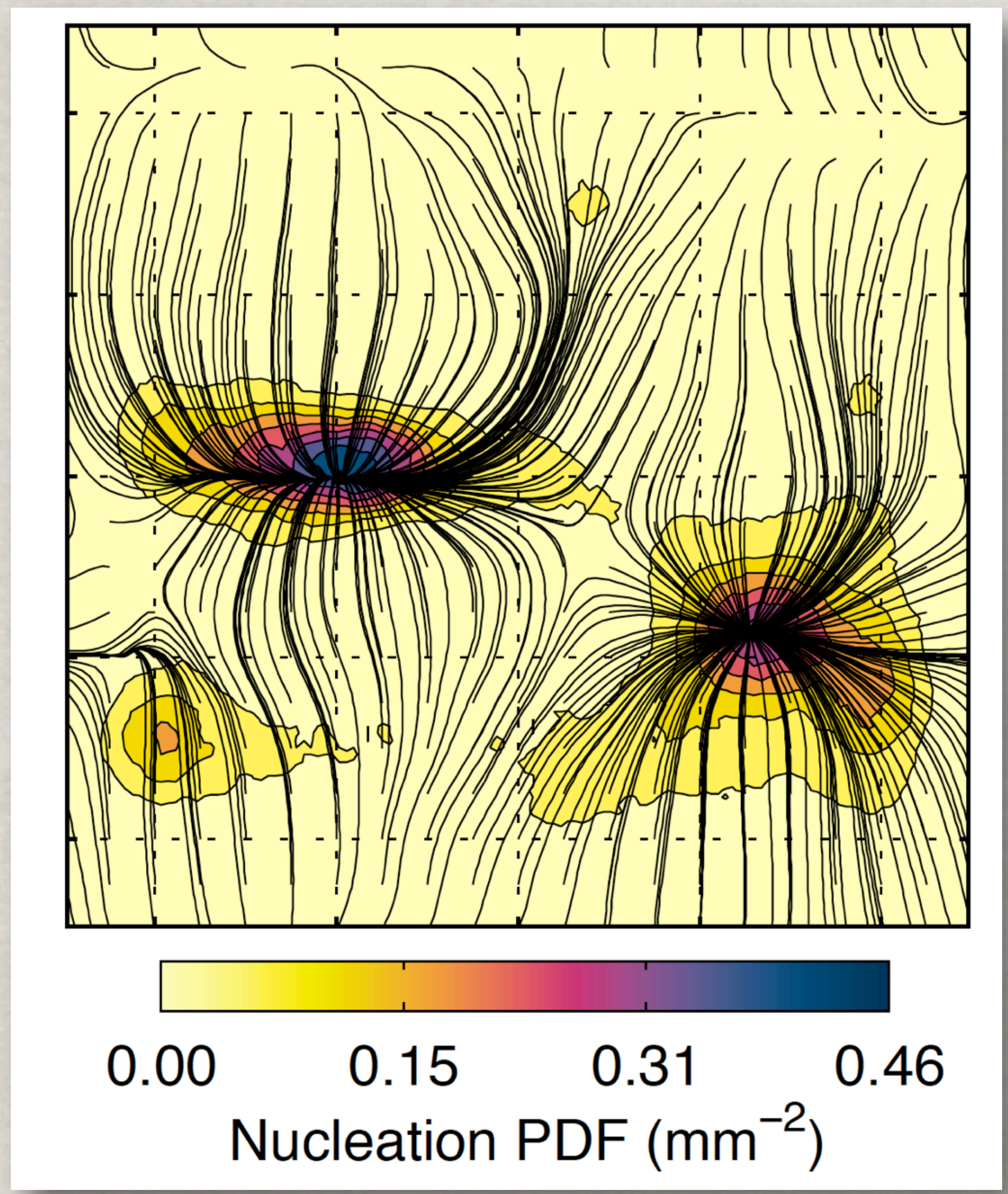
What makes one region a nucleation site?

Not a local statistical property of the network

Not a local dynamical property of the network

AVERAGED NOISE FLOW AND SELECTION OF NUCLEATION SITES

Average noise flow of IAs



What makes one region a nucleation site?

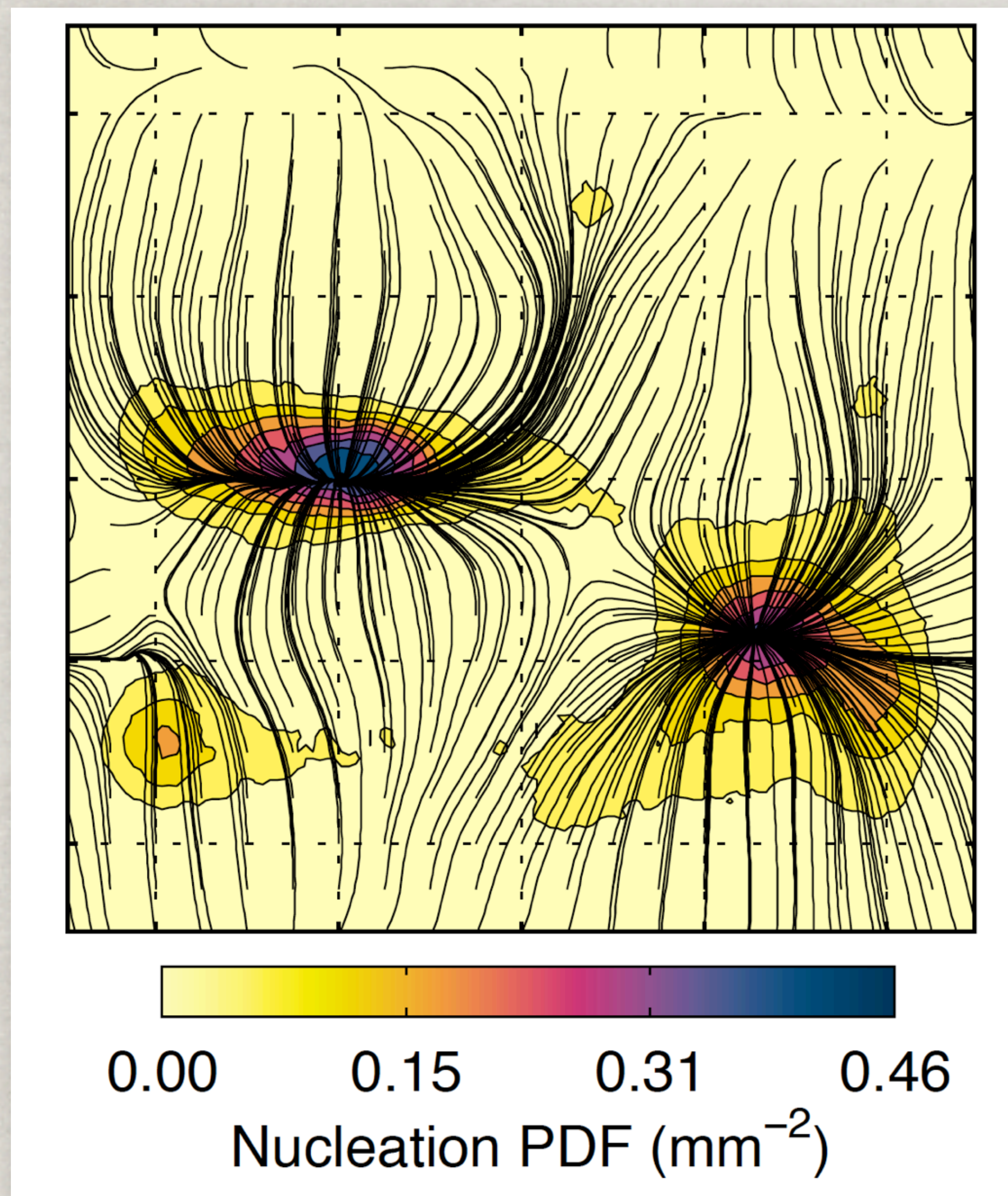
Not a local statistical property of the network

Not a local dynamical property of the network

A non-local, collective phenomenon:

AVERAGED NOISE FLOW AND SELECTION OF NUCLEATION SITES

Average noise flow of IAs



What makes one region a nucleation site?

Not a local statistical property of the network

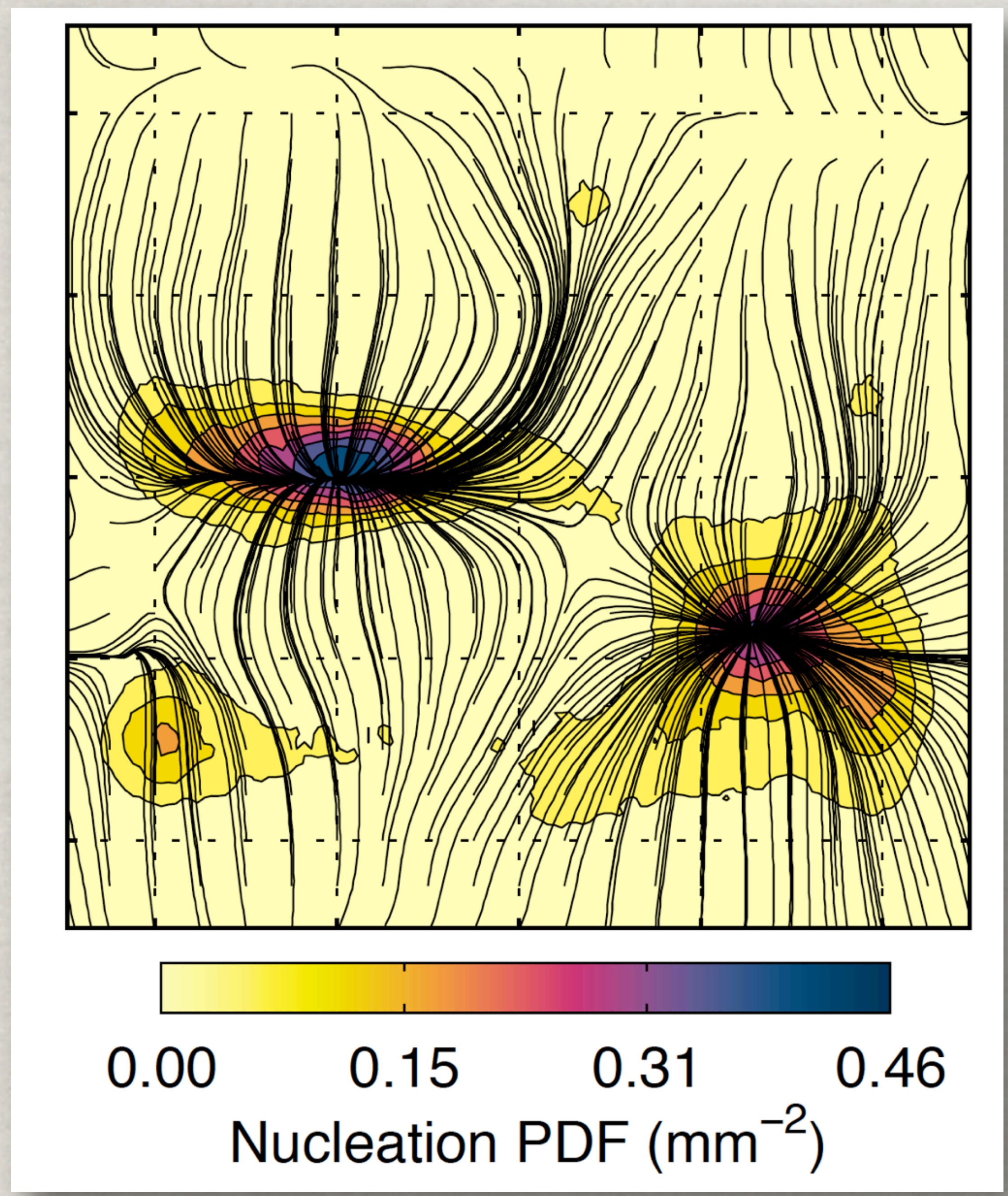
Not a local dynamical property of the network

A non-local, collective phenomenon:

being at the confluence of paths of high amplification

AVERAGED NOISE FLOW AND SELECTION OF NUCLEATION SITES

Average noise flow of IAs



What makes one region a nucleation site?

Not a local statistical property of the network

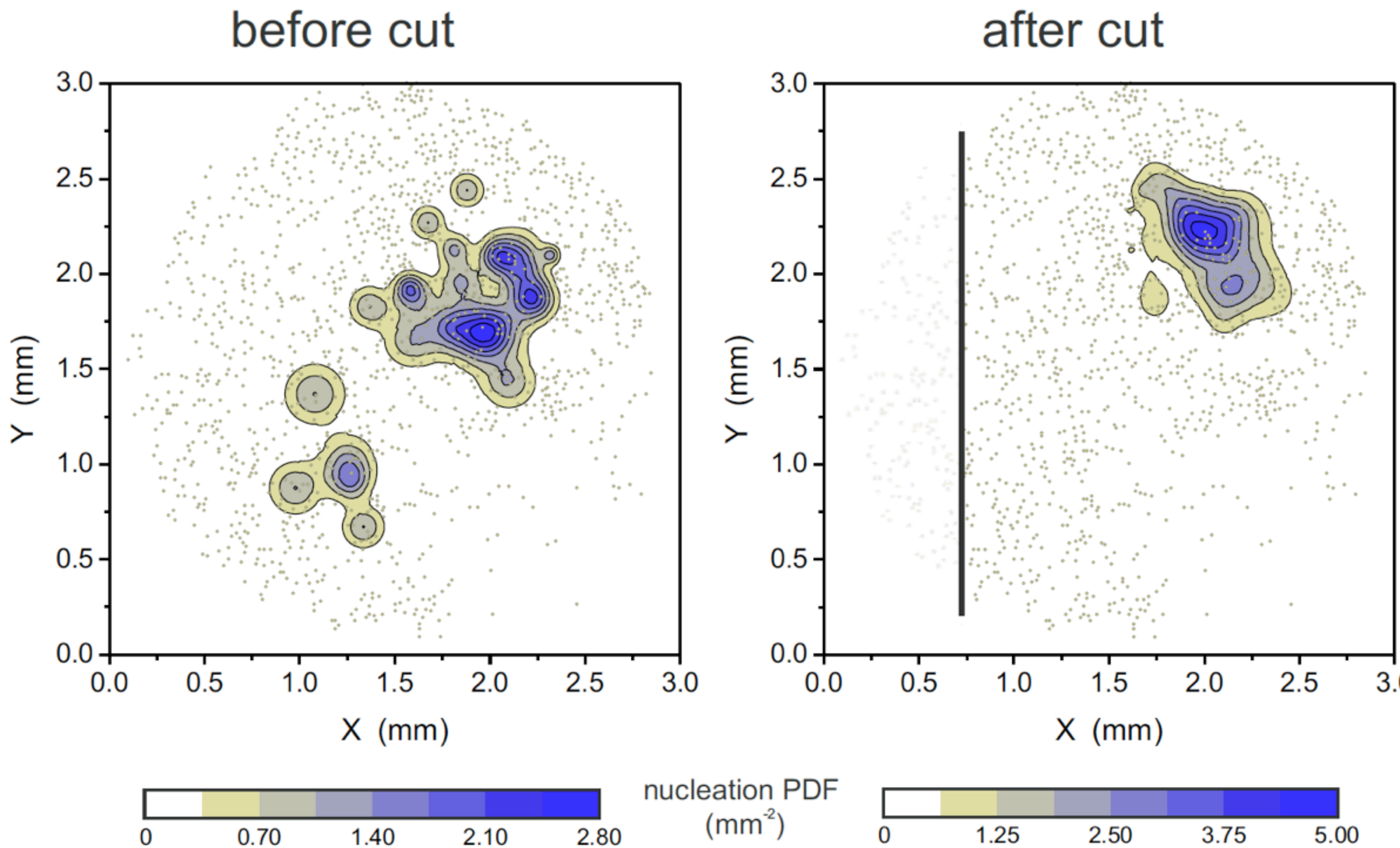
Not a local dynamical property of the network

A non-local, collective phenomenon:

being at the confluence of paths of high amplification

Nucleation sites are ‘sinks’ of the averaged flow of large avalanches

EXPERIMENTAL TEST OF NON-LOCALITY



A PHENOMENOLOGICAL MODEL FOR NOISE FOCUSING

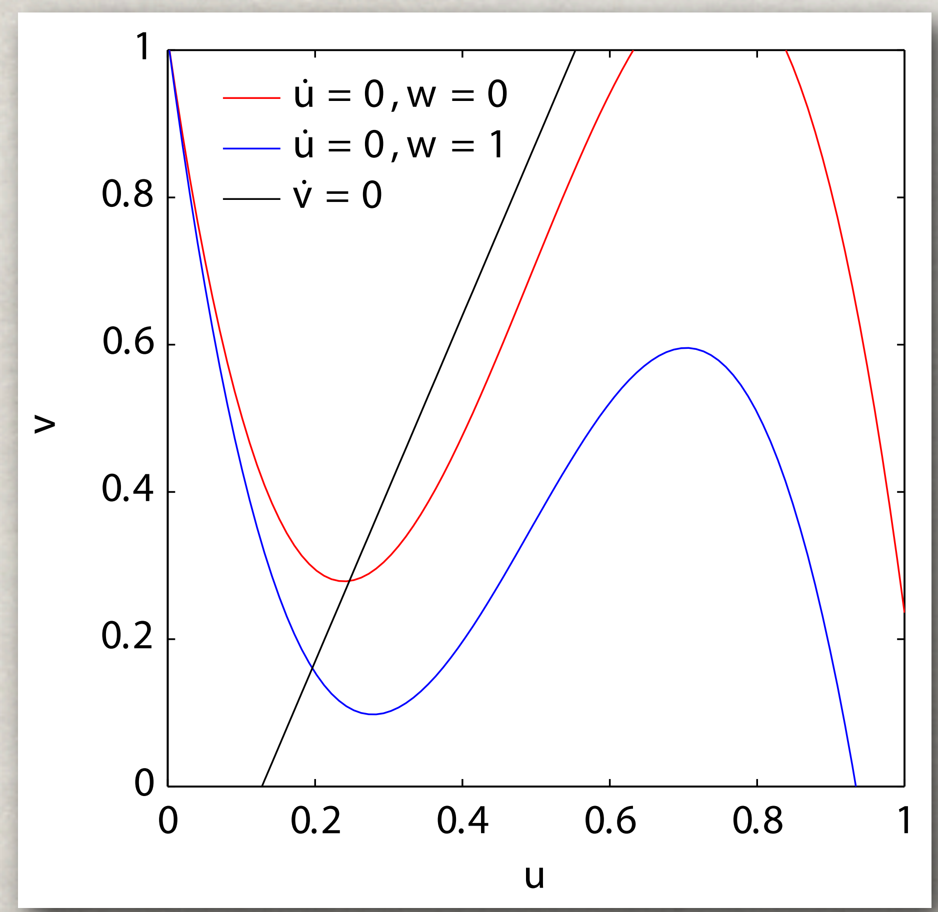
$$\dot{u} = f(u) - \kappa v + (1-w)(D\Delta u - \vec{\nabla}\cdot(u\vec{V}) + \alpha u) + \xi$$

$$\dot{v} = \gamma(u + g - hv)$$

$$\dot{w} = -\frac{1}{\tau_D} w + \beta u^{\nu}(1-w)$$

with $f(u) \equiv au^3 + bu^2 + cu + d$

nullclines



A PHENOMENOLOGICAL MODEL FOR NOISE FOCUSING

$$\dot{u} = f(u) - \kappa v + (1-w)(D\Delta u - \vec{\nabla}\cdot(u\vec{V}) + \alpha u) + \xi$$

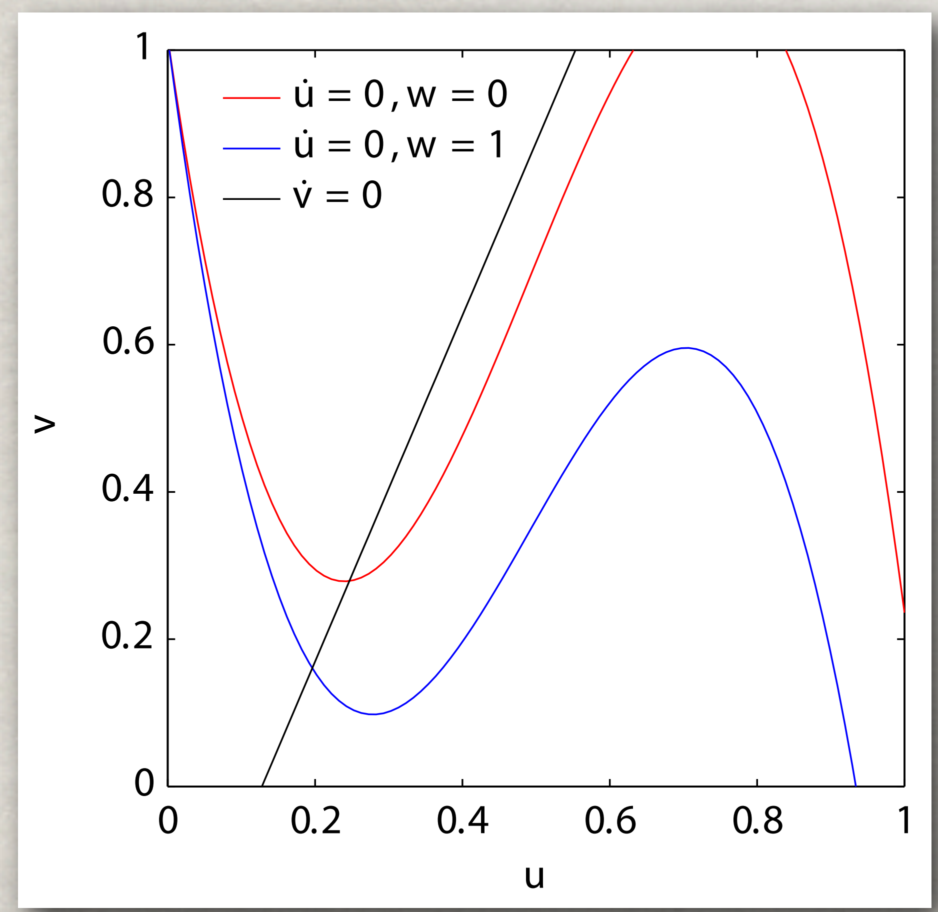
$$\dot{v} = \gamma(u + g - hv)$$

$$\dot{w} = -\frac{1}{\tau_D} w + \beta u^{\nu}(1-w)$$

with $f(u) \equiv au^3 + bu^2 + cu + d$

$\vec{V}, \ \alpha$ new (space-dependent) transport and kinetic parameters

nullclines



A PHENOMENOLOGICAL MODEL FOR NOISE FOCUSING

$$\dot{u} = f(u) - \kappa v + (1-w)(D\Delta u - \vec{\nabla}\cdot(u\vec{V}) + \alpha u) + \xi$$

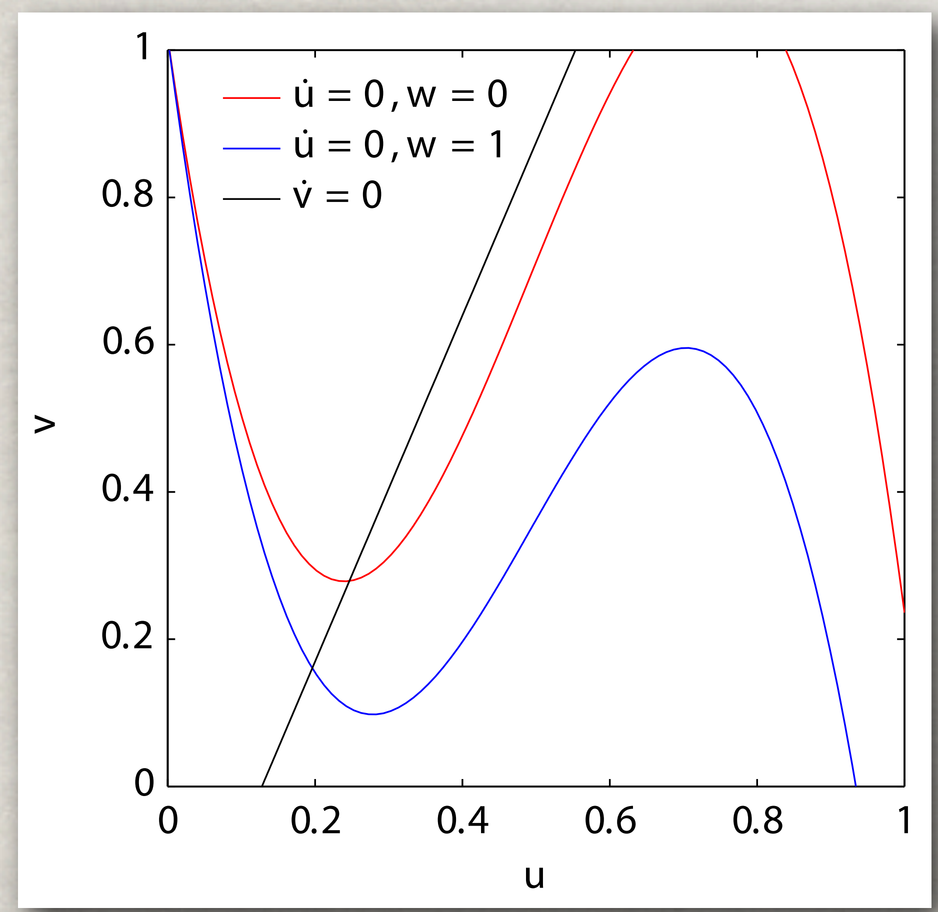
$$\dot{v} = \gamma(u + g - hv)$$

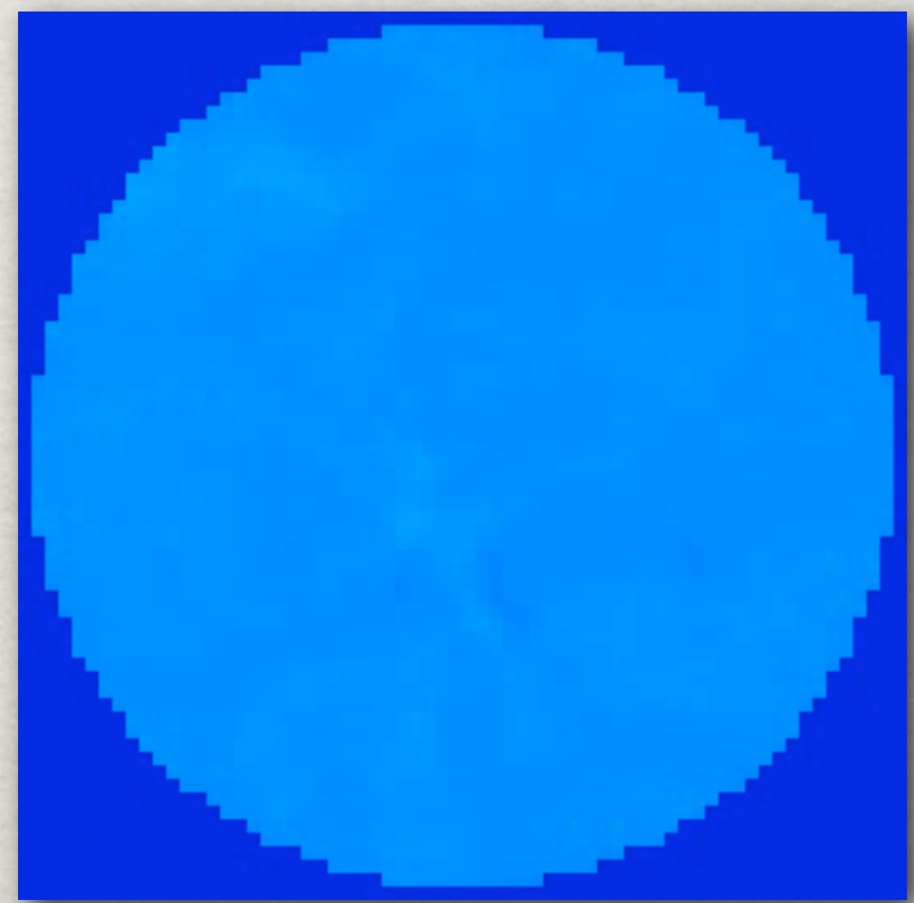
$$\dot{w} = -\frac{1}{\tau_D}w + \beta u^\nu (1-w)$$

with $f(u) \equiv au^3 + bu^2 + cu + d$

$\vec{V}$, α new (space-dependent) transport and kinetic parameters

nullclines





CONCLUSIONS

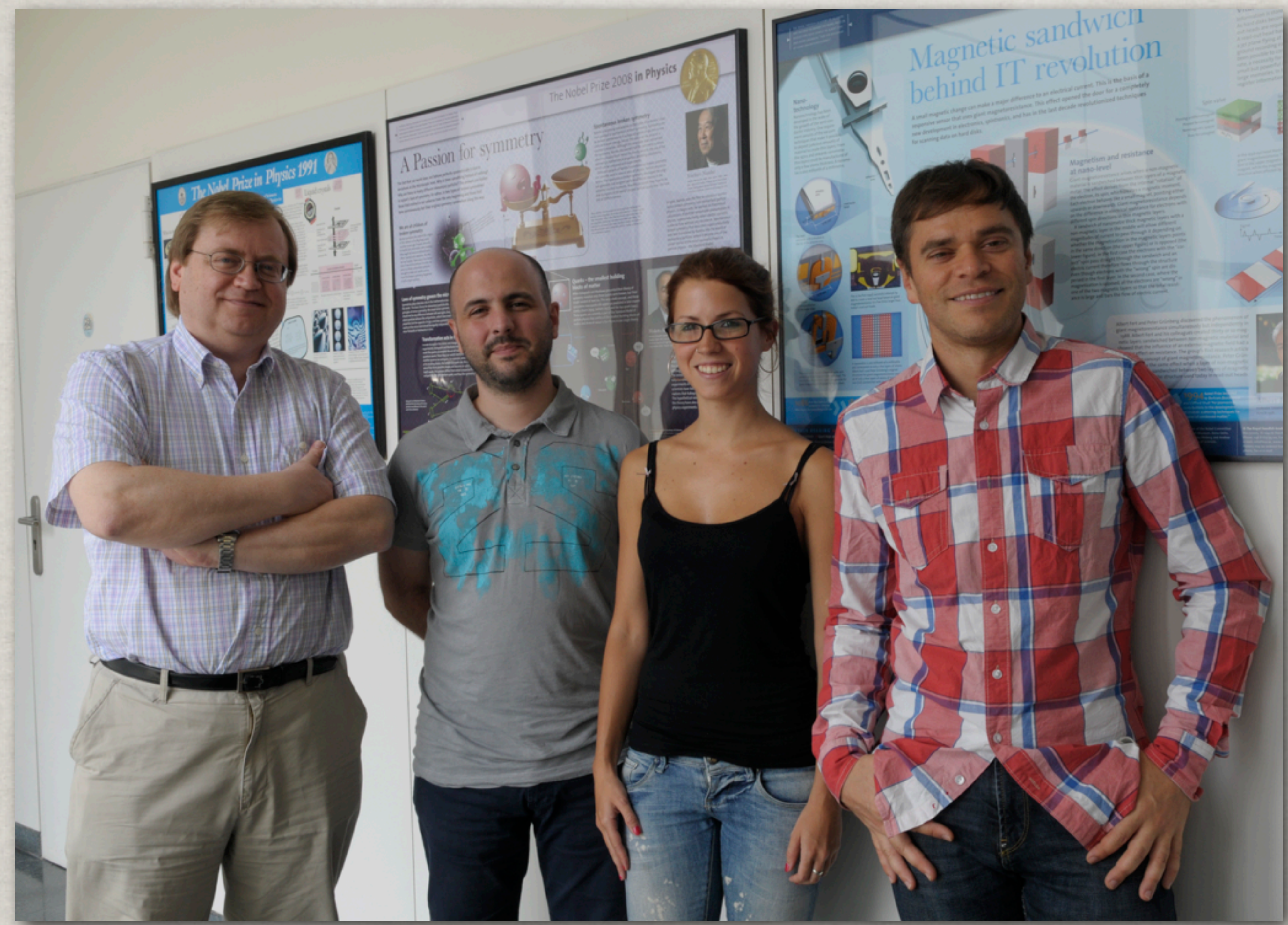
Coherent spontaneous activity in cultures is explained in terms of wave nucleation (no 'leaders' required).

Noise is structured in avalanches with self-similar statistics and endows the network with a non-trivial hierarchical structure.

Integrate-and-fire dynamics plus metric correlations leads to strong spatio-temporal localization of noise activity: noise focusing.

The strong sensitivity of noise amplification to network details defines a nontrivial pattern of noise flow, an inherently collective and non-local (emergent) phenomenon.

Implications in 'network reconstruction' and other 'integrate-and-fire networks' (rumor propagation in social networks)



J.G.Orlandi S. Teller J. Soriano E. Alvarez-Lacalle

THANKS !