Lecture 9: Percolation in Living Neuronal Networks

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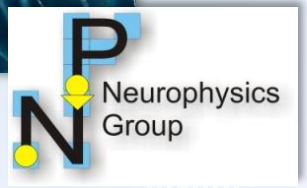
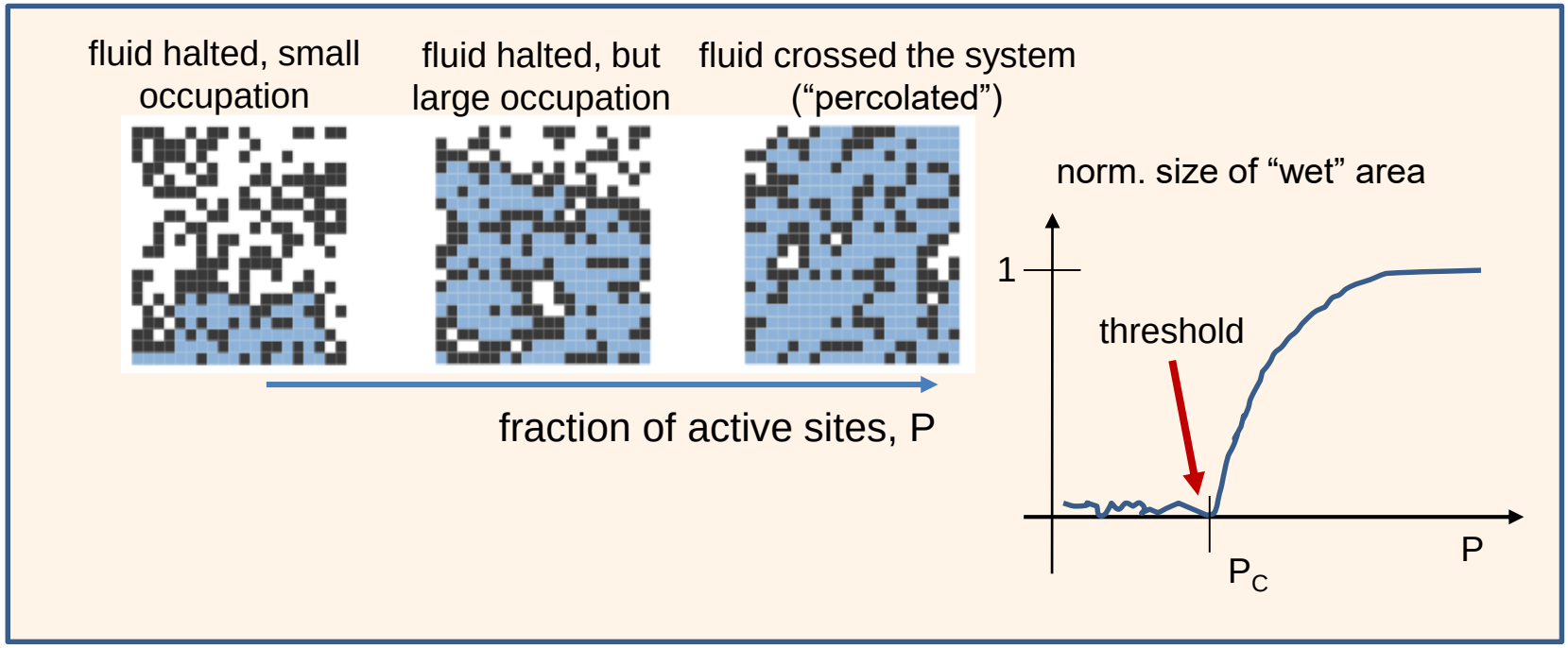


1. Percolation

■ Percolation is a classical problem in Statistical Physics.

One typically pictures a system of interconnected sites that can have two states, active or inactive. Active sites allow the flow of some observable (information, a fluid…) across the system, while inactive ones block it.

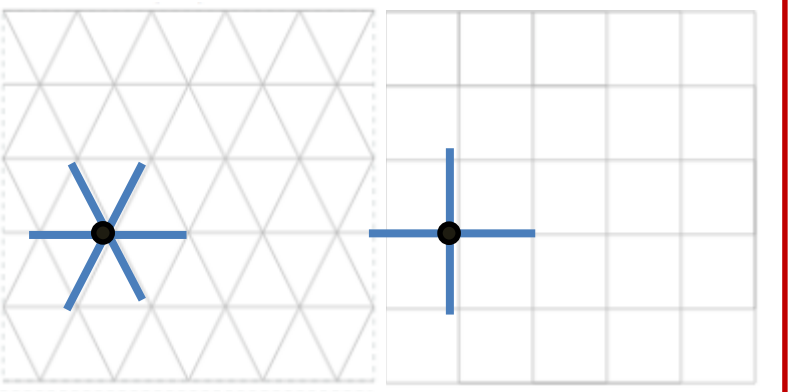
What minimum fraction of sites P_C must be active for the observable to cross the entire system? How much observable is present as the probability of occupation increases?



1. Percolation

■ From the point of view of network science, one generally views the problem as occurring in a network of **nodes** and **links**.

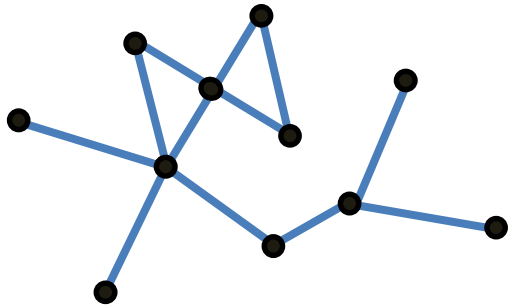
■ For example, in classical 2D lattices:



6 links per node (constant K)

4 links per node (constant K)

General network



(varying connectivity per node, one should considerer <K>)

■ In general, on distinguishes between **“site percolation”** when the nodes set the rules (active/blocked) for percolation; or **“bond percolation”** when the connections between nodes are the ones setting the rules (connected/disconnected).

1. Percolation

■ The percolation threshold depends on the structure of the underneath network as well as on the dimensionality of the system.

Bond percolation in triangular lattice, P_C = ½; square lattice, P_C = 0.59.

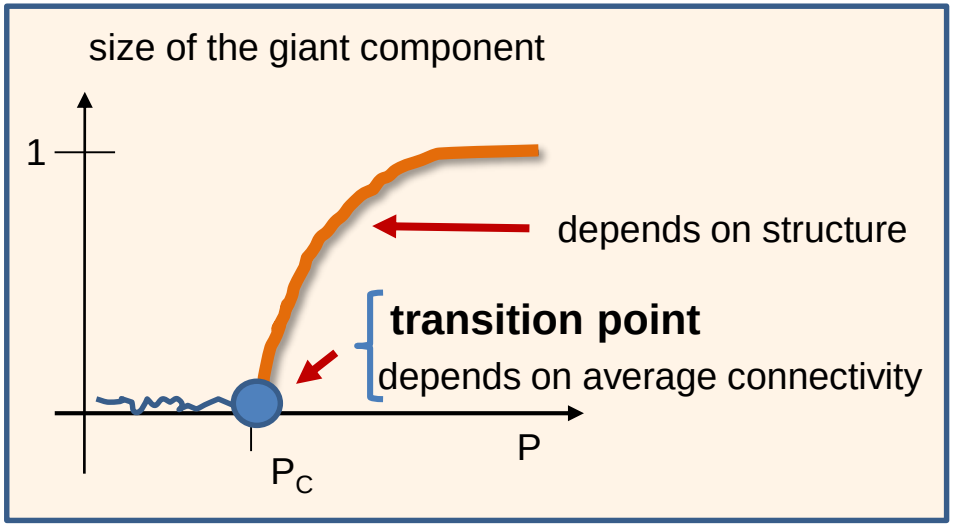
Conceptually, one can generally view the following trend:

▫ The percolation point is in general related to the average connectivity between nodes.

▫ The curve describing the growth of the observable's size depends on the details of the connections among nodes (e.g. the distribution of connections in the network).

■ The size of the observable is often termed '**giant component**'.

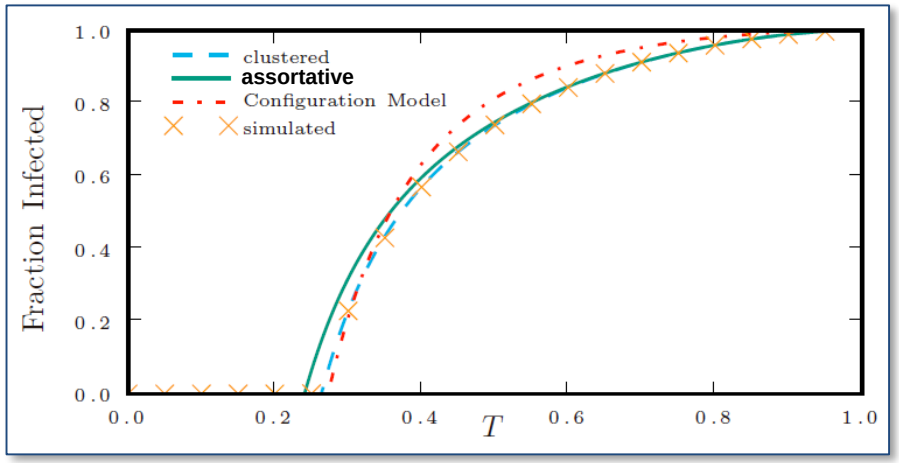
■ Percolation is viewed as a continuous phase transition, with the giant component growing rapidly above transition.



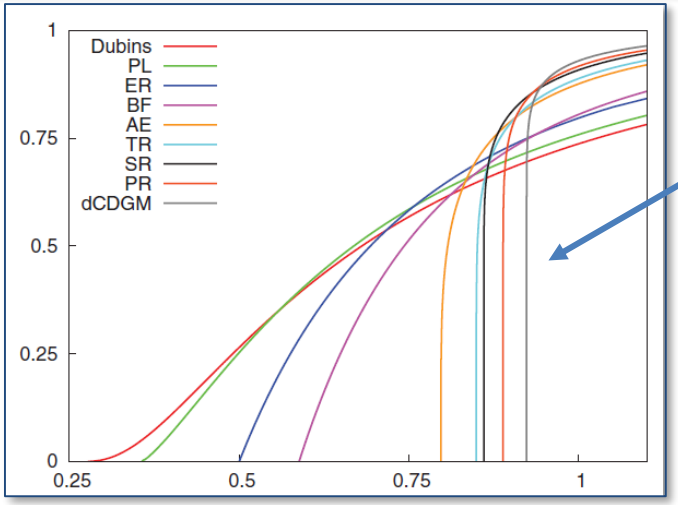
2. Percolation in complex networks

■ Percolation has caught the attention of scientists in problems that range from oil recovery in porous media to disease spreading. The interest is both characterizing the transition point and the growth of the giant component.

▫ Example 1: In **epidemics** one studies the epidemic threshold T in different network models, and the growth of the fraction of infected. In this example, an assortative structure reduces the epidemic threshold.



▫ Example 2: **'Explosive percolation'** is a new paradigm that goes beyond standard statistical physics, and applies to networks where **the addition of a link is not random**, but chosen to maximize connectivity. Such a 'selection rule' leads to a sharp growth of the giant component with just the addition of a single link.

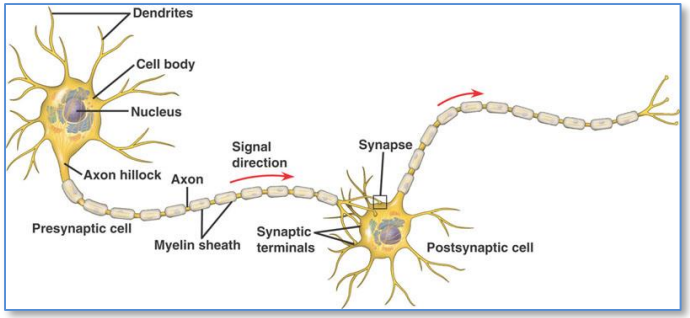


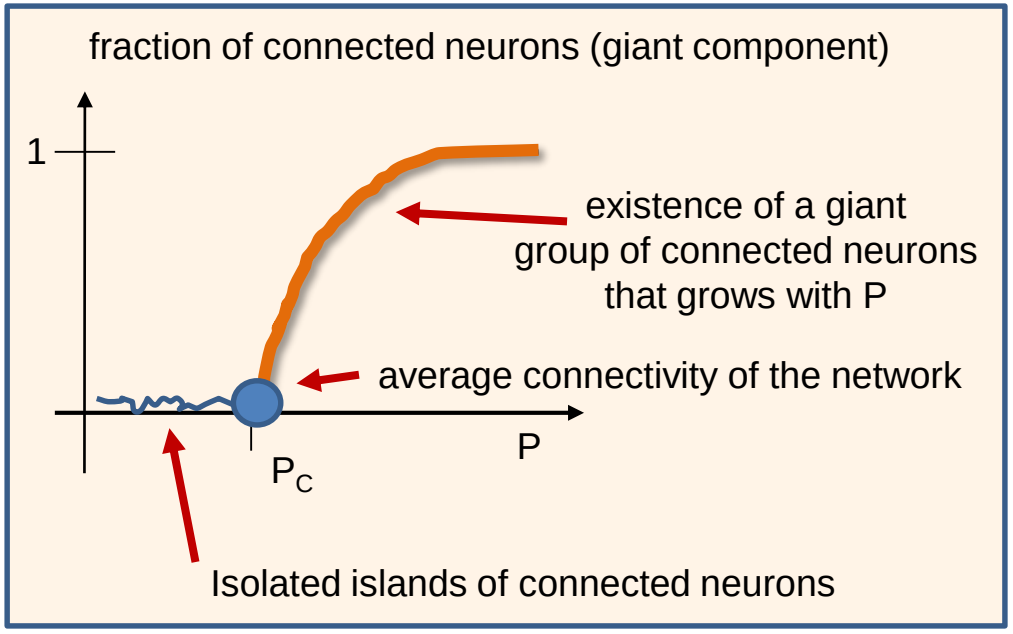
3. Percolation and neuroscience

■ Neuronal networks can be well described by nodes and links.

In the context of **resilience**, one can ask how many neurons or synaptic connections a neuronal network can loose to stop functioning.

In the context of **connectivity**, one can devise methods to get information of network structure by studying the properties of the percolation threshold and the growth of the giant component.





4. Experiments on percolation in neuronal cultures

■ The detailed biological network structure is unknown in a living neuronal circuit, and its characterization often requires the destruction of the circuit (e.g. fixation of the tissue and labeling of connections).

■ Percolation experiments allow the monitoring of the network without damaging it. The key points for such an idea are:

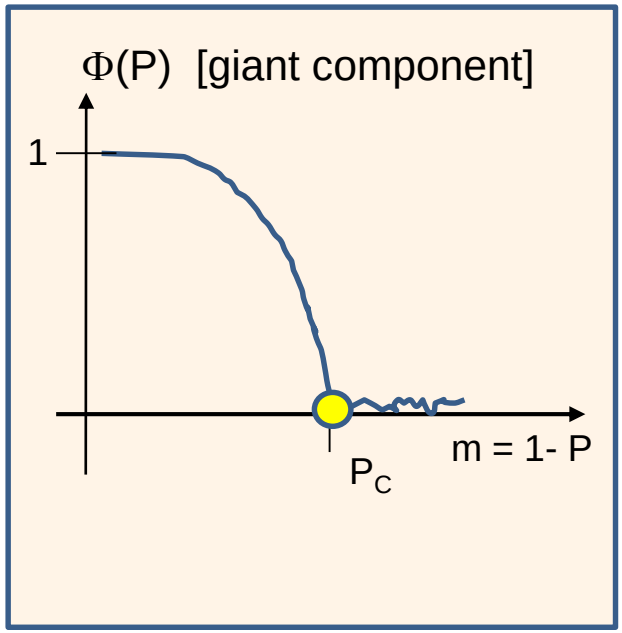
▫ Neuronal networks can be well described by nodes and links, whose behavior is known.

▫ Connectivity biological blueprint is fixed, but the strength of the connections can be modified through biochemical action, and effectively one can gradually disintegrate the network without causing biological damage.

↳ **Control parameter m = 1 - P**

▫ Neurons can be externally stimulated, so that the response of the network for different connectivity conditions can be quantified.

↳ **Order parameter Φ(P).**

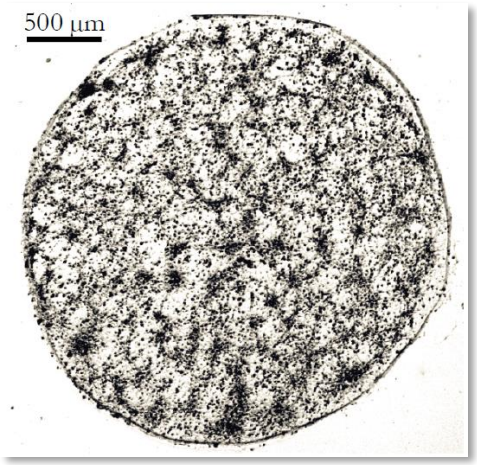


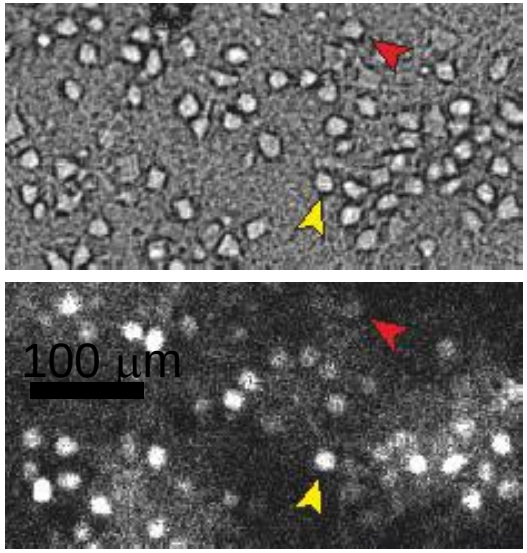
4. Experiments on percolation in neuronal cultures

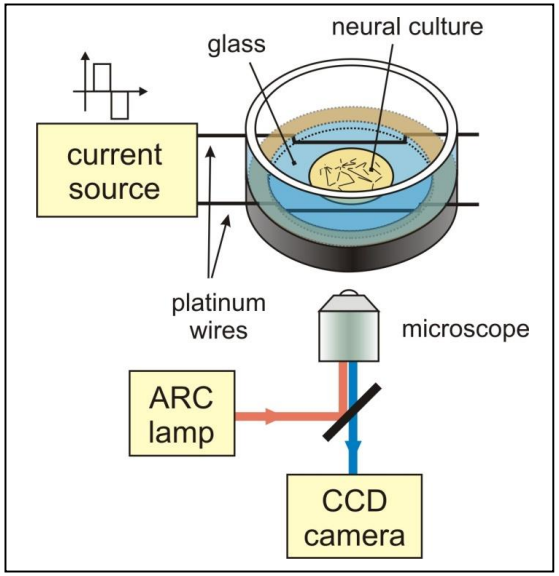
■ We consider the homogeneous cultures and the calcium imaging technique introduced in **Lecture 8**.

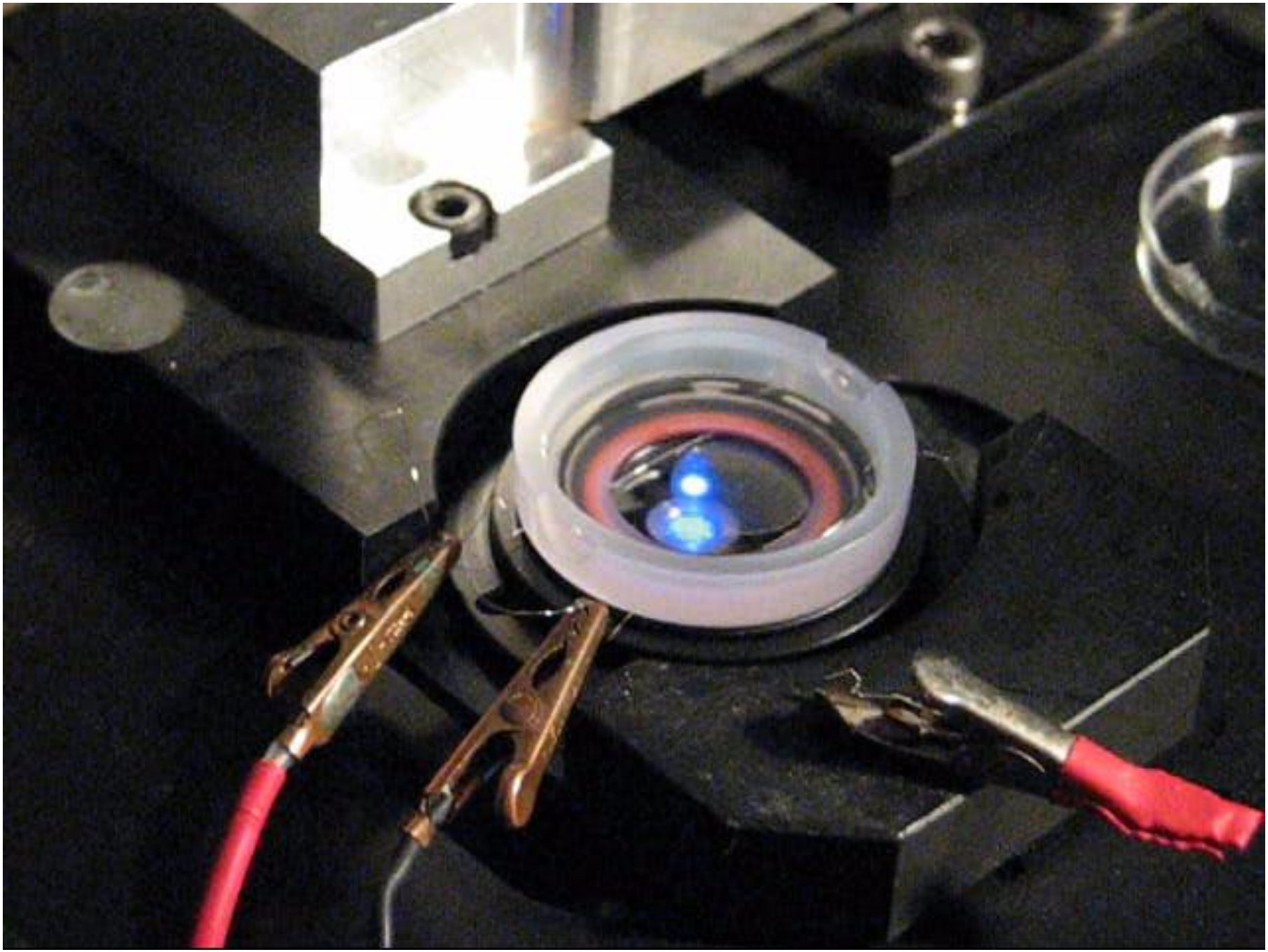
■ Instead of monitoring activity, an electric stimulation is applied to excite the neurons and count how many get activated. Key approach:

Global electrical stimulation
+
gradually lower synaptic coupling



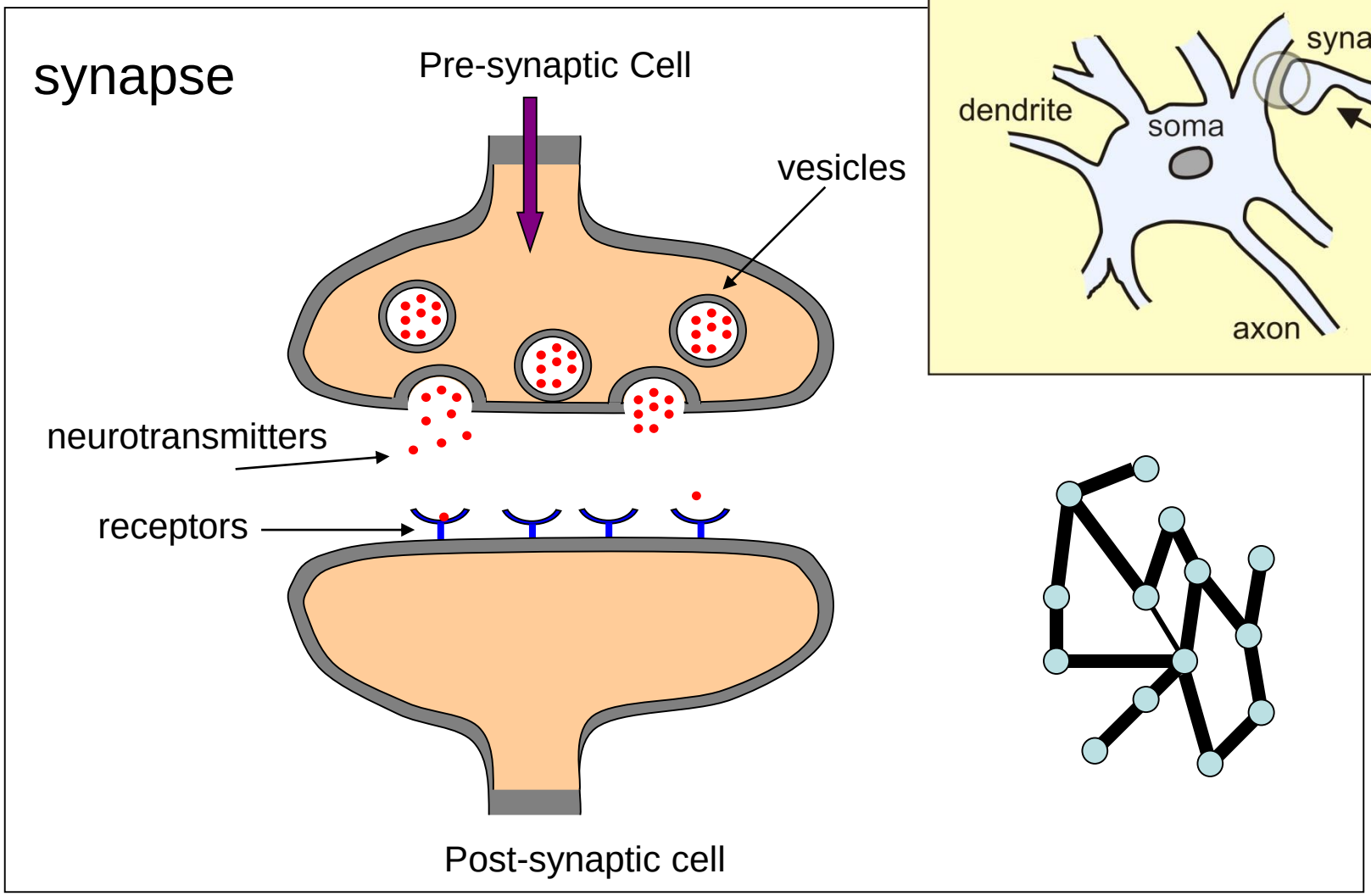






4. Experiments on percolation in neuronal cultures

■ Reduction (without actual damage) of neuronal connectivity by blocking receptors of specific neurotransmitters.



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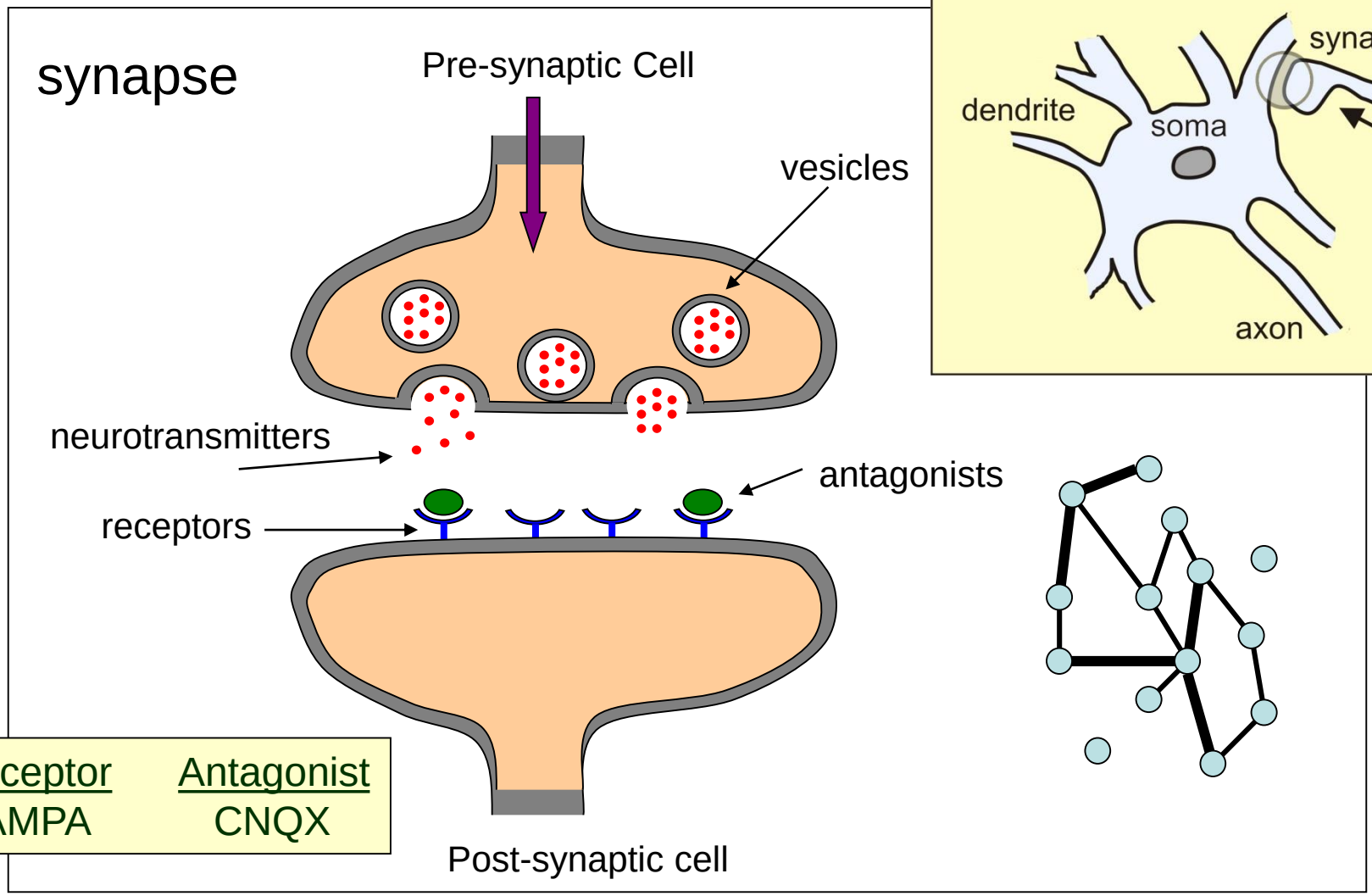

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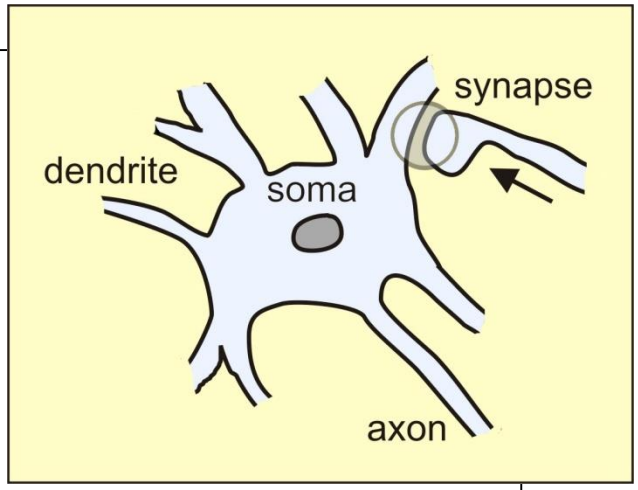

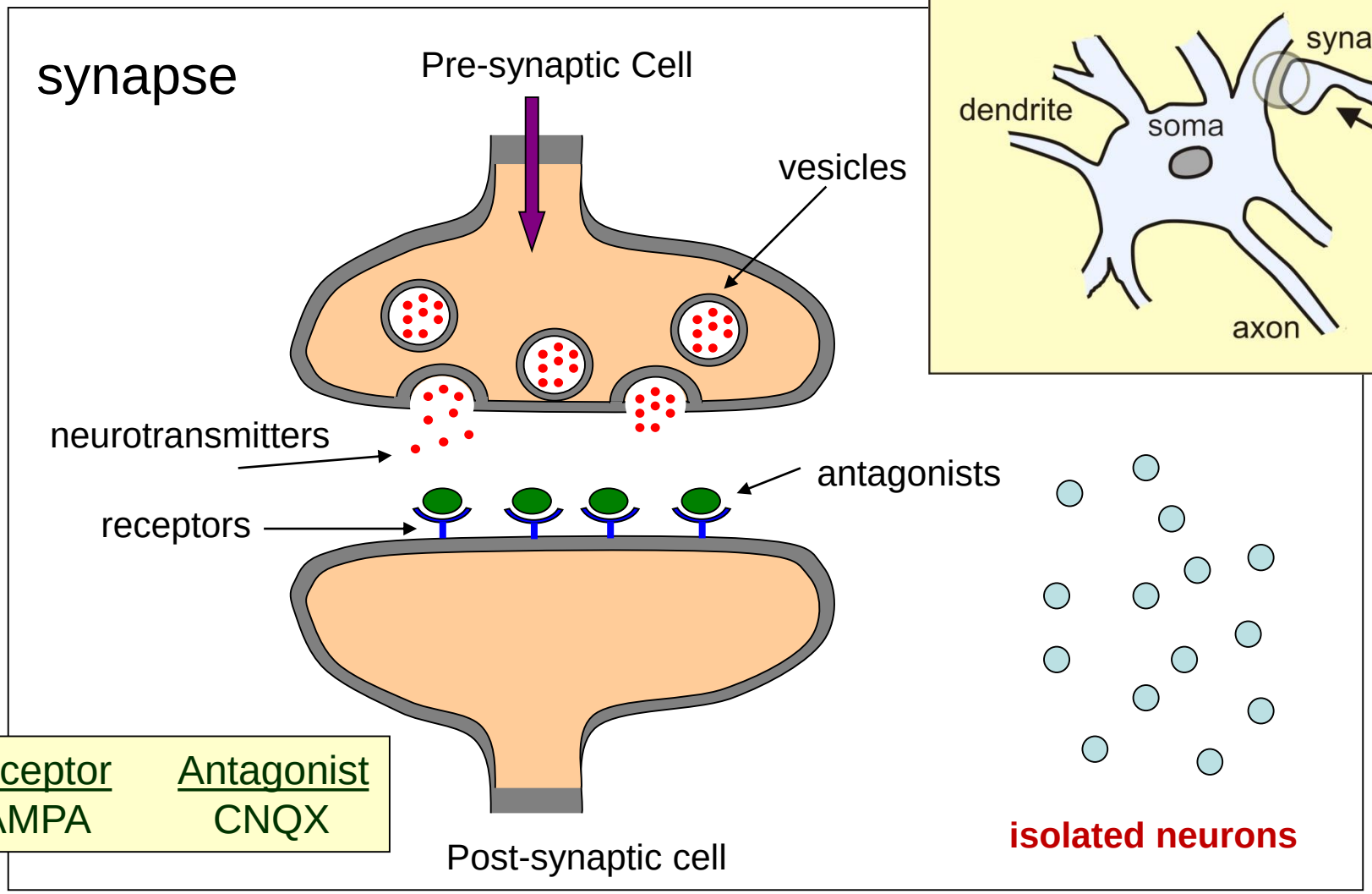

Receptor	Antagonist
AMPA	CNQX

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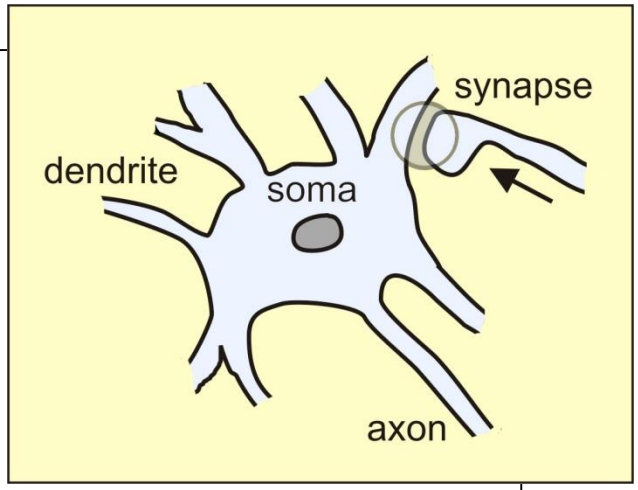


synapse

Pre-synaptic Cell

vesicles

neurotransmitters

antagonists

receptors

Post-synaptic cell

Receptor	Antagonist	Target
AMPA	CNQX	**Excitation (80%)**
$GABA_A$	bicuculline	**Inhibition (20%)**

Receptor	Antagonist
AMPA	CNQX

4. Experiments on percolation in neuronal cultures

■ The bond percolation concept has to be revised since neurons are "integrate and fire units", i.e. they need a **quorum of inputs** to fire.

One needs to introduce a new control parameter to account for this behavior:

m : number of inputs needed to fire.

$$m = \frac{V_T}{g_{\mathrm{syn}}}$$

← Voltage threshold (30 mV)

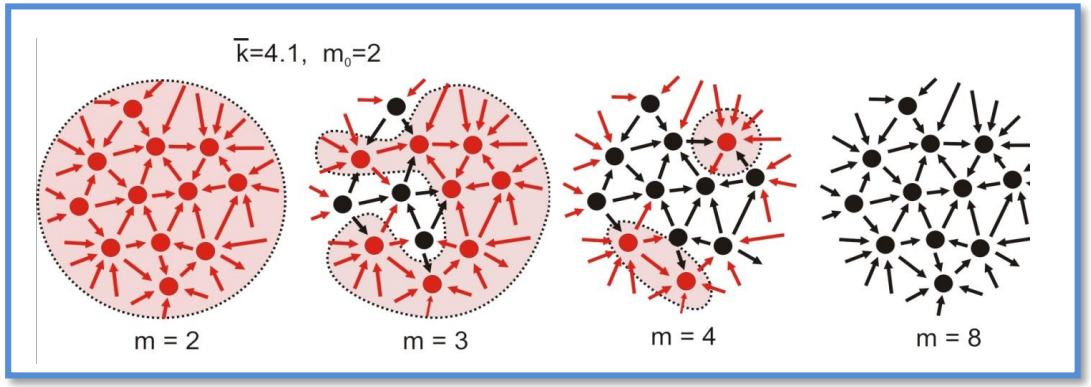
← synaptic voltage (2 mV)

$$g_{syn} \approx \frac{g_0}{1 + [CNQX] / K_d}$$

g_{syn} decreases with the amount of blocking (and m grows)

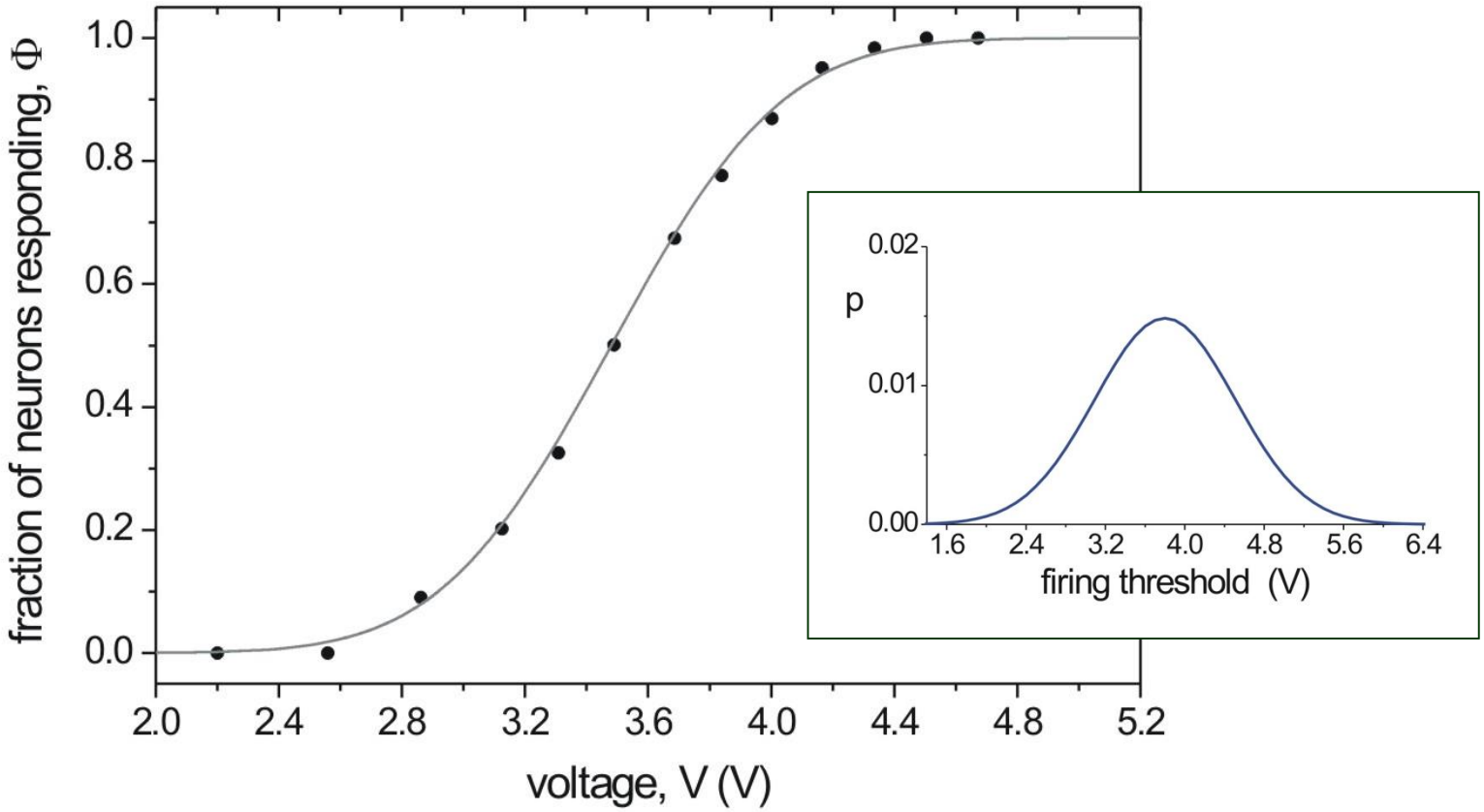
$$m = m_0 (1 + [CNQX] / K_d)$$

$m_0 = 15$



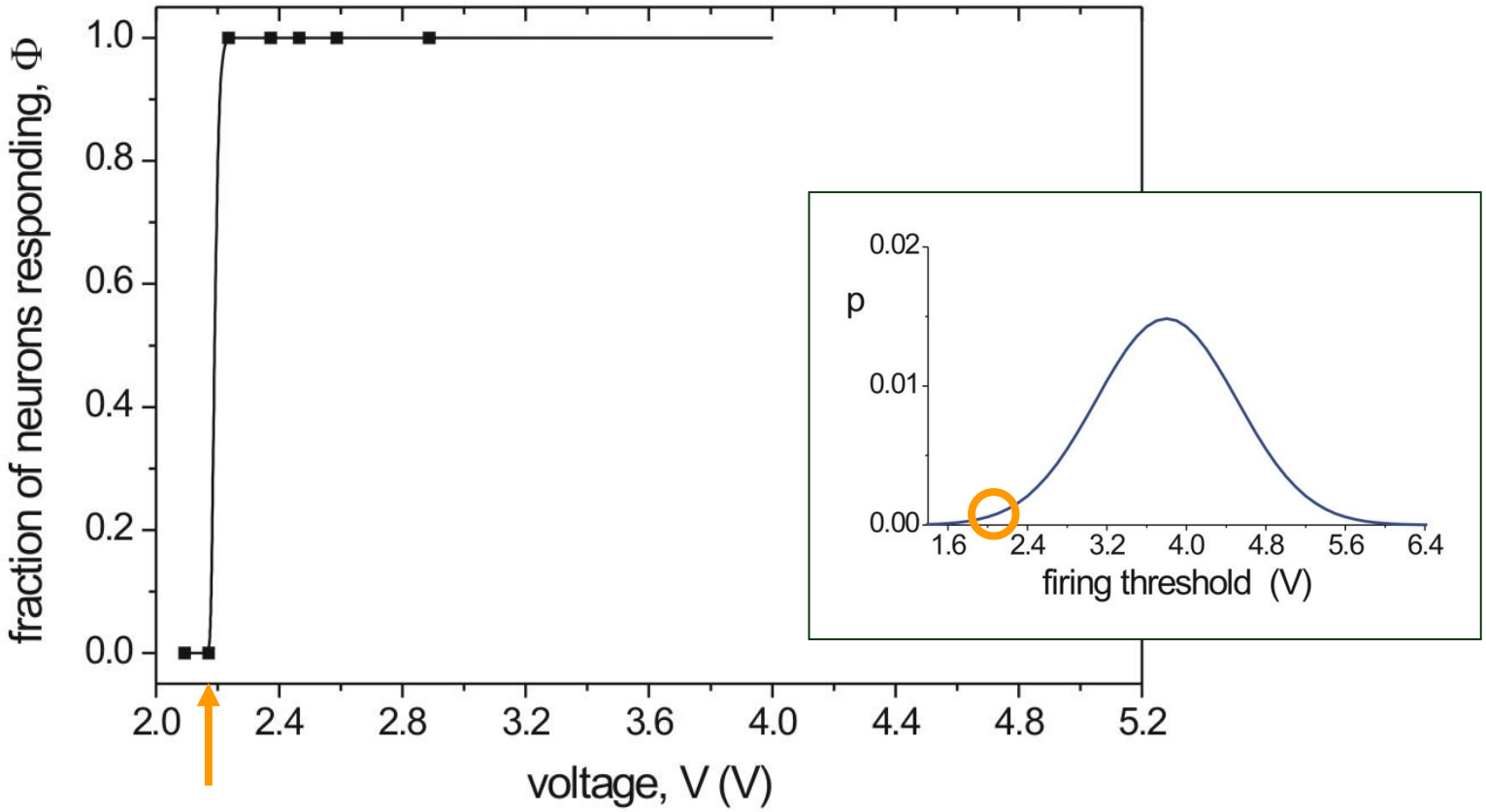
5. Network response upon disintegration

■ A **fully disconnected** network gives a response that reveals the excitability of each neuron.



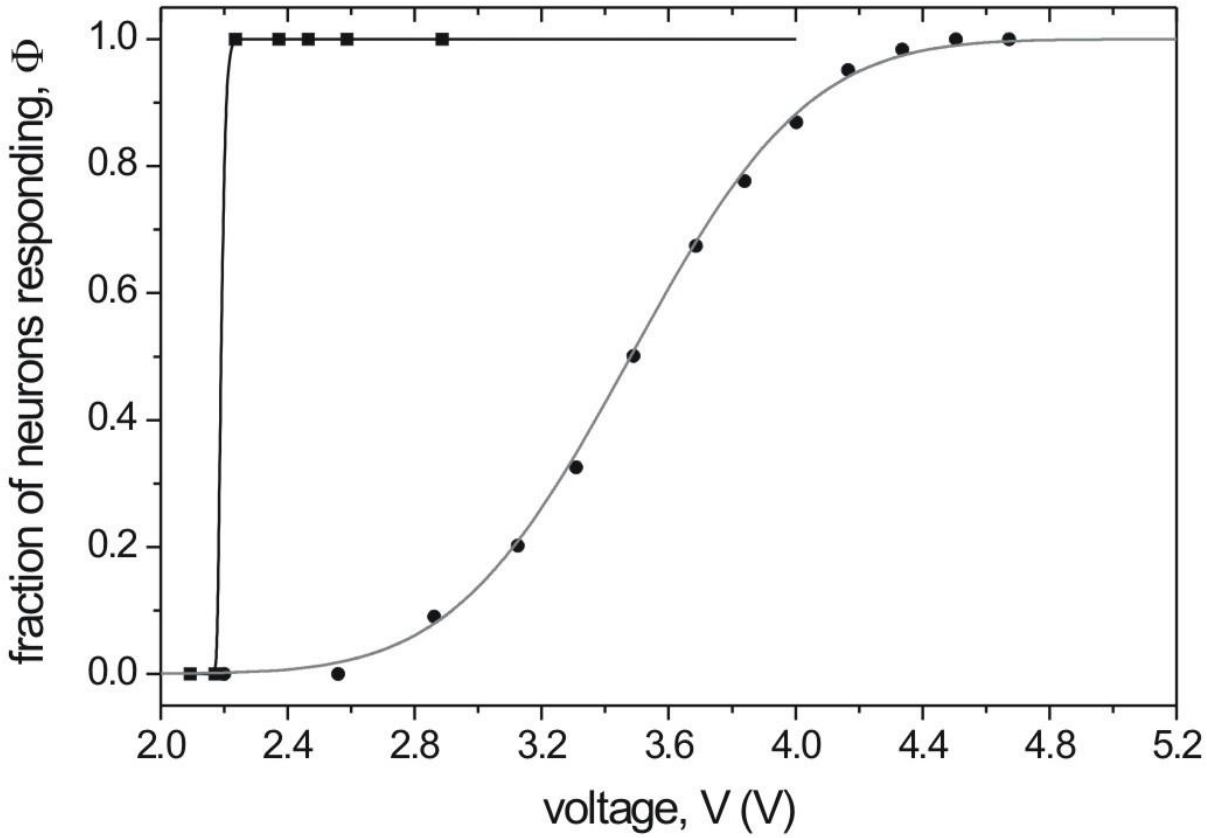
5. Network response upon disintegration

- **Fully connected** shapes a “jump” since a small activation triggers all neurons.



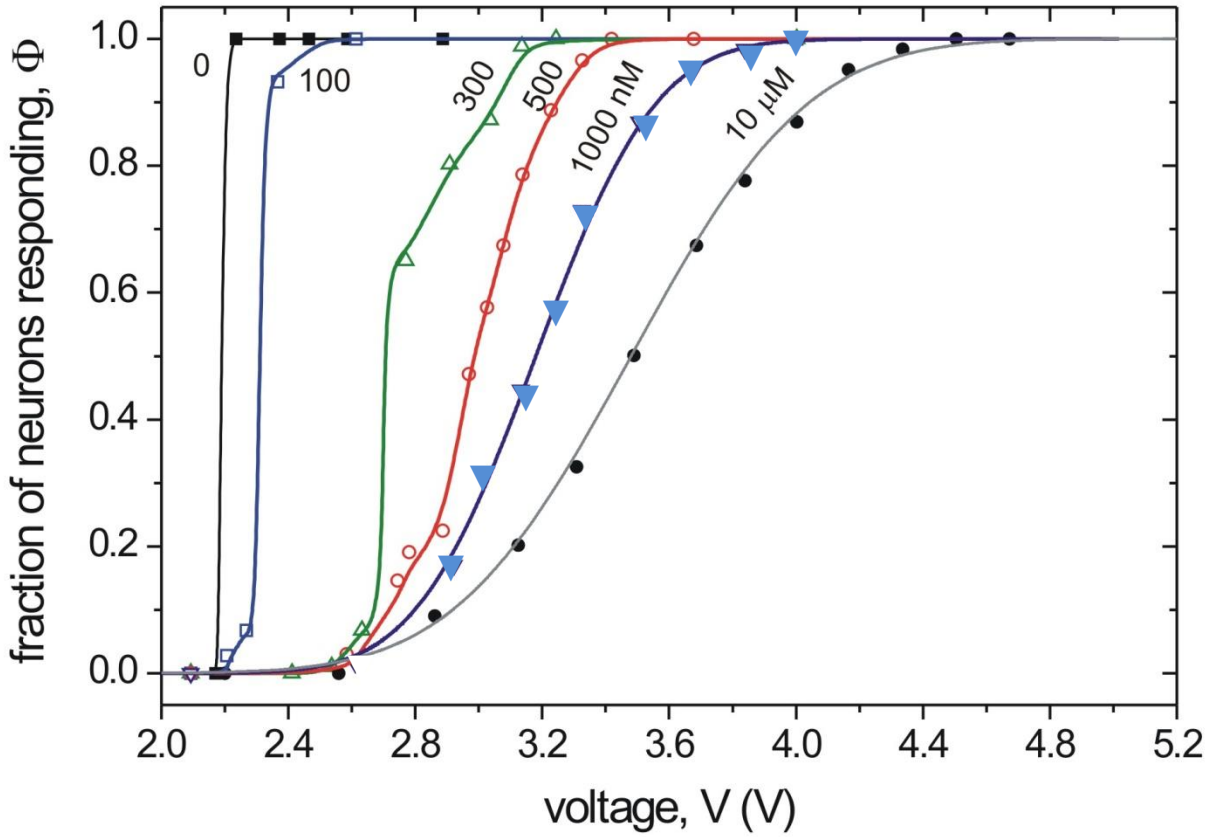
5. Network response upon disintegration

- And in between?



5. Network response upon disintegration

- As disintegration progresses, the jump (giant component) shrinks.



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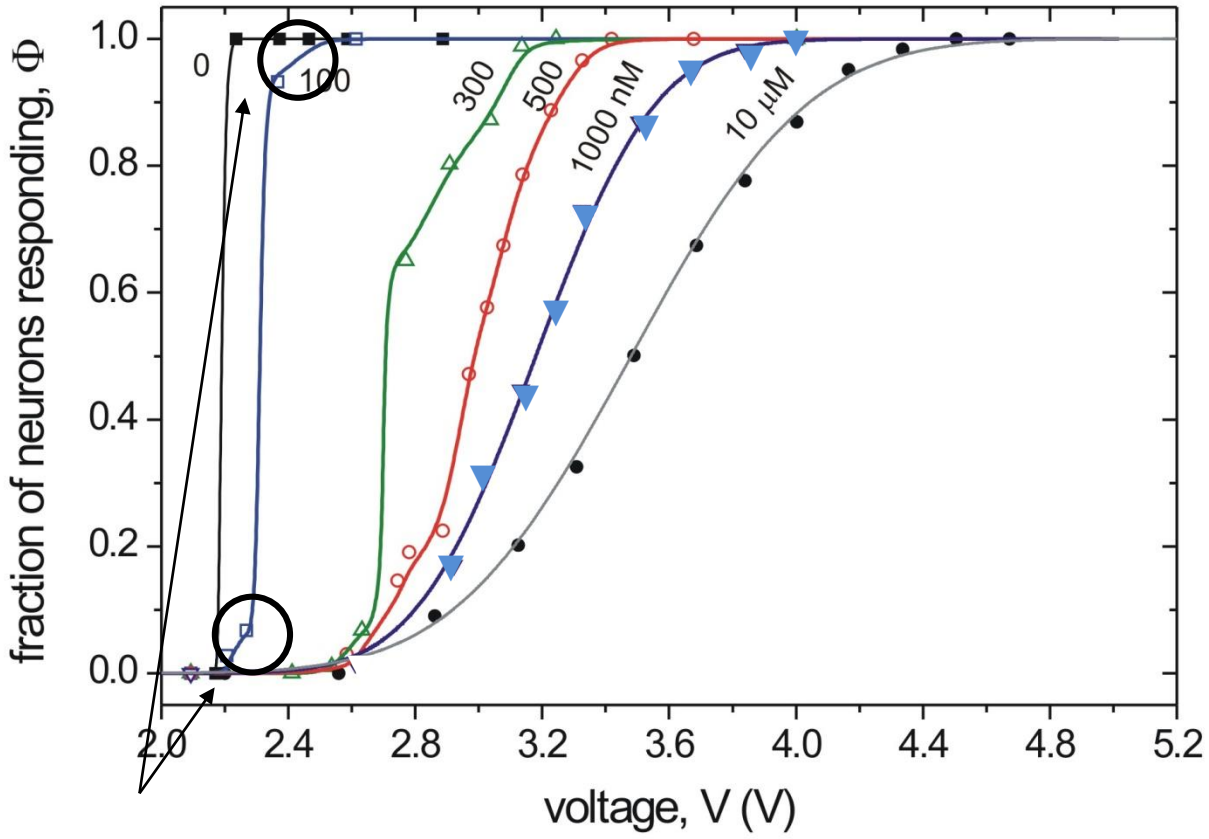
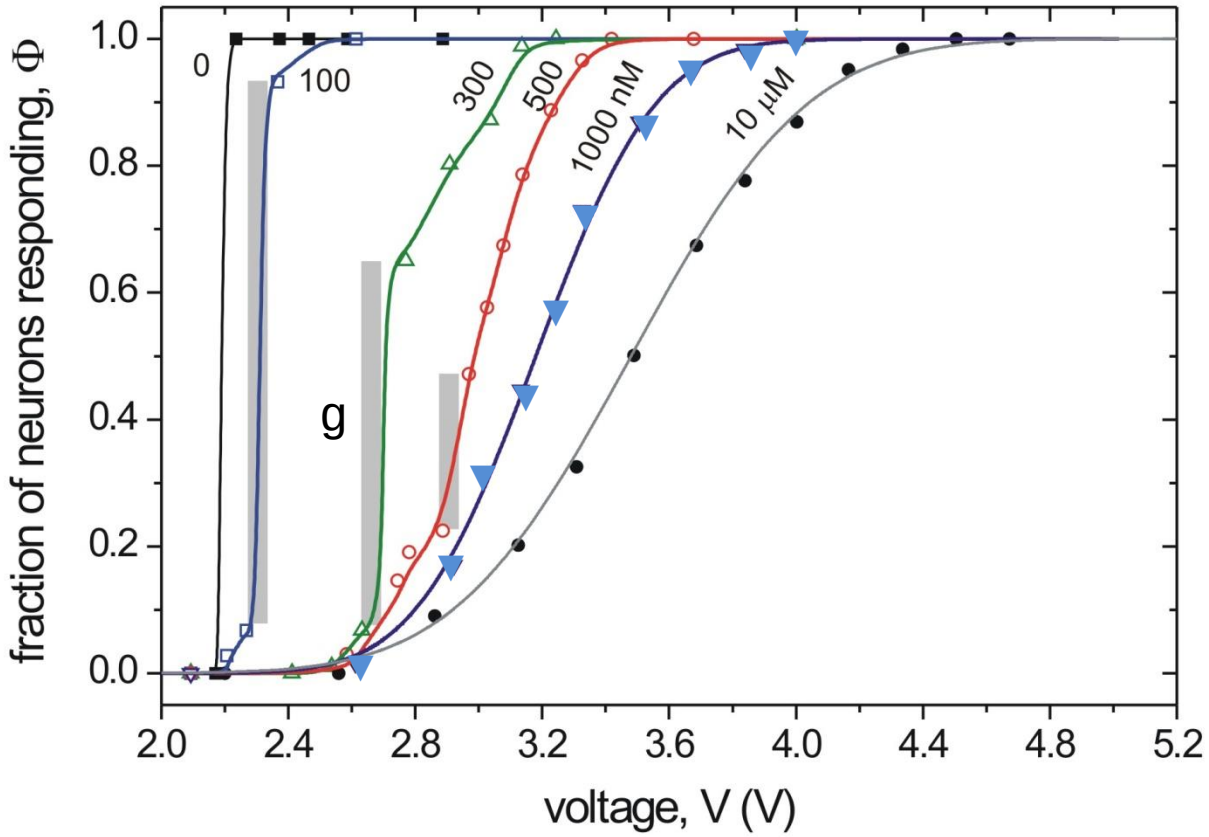


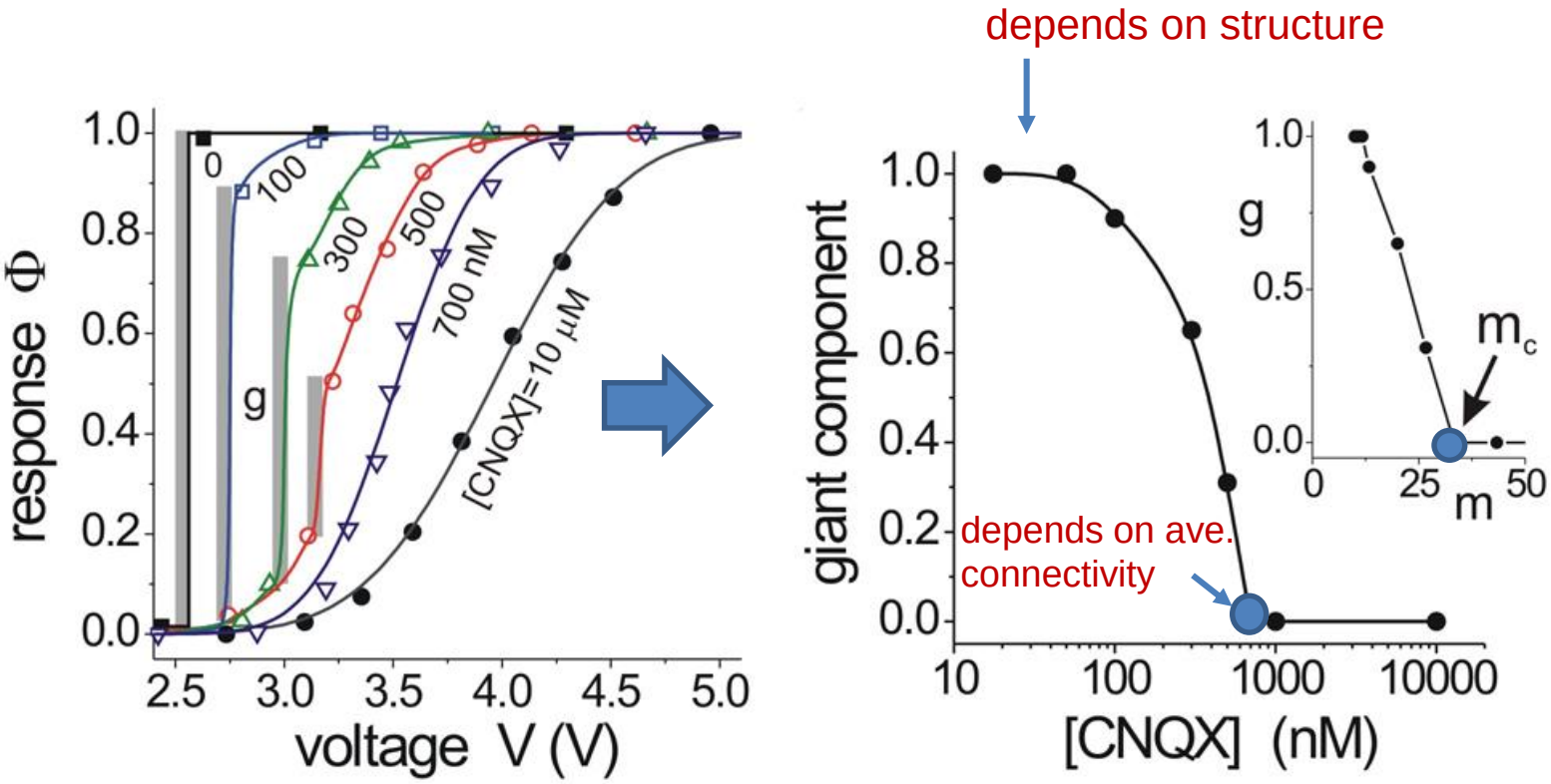
small groups of connected neurons

5. Network response upon disintegration

- As disintegration progresses, the jump (giant component) shrinks.



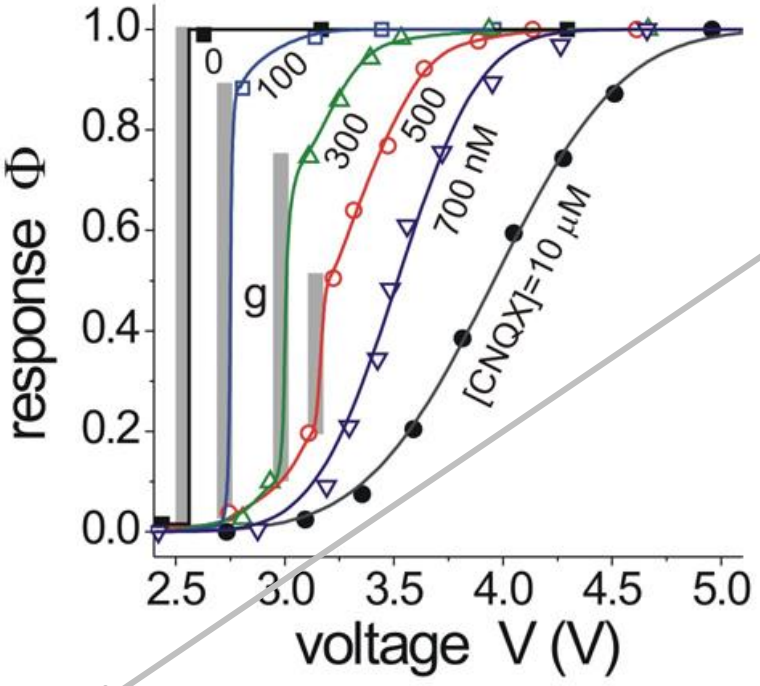
6. Extracting average connectivity

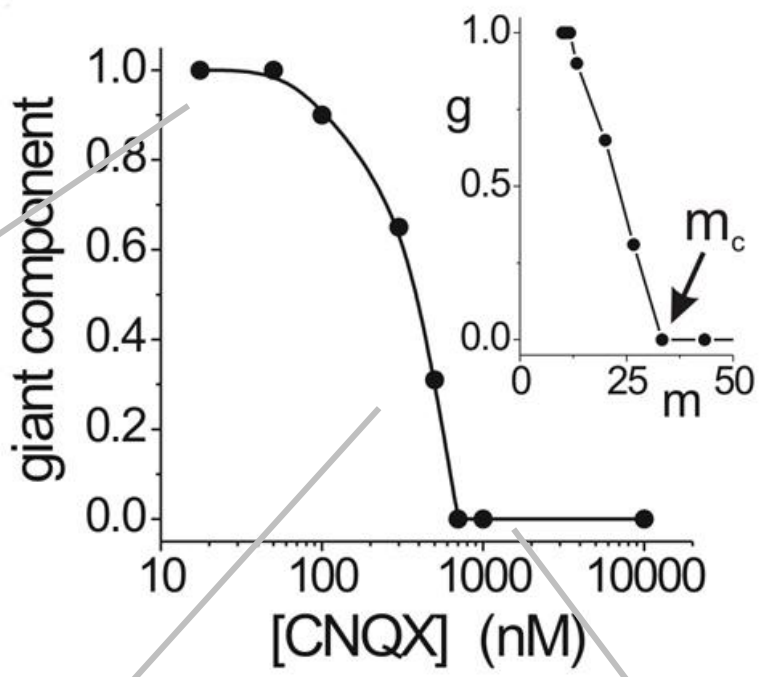


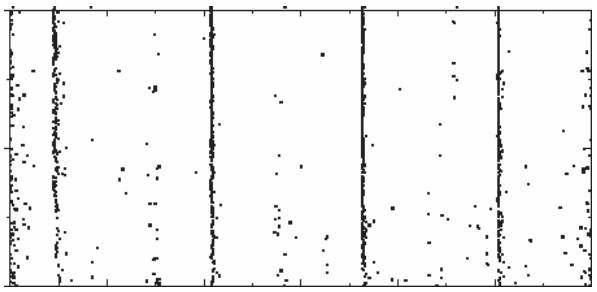
Disintegration parameter: $m = m_0 (1 + [CNQX] / K_d)$

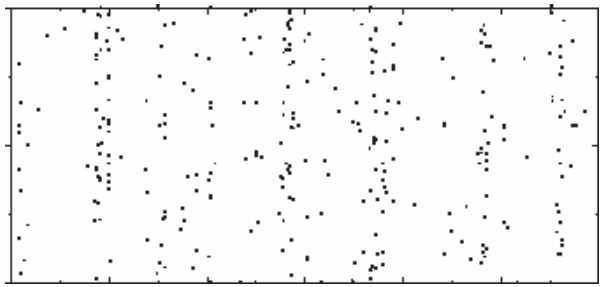
6. Extracting average connectivity

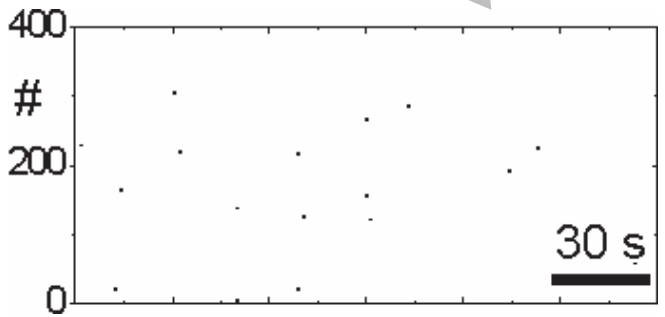
- We can actually relate the behavior at different disintegration points with the dynamics. It gives an idea of the importance of connectivity for dynamics.







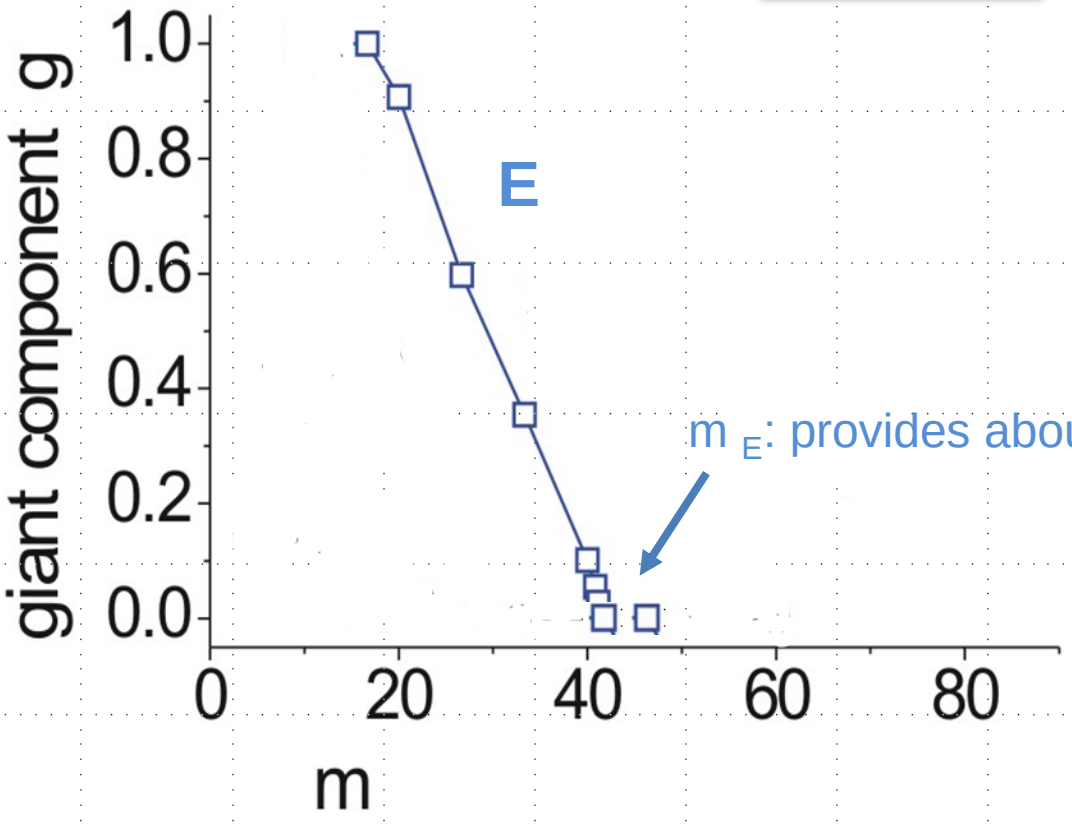




6. Extracting average connectivity

■ One can get two disintegration curves, for inhibition blocked (**E-only connections**) …

$$m_E \simeq \bar{k}_E.$$



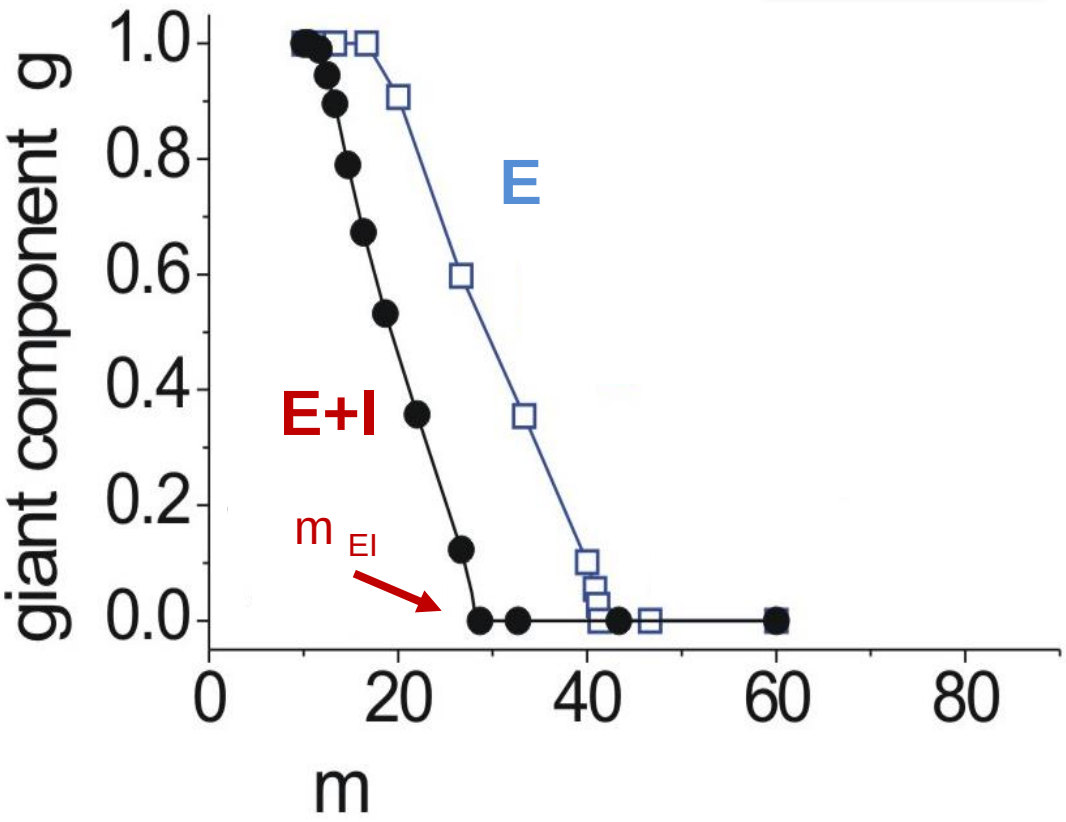
m $_E$: provides about **200 connections / neuron**

6. Extracting average connectivity

- One can get two disintegration curves, for inhibition blocked (**E-only connections**) … and for inhibition active (**E+I connections**), providng:

$$m_E \simeq \bar{k}_E.$$

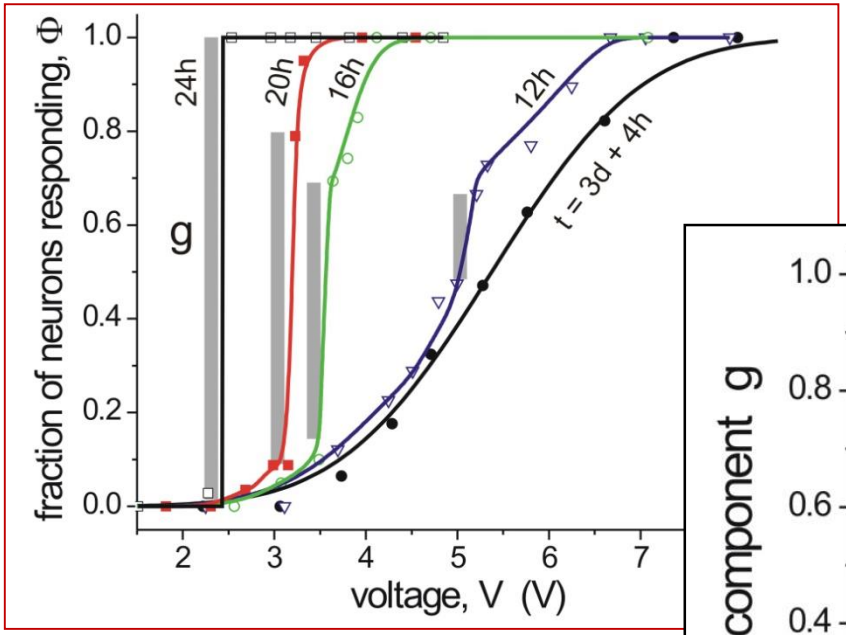
$$m_{EI} \simeq \bar{k}_E - \bar{k}_I$$

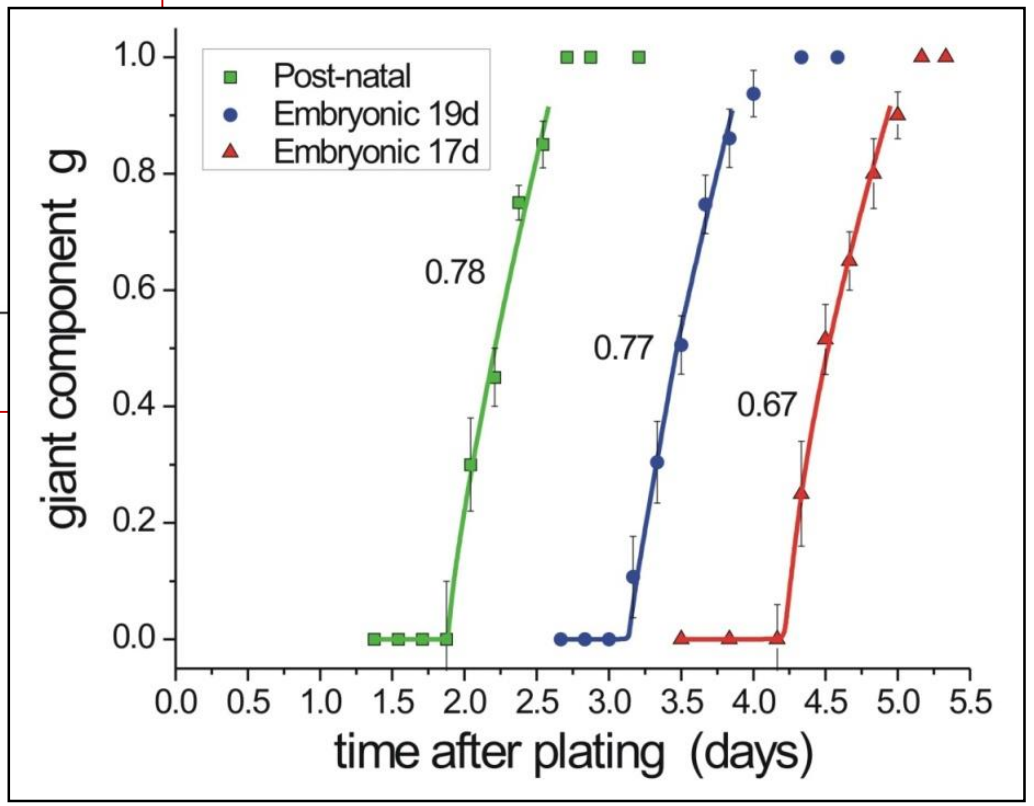


Leads to:
Excitation: 70-80%
Inhibition: 30-20%

6. Extracting average connectivity

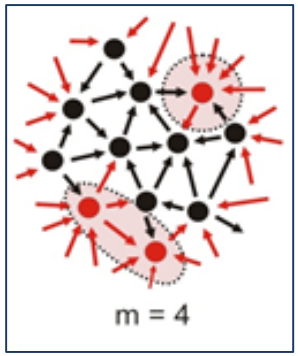
■ One can also quantify the development along time. The formation of new connections upon maturation works as the inverse of CNQX.





7. Distribution of connections

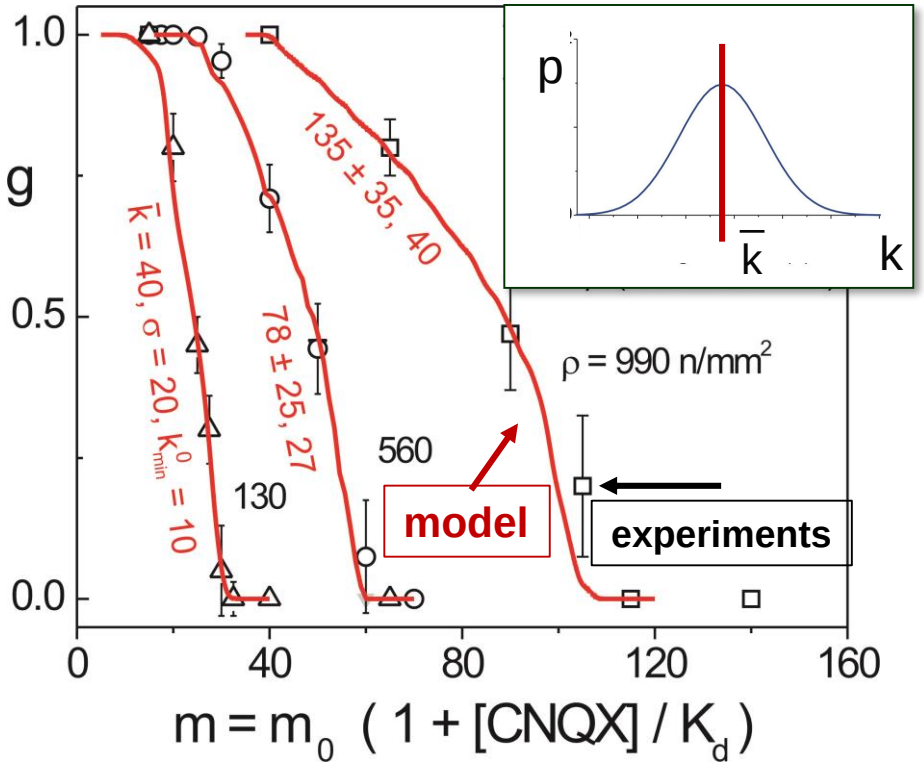
■ Percolation excludes dynamics, and therefore a model and simulations are relatively simple. One just has to be aware of the **quorum effect** for firing.



▫ Simulations allow testing different connectivity blueprints and compare with experiments.

▫ Results show that a Gaussian connectivity is the most probable configuration.

▫ Makes sense? **Yes**, neurons in a homogeneous culture essentially connect to nearby neighbors, and in a similar manner everywhere.



8. Other resources from Physics: Ising Model

■ In an Ising model, spins with states {1, -1} interact to one another upon an external drive. It is very similar to our culture, but using {0,1} as states of the neuron (inactive=0; active=1).

$$\mathcal{H} = -\sum_{i=1}^{N} s_i \left(J \left[\sum_{\{j_E\}_i} s_j - \gamma \sum_{\{j_I\}_i} s_j \right] + h_i + H^* \right)$$

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$s_i = \{1,0\}$

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sensitivity to H

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Mean field approach
(any neuron sees the same neighborhood)

$$M \equiv \langle s \rangle$$

$$M = \int_{k_i=-\infty}^{k_i=+\infty} \rho(k_i)\Phi\left(\frac{\frac{J_0[p_E - \gamma p_I]}{m} k_i M + H - H_0}{\sigma_h} \right) dk_i$$

8. Other resources from Physics: Ising Model

■ In an Ising model, spins with states {1, -1} interact to one another upon an external drive. It is very similar to our culture, but using {0,1} as states of the neuron (inactive=0; active=1).

$$\mathcal{H} = -\sum_{i=1}^{N} s_i \left(J \left[\sum_{\{j_E\}_i} s_j - \gamma \sum_{\{j_I\}_i} s_j \right] + h_i + H^* \right)$$

Mean field approach
(any neuron sees the same neighborhood)

$$M \equiv \langle s \rangle$$

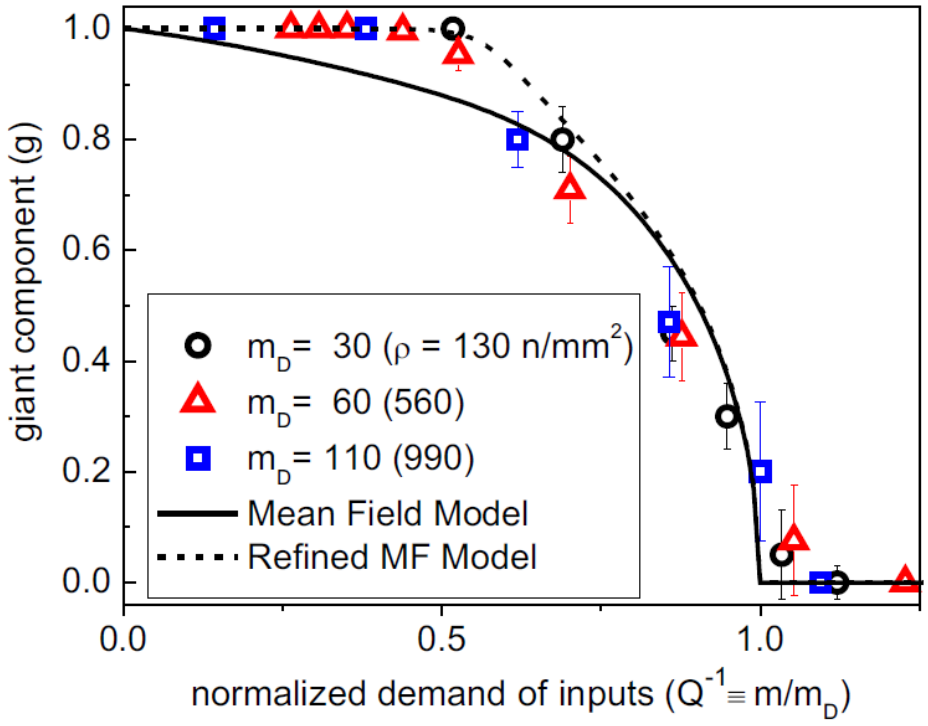
$$M = \int_{k_i=-\infty}^{k_i=+\infty} \rho(k_i) \Phi \left(\frac{\frac{J_0[p_E - \gamma p_I]}{m} k_i M + H - H_0}{\sigma_h} \right) dk_i$$

Connectivity layout

8. Other resources from Physics: Ising Model

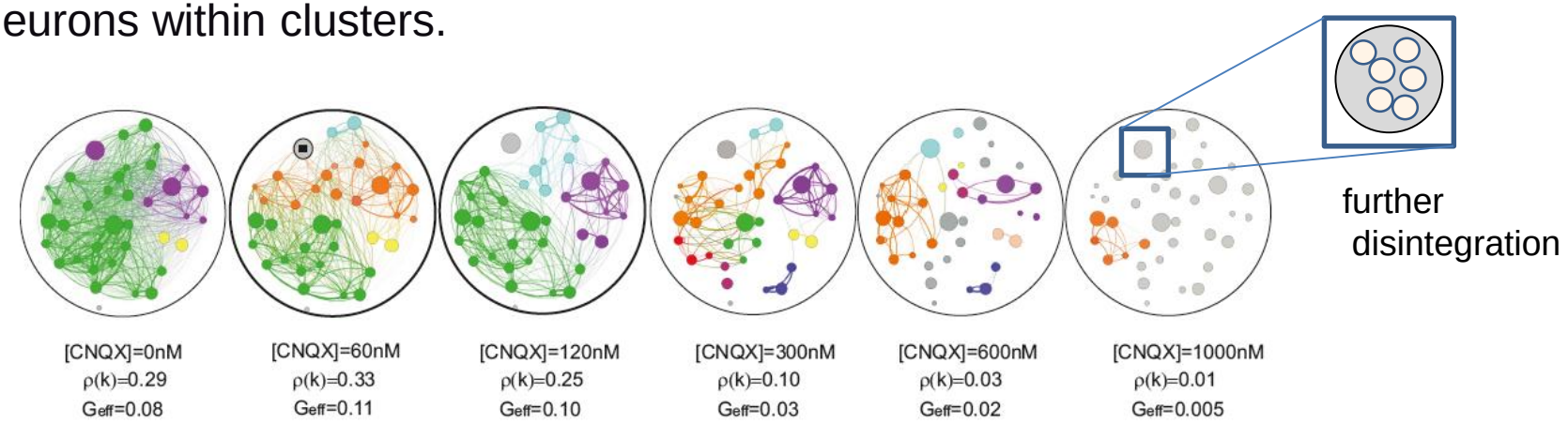
■ In an Ising model, spins with states {1, -1} interact to one another upon an external drive. It is very similar to our culture, but using {0,1} as states of the neuron (inactive=0; active=1).

▫ The Ising model approaches the experimental results well. The differences allow for interesting refinements to be included!

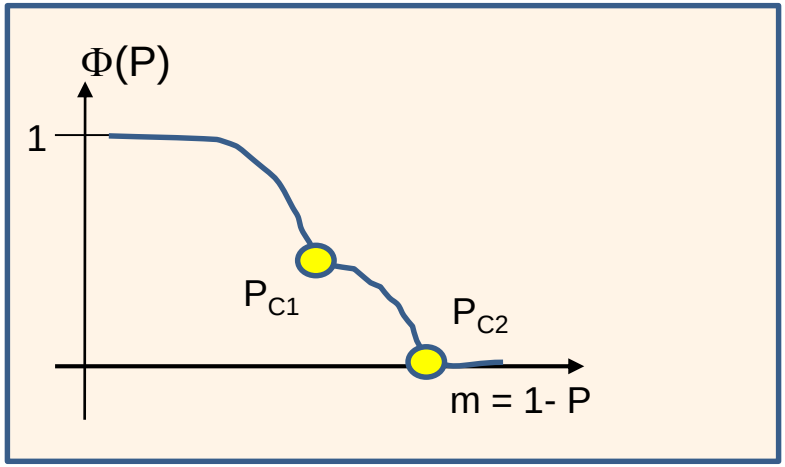


9. Final remark. Percolation in more complex networks

■ We can revisit the clustered networks described in **Lecture 7** and study their controlled disintegration through CNQX. In this case we observe something interesting: the emergence of 2 percolation transitions, one corresponding to the disconnection among clusters, and another one to the disconnection of neurons within clusters.



▫ The percolation curve captures the two spatial scales of the system, and therefore this framework could serve to unravel the degree of hierarchical organization in neuronal networks.



End of lecture 9

TAKE HOME MESSAGE:

- Percolation is a classic resource from Statistical Physics that can be translated into neuroscience to unravel interesting information about the structure of a neuronal network in a non-invasive way.

- The transition point conveys information on the average connectivity, while the transition curve reflects the distribution of connections.

- Other classical resources from Statistical Physics (spin models, mean field..) are slowly providing new tools for connectivity inference.

Questions and discussion aspects:

- We treated bond percolation. How about site percolation?

- In this examples I have not use at any moment the fact that neurons are embedded in a metric space. How do you think I can further use this information?

- Do you think I observe other statistical physics phenomena in the experiments, such as hysteresis or avalanches?

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