# Shaping connectivity and dynamics of neuronal networks with physical constraints

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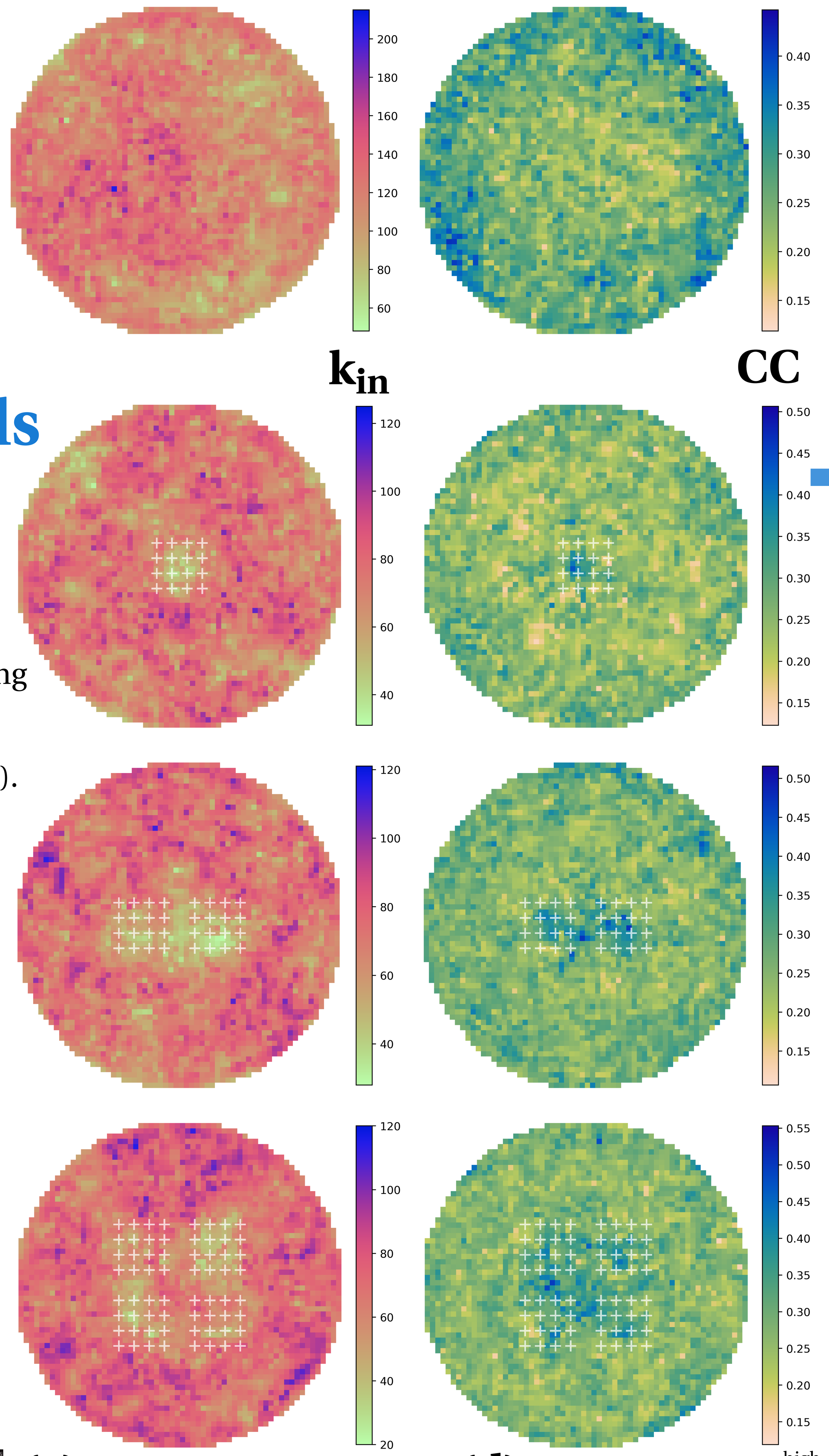
## Summary


- **Simulations** permit precise modeling of networks' geometry and dynamics.
- **Functional networks** can be obtained using calcium imaging of 3D cultures.
- **Network properties tuned by** density or arrays of obstacles.


## Simulations of neuronal growth in 2D

We study local network properties in simulations of 2500 neurons growing in a disk of diameter 4 mm. The density of neurons is about 200 neurons/mm$^2$ which corresponds to that seen in experiments on primary cultures.

Figures on the right represent the average values of in-degree ( $k_{in}$ ) and clustering coefficent ( CC ) in square regions of side 0.63 mm, containing ~80 neurons.

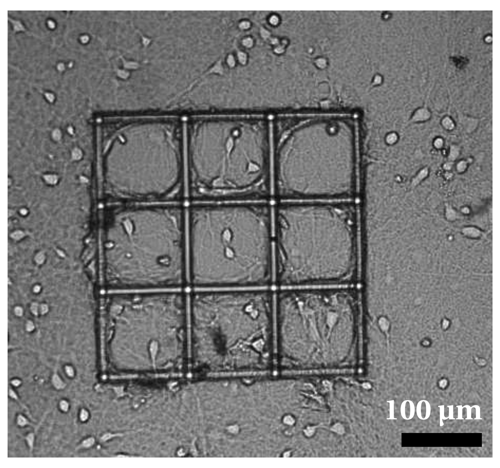


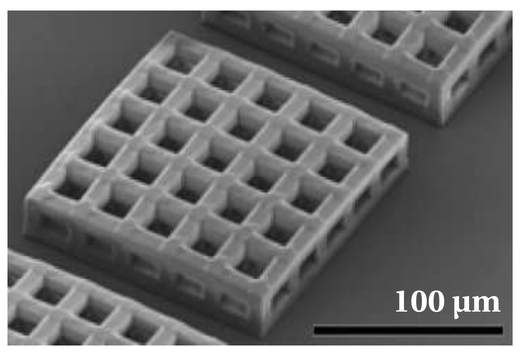

## Cultures on scaffolds

The structure of the culture substrate allows to ***guide neurite growth*** cones and neuronal connectivity pattern *in vitro* [1,2,3].

We employ 3D printed scaffolds within the Mesobrain project to stabilise ***fragile*** cultures and build 3D cultures ***mimicking cortical columns*** *in vitro*. [ ***mesobrain.eu*** ]

Left: Bright field image of neurons growing on scaffold. Right: SEM image of two level *box shaped* scaffolds.



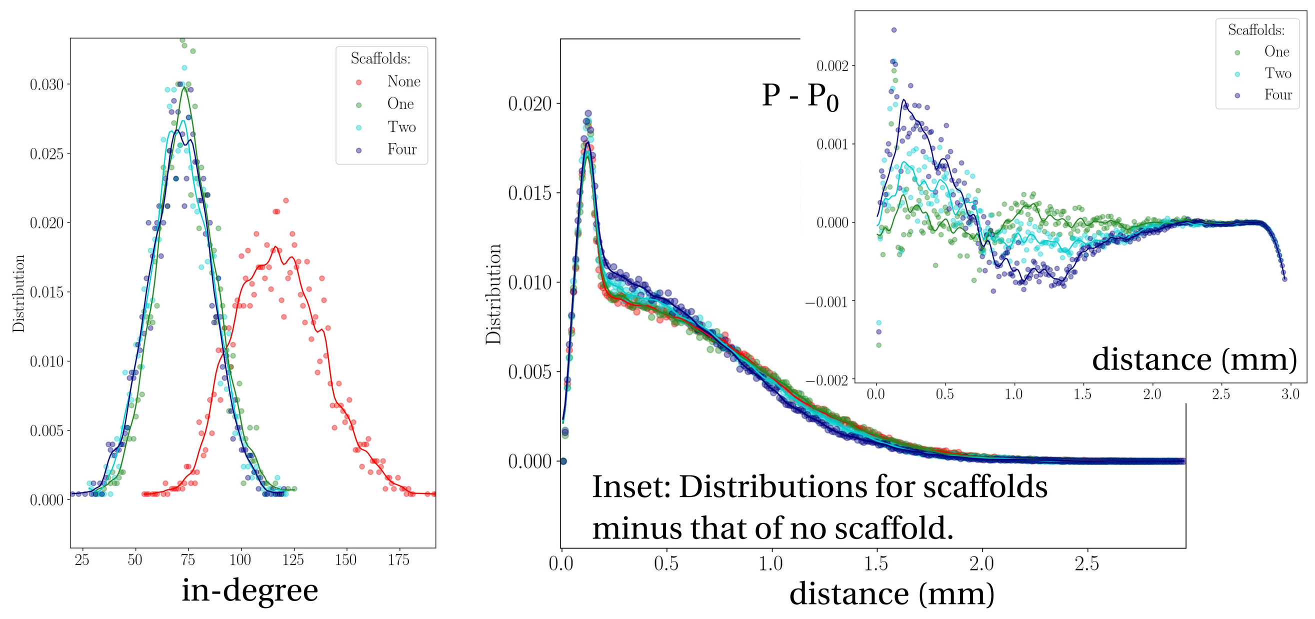




## Simulations with 2D scaffolds

The box-like scaffold structure is modeled by a 4x4 array of cross shaped obstacles. Data for simulations of one, two and four scaffolds placed in center of the circle are presented.

In all three cases the in-degree ($k_{in}$) is reduced and the clustering coefficent ( CC ) is enhanced in the vicinity of the obstacles.

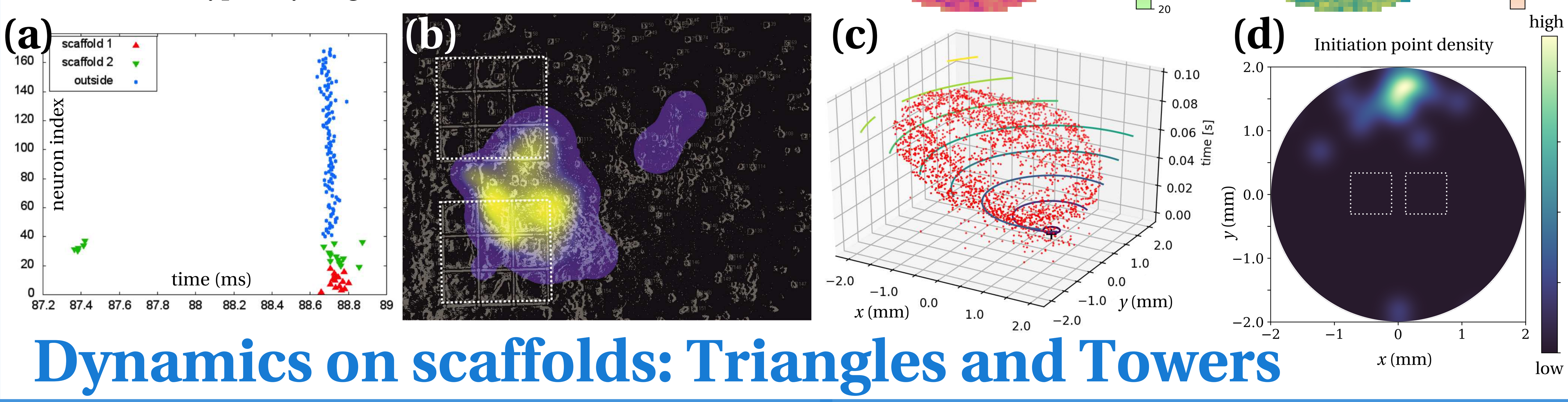
Distributions of in-degrees (left) and connection lengths (right).




Dynamics for two scaffold geometry ( exp. & sim. ).

**In experiments** activity propagates across the field of view **(a)**, and initiation points lie within and outside of scaffolds **(b)**.

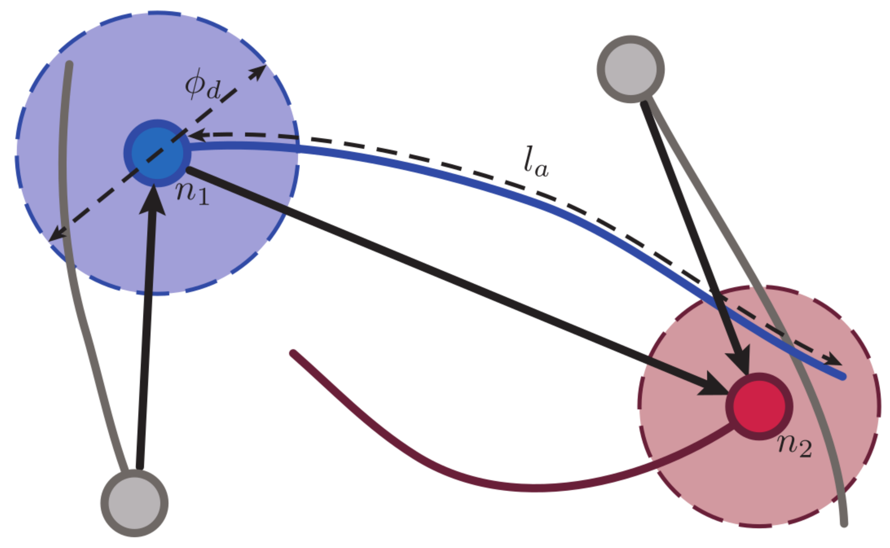
**In simulations** activity propagates also **(c:** spike times and wave fit), and typically originates outside scaffolds **(d)**.




## Model

**Network growth**

Randomly position neurons on in a defined area. Osbtacles are modeled as excluded areas. Dendritic trees are modeled as circular areas with radius ($\phi_d$) drawn from a normal distribution. Axons grow at random angles and follow a biased random walk with $\bar{l}_a$=1.1 mm, as in [4].




**Neuron dynamics**

A quadratic integrate and fire model with adaptation was used for the soma dynamics [4,5]. A generated spike is transmitted as a current and the synapse model includes depression [4].

$$C\dot{v} = k(v - v_r)(v - v_t) - u + I + \eta$$

$$\tau_a \dot{u} = b(v - v_r) - u$$

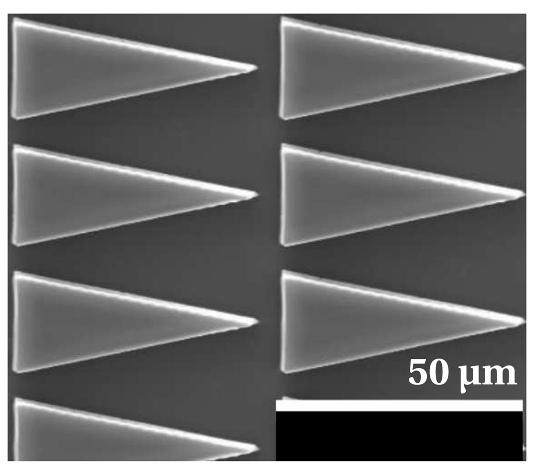
$$\text{if } v \geq v_p, \quad \text{then } v \leftarrow v_c, \leftarrow u + d$$

where $v$, $v_r$, $v_t$ are the soma membrane, resting & threshold potentials, $u$ is an inhibitory current, $I$ contains synaptic inputs and $\eta$ is a noise term.

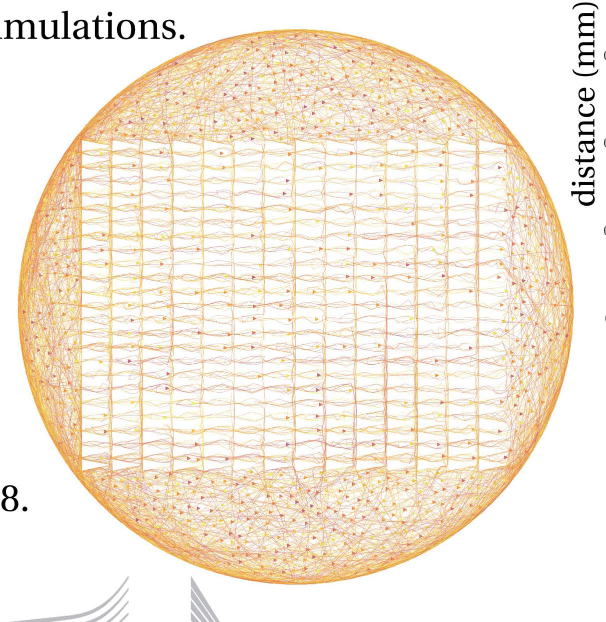
## Dynamics on scaffolds: Triangles and Towers

An array (24x24) of triangles disposed in a circle favours connections at small angles.

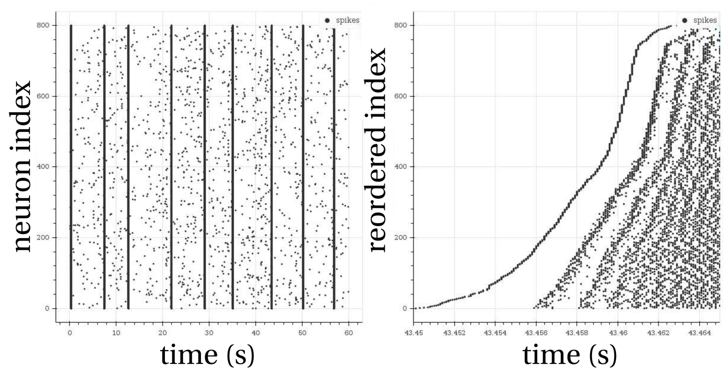
Electronmicrograph of triangular scaffolds.



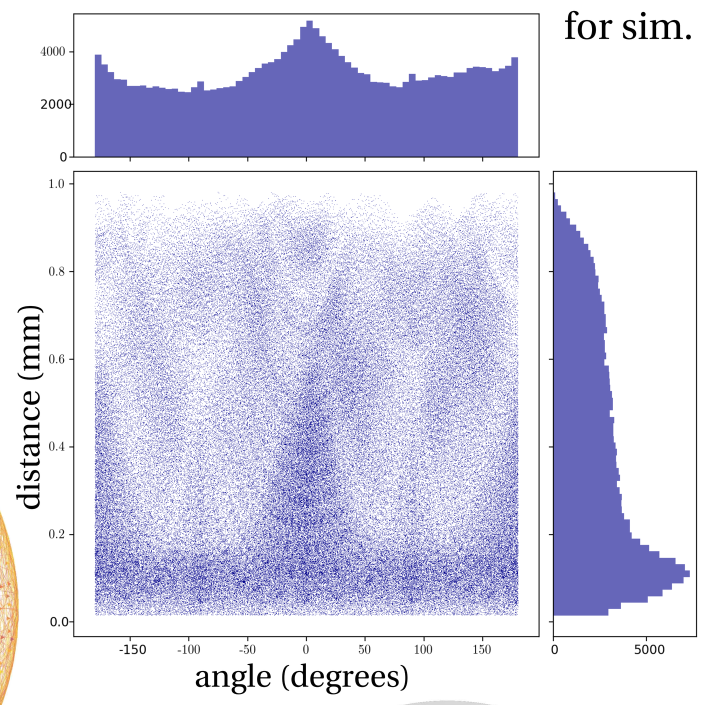

Neuron positions and axonal paths in simulations.



Left: Raster plot for simulation with triangles. Right: Reordered by spike time.




Distribution of lengths versus angles for sim.




Neurons were grown on tower-like scaffolds.

Activity was measured using Ca-fluorescence and the functional network was inferred with GTE as in [6].

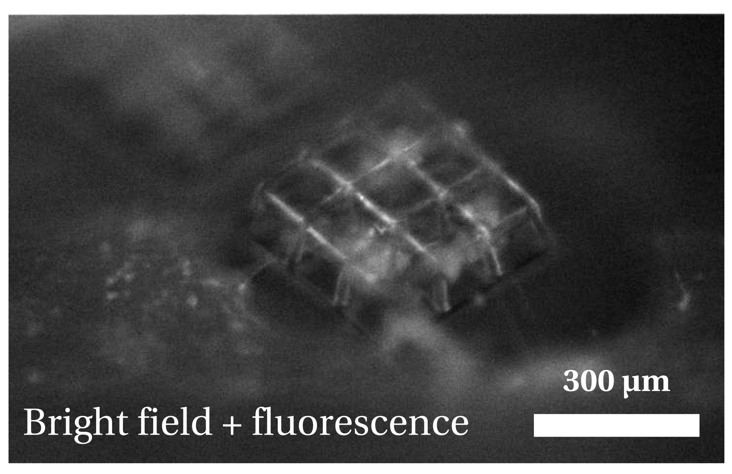
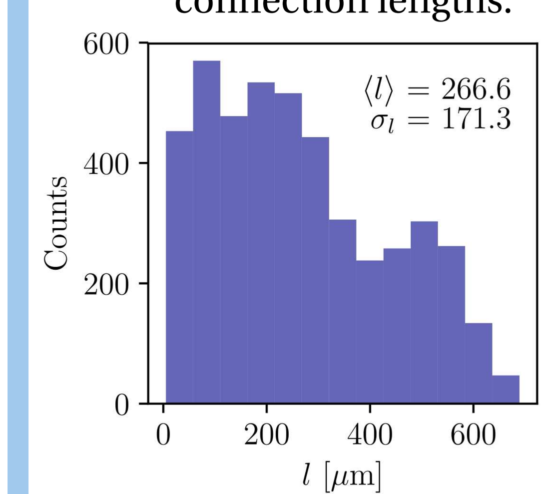
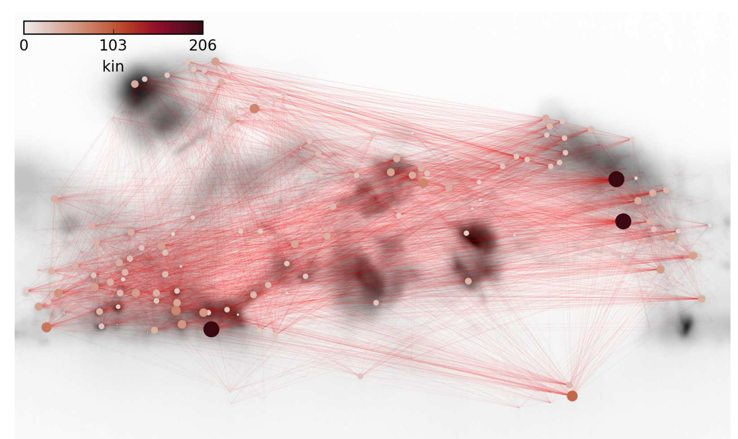



Image of neurons growing on scaffold.

Distribution of connection lengths.




Inferred functional network.



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