The remarkable effect of network topology on calcium wave propagation in astrocyte networks

Jules Lallouette, Mati Goldberg, Maurizio de Pittà, Eshel Ben-Jacob, Hugues Berry

The remarkable effect of network topology on calcium wave propagation in astrocyte networks

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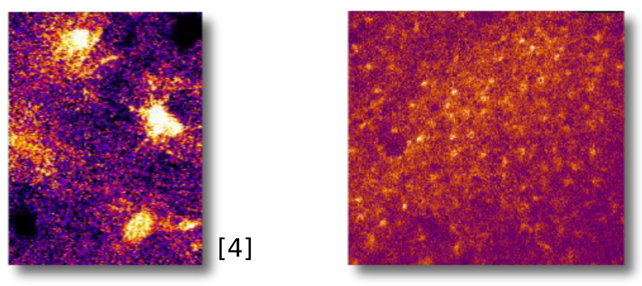
Calcium waves and network topologies

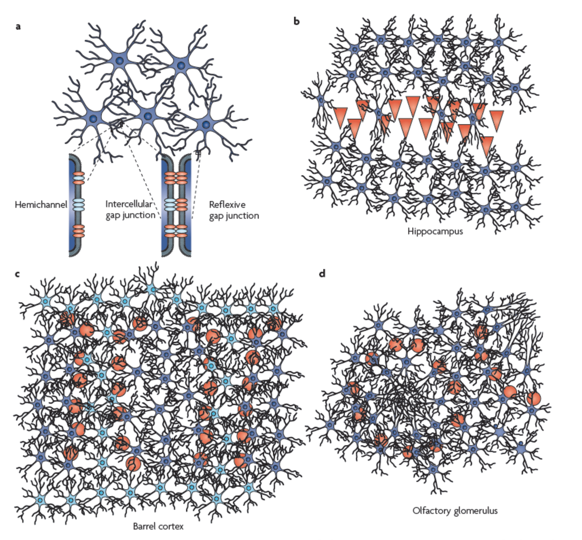
In astrocyte networks, the reported speed and extent of propagation of intercellular calcium signals can largely vary. Of course, this variability in the propagation patterns may reflect different intracellular properties (biochemical, signaling). But experimental evidence also suggests that the way astrocytes connect to each other in the network (topology) varies depending on the brain region. Such different topologies may already bring forth, by themselves, different modes of intercellular calcium propagation.

Different types of waves

Wave Type [exper. ref]	Activated cells	Speed ($\mu m.s^{-1}$)
Locally synchronized [1]	~ 10	N.A.
Spatially restricted [2]	~ 40	~ 15
Regenerative [3]	∞	~ 35
Glissandi [4]	∞	~ 60



Different topologies



source : Giaume et al. (2010)

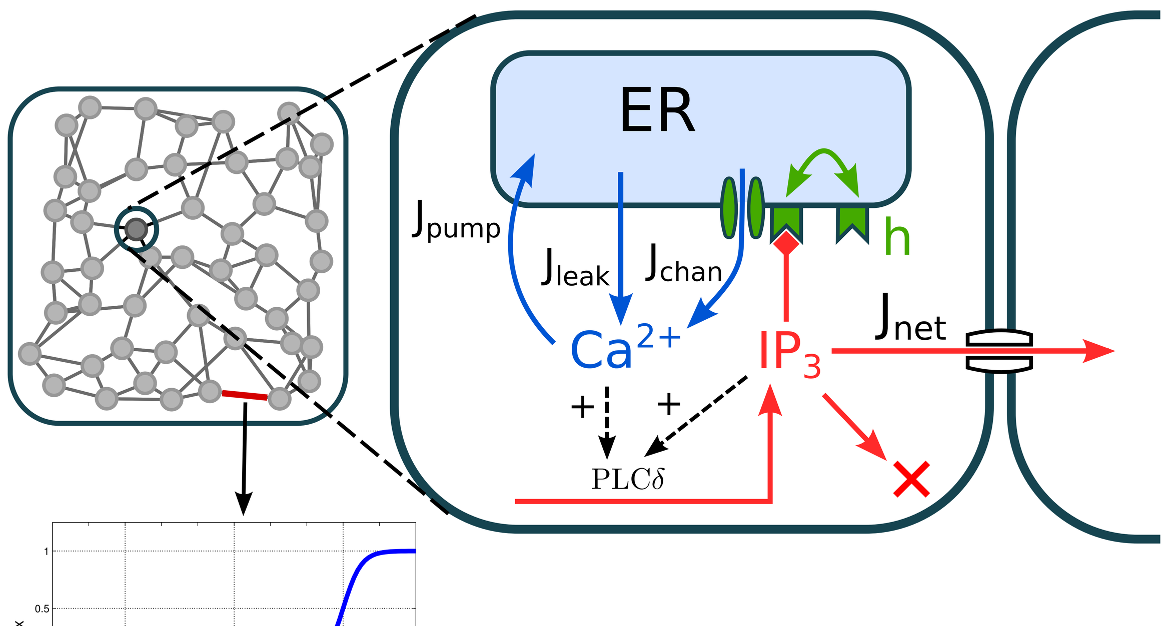
Can we account for the different wave properties by the different topologies ?

Calcium Dynamics model

$$\frac{dC^i}{dt} = J_{chan}(C^i, h^i, IP_3^i) + J_{leak}(C^i) - J_{pump}(C^i)$$

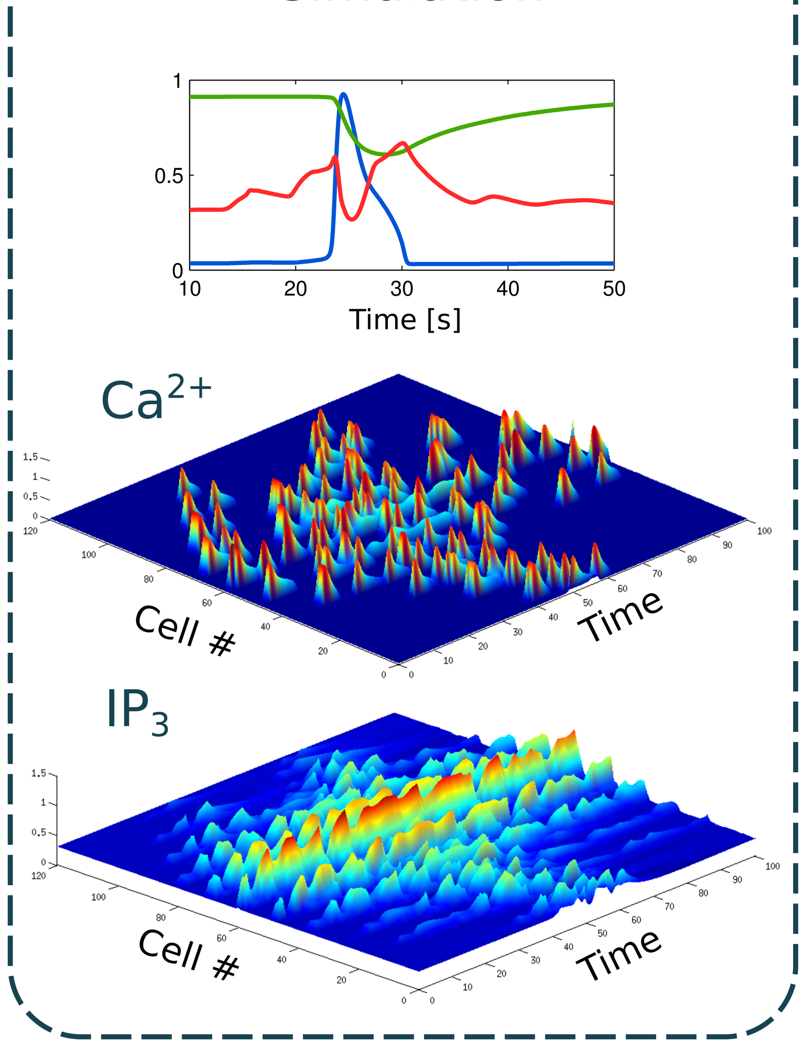
$$\frac{dh^i}{dt} = (h_\infty(C^i, IP_3^i) - h^i)/\tau_h(C^i, IP_3^i)$$

$$\frac{dIP_3^i}{dt} = P_{PLC\delta}(C^i, IP_3^i) - D_{3K}(C^i, IP_3^i) - D_{5P}(IP_3^i) + J_{net}^i$$



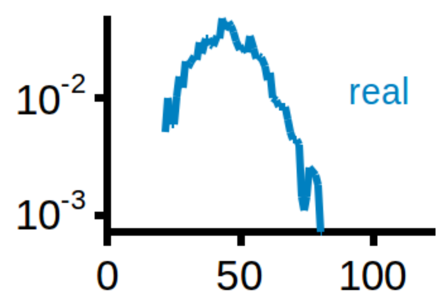
$$J_{j\to i} = \frac{F}{2}\left(1 + \tanh\left(\frac{|\Delta_{ji}IP_3| - IP_3^{thr}}{IP_3^{scale}}\right)\right)\frac{\Delta_{ji}IP_3}{|\Delta_{ji}IP_3|}$$

Simulation

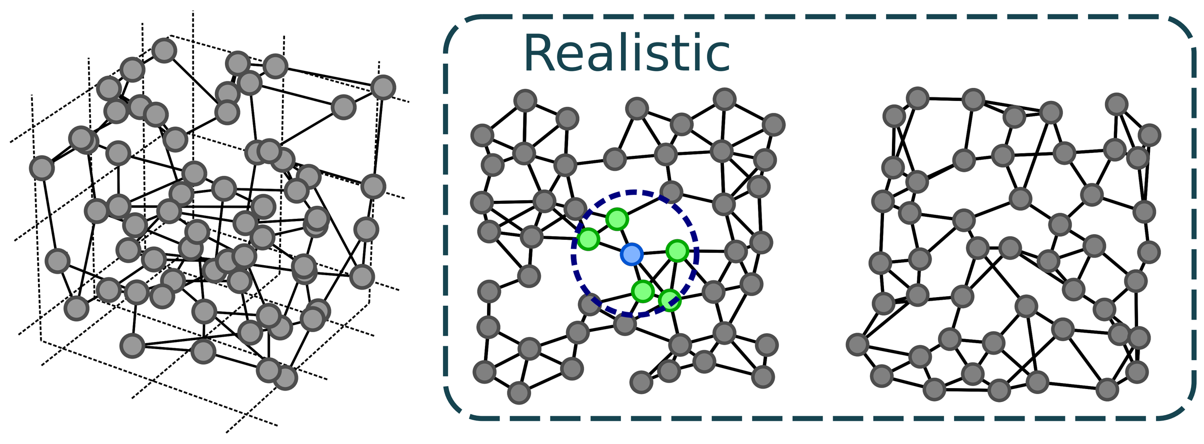


3D Network topologies

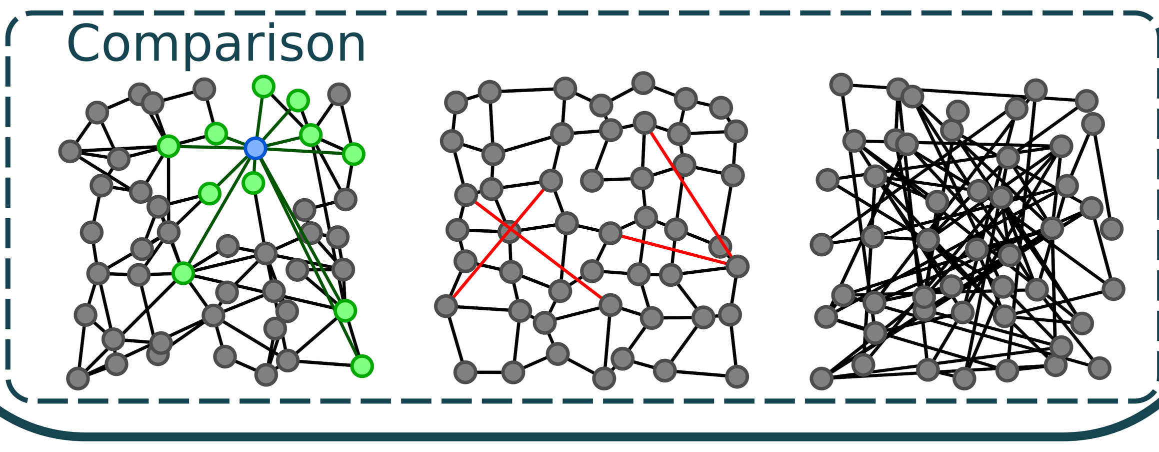
- Stimulation of the center cell with IP3 during the whole simulation.
- Several classes of spatial networks tested.



Realistic

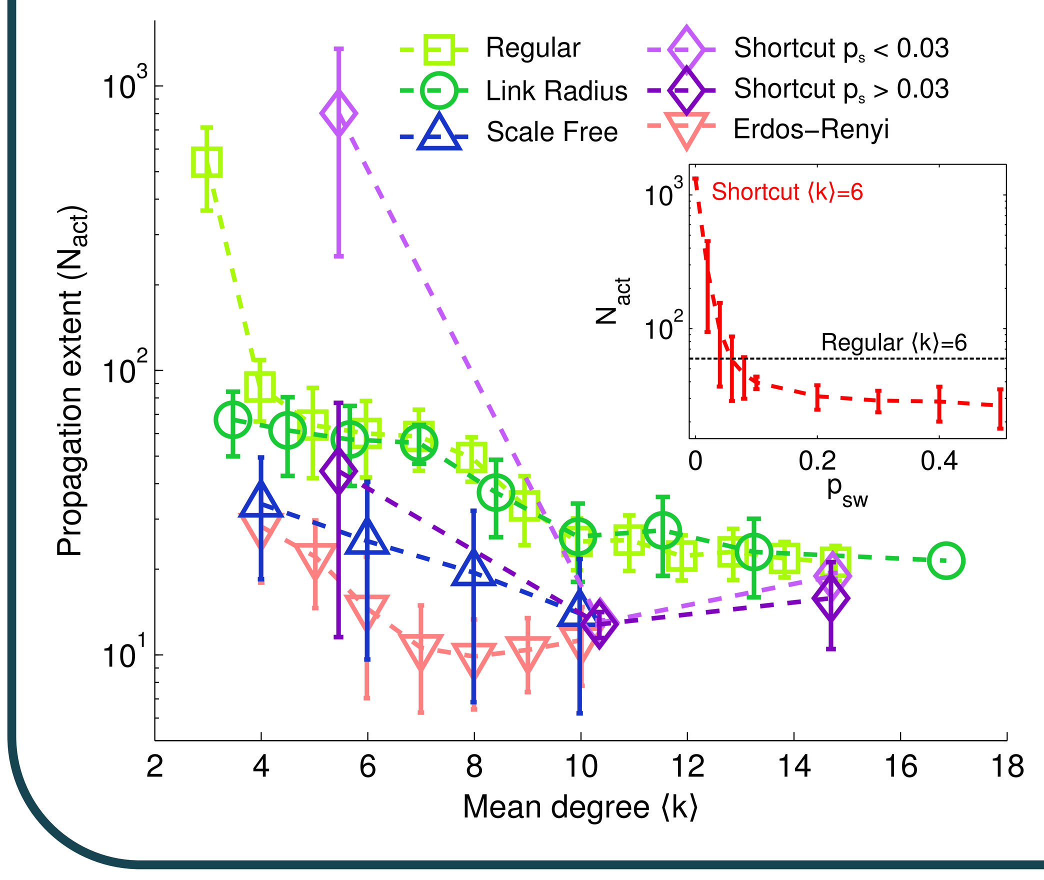


Comparison

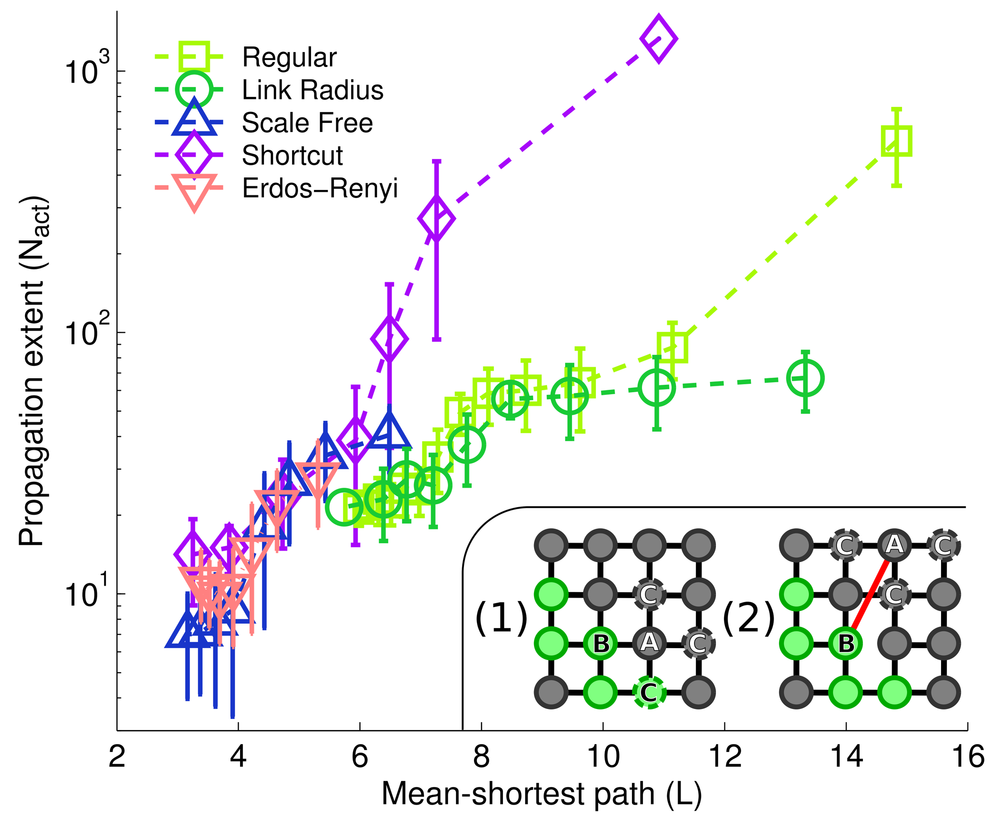


Influence of topology

Low mean degrees increases propagation

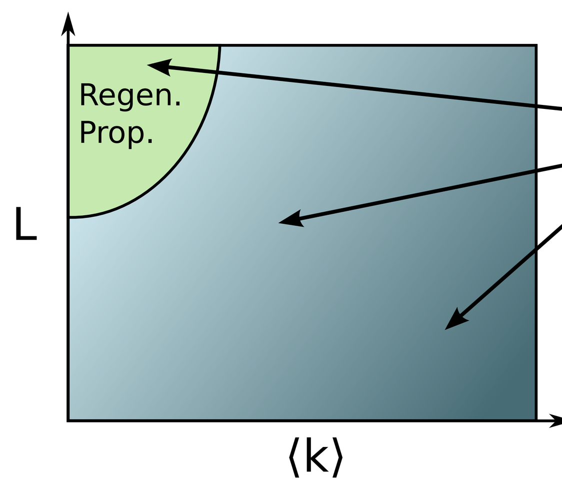


High mean-shortest path increases propagation



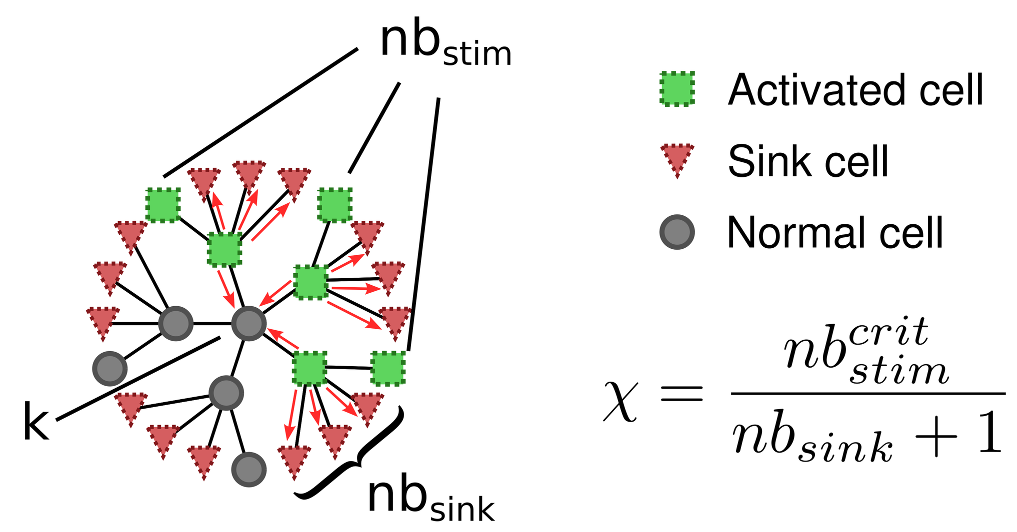
- The major classes of observed propagations can be emulated by a mere variation of the connection topology.
- Calcium wave propagation is favored when the connections between astrocytes are few and mainly restricted to small inter-cell distances.
- Propagation is improved when the mean-shortest path of the network is large.

Schematically :



Wave Type [exper. ref]	N_{act}	$\langle k \rangle$	L
Regenerative [3, 4]	~ 500	~ 3	~ 14
Spatially restricted [2]	~ 40	~ 7	~ 8
Locally synchronized [1]	~ 10	~ 8	~ 4

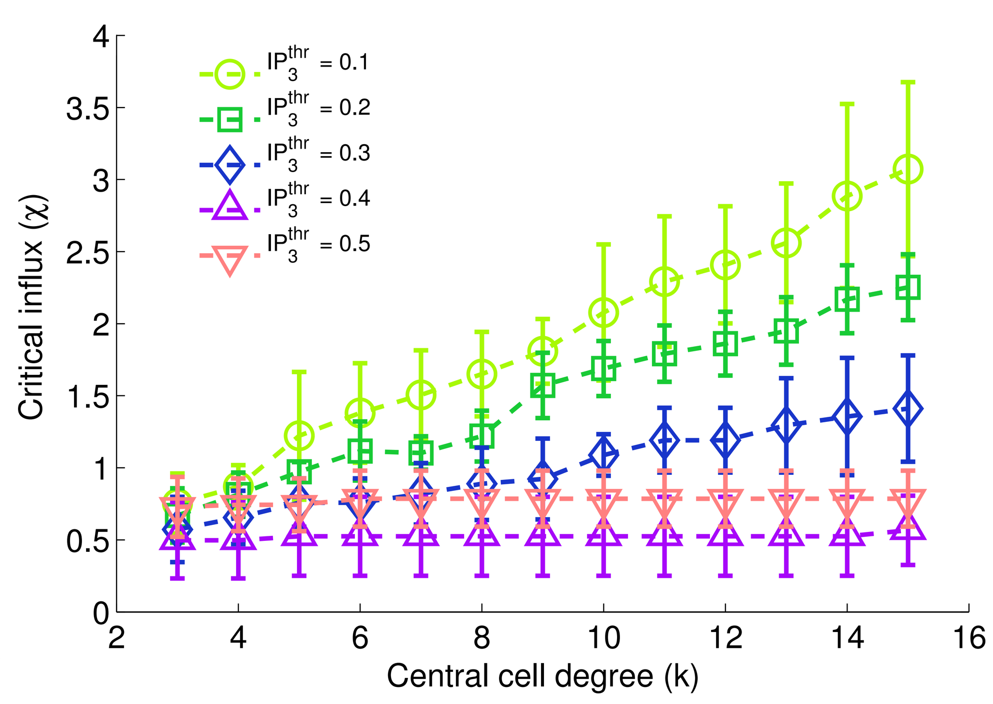
Local rule of propagation



$$\chi = \frac{nb_{stim}^{crit}}{nb_{sink} + 1}$$

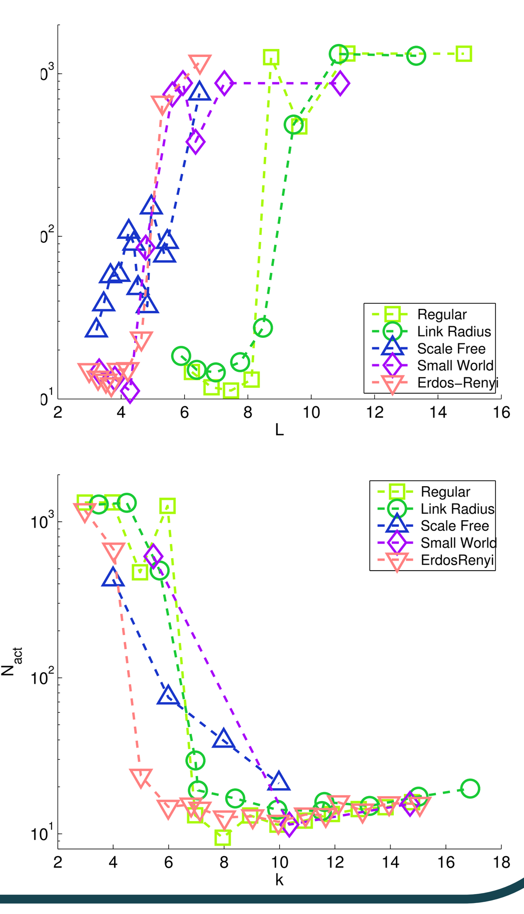
- Activated cells leak IP_3 to their inactive neighbors which act as sinks
- Unactictivated cells receive IP_3 from all their active neighbors and get activated if the IP_3 total influx χ crosses a threshold

Effect of link parameters



$$\chi = A(IP_3^{thr})k + B(IP_3^{thr})$$

Simplified model



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