Cellular criticality

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CONICET

UNC Universidad Nacional de Córdoba

I F E G

Statistical Mechanics for Complexity 2023
80th birthday of C. Tsallis celebration

Collaborators

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Universidad Nacional de San Martin, Buenos Aires, Argentina (CONICET)

- Orlando Billoni

Universidad Nacional de Córdoba , Argentina (IFEG-CONICET)

- Nahuel Zamponi

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- Emiliano Zamponi

University of Colorado-Boulder, USA

MITOCHONDRIA

- Set of tubular shaped organelles (mitochondrion) found in the cells of most eukaryotic organisms.

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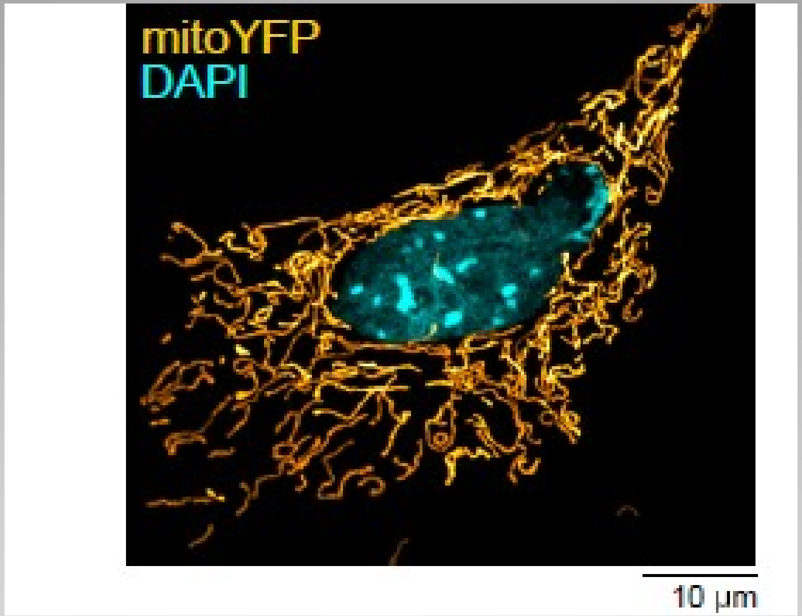
- Main function: ATP (adenosine triphosphate) generation
- Origin (endosymbiotic theory): symbiosis between prokariotic cells (bacteria) and a primitive eukaryotic cell that started about 2.3 billion years ago.
- Other functions: participate of several cellular processes, such as apoptosis (programmed cell death), phospholipids synthesis, regulation of membrane potential, etc..

MORPHOLOGY



AGENTS BASED MODEL: MEAN FIELD

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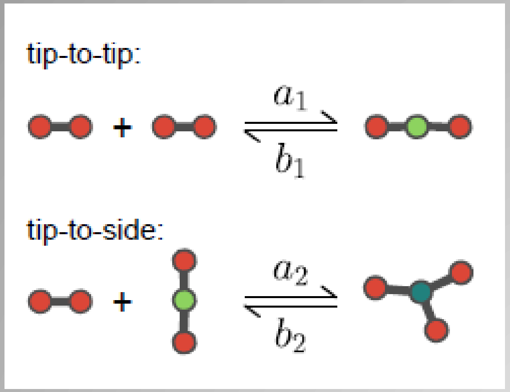
Emergence of the Mitochondrial Reticulum from Fission and Fusion Dynamics

Valerii M. Sukhorukov[1,2]*, Daniel Dikov[3,4], Andreas S. Reichert[3,4], Michael Meyer-Hermann[1,5]*



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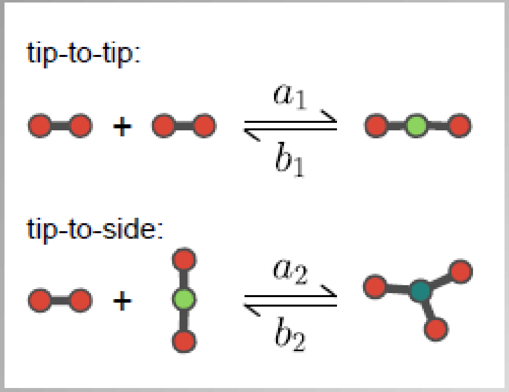

X_k : nodes with degree $k = 1,2,3$

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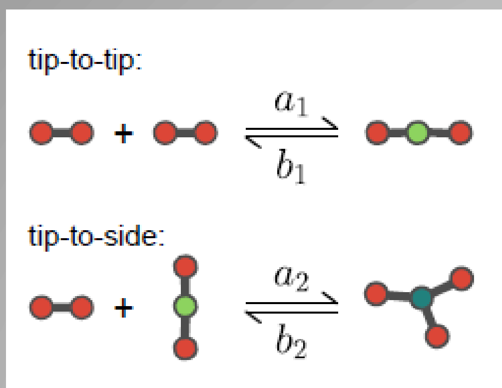

X_k : nodes with degree $k = 1,2,3$

tip-to-tip fusion (a_1) and fission (b_1):

$$2X_1 \underset{b_1}{\overset{a_1}{\rightleftarrows}} X_2$$

tip-to-side fusion (a_2) and fission (b_2):

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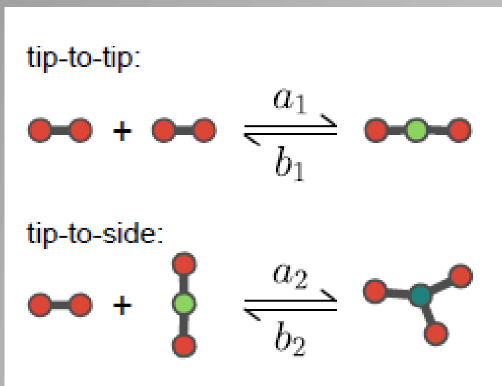

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$b_2 = (3/2)b_1 \equiv (3/2)b$ $\quad$ $c_1 \equiv a_1/b$ and $c_2 \equiv a_2/b$

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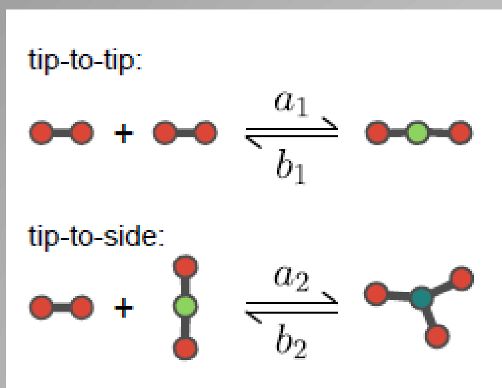

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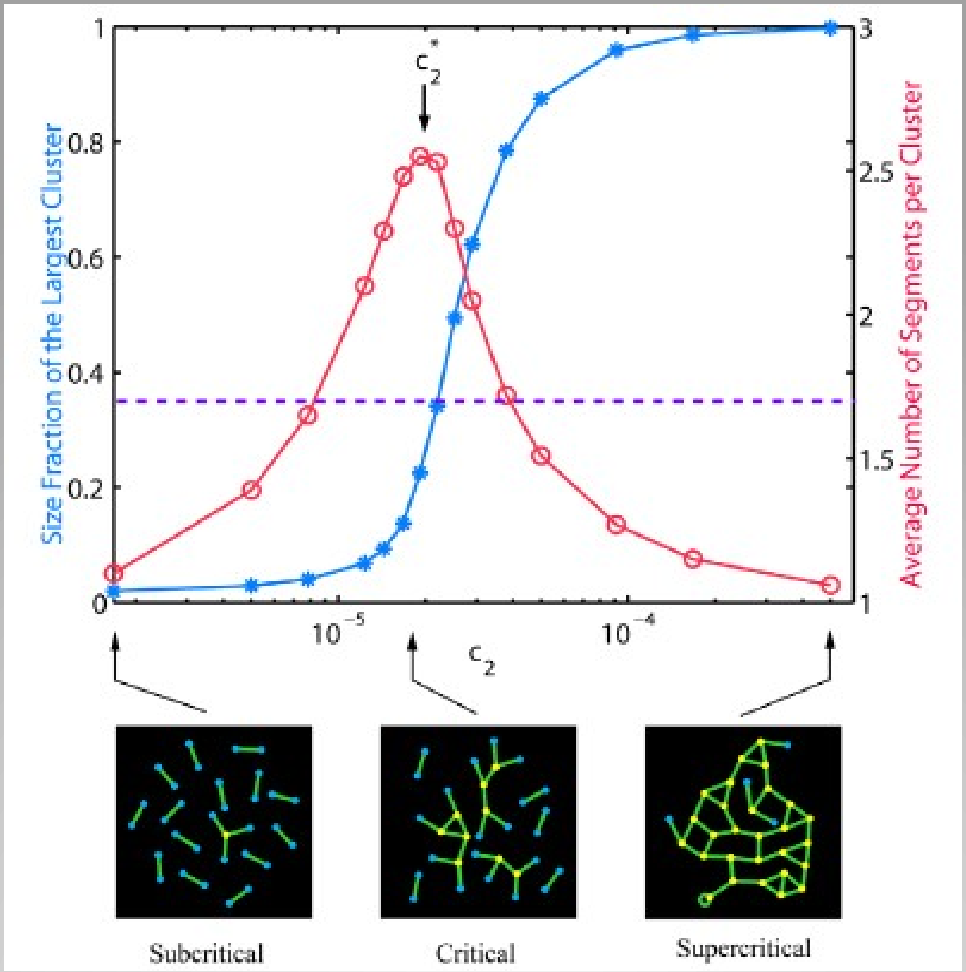
$b_2 = (3/2)b_1 \equiv (3/2)b$ $\quad$ $c_1 \equiv a_1/b$ and $c_2 \equiv a_2/b$

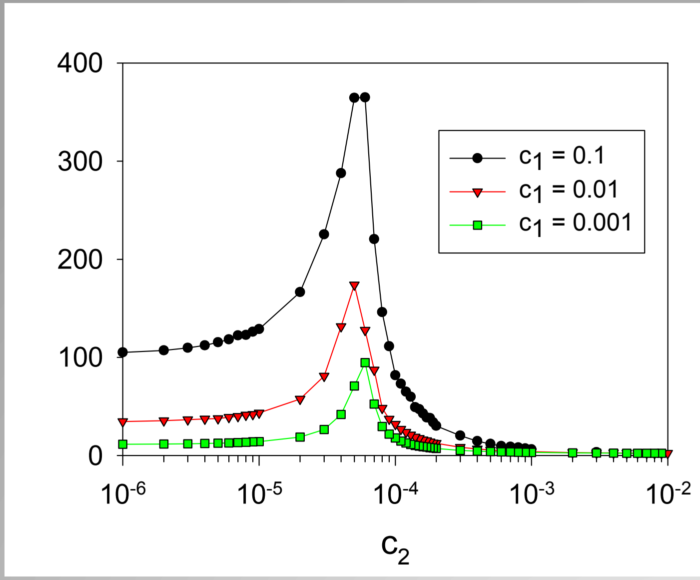
Dynamics: Gillespie algorithm with N_e dimers

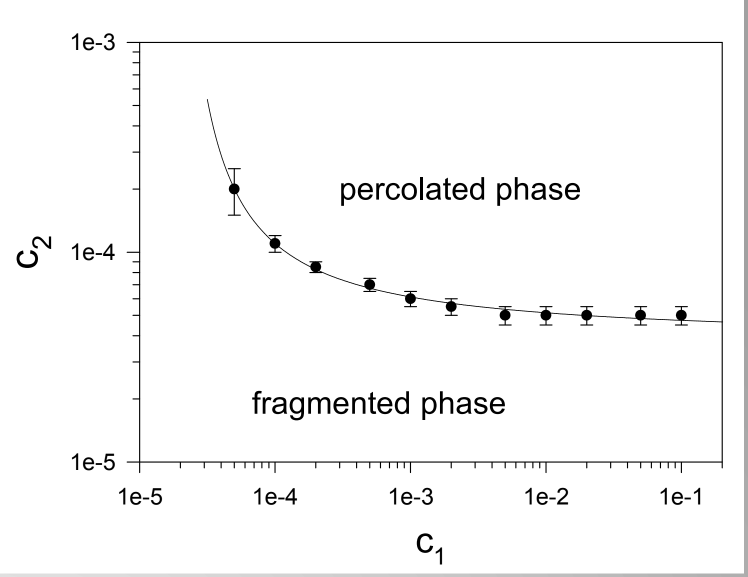


$c_1 = 0.1$ - $N_e = 3 \times 10^4$

PHASE DIAGRAM

$N_e = 15000$





$$\langle s \rangle = \frac{\sum_s' N_s s^2}{\sum_s' N_s s}$$

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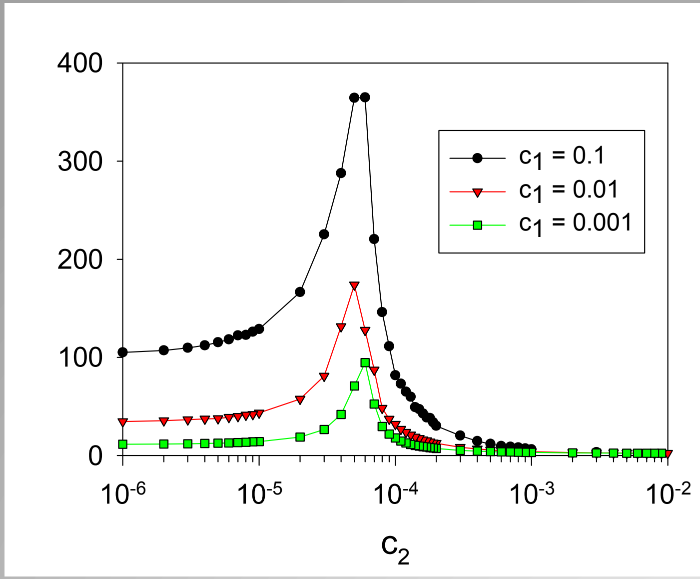
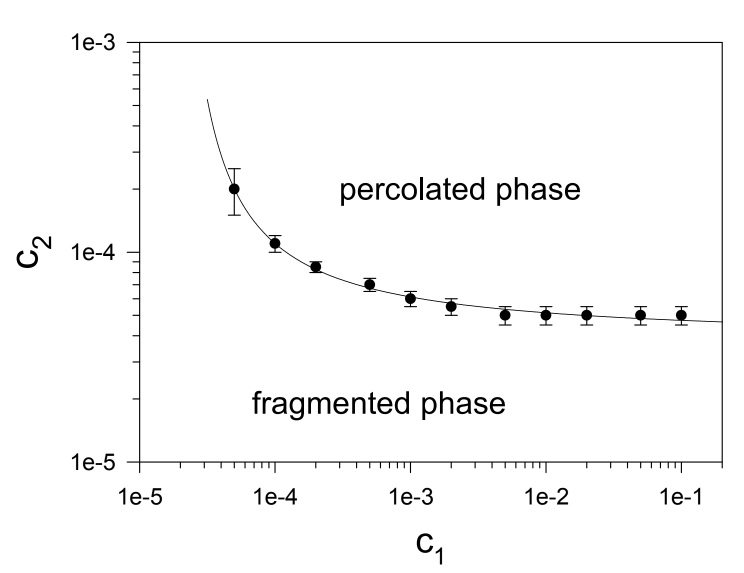


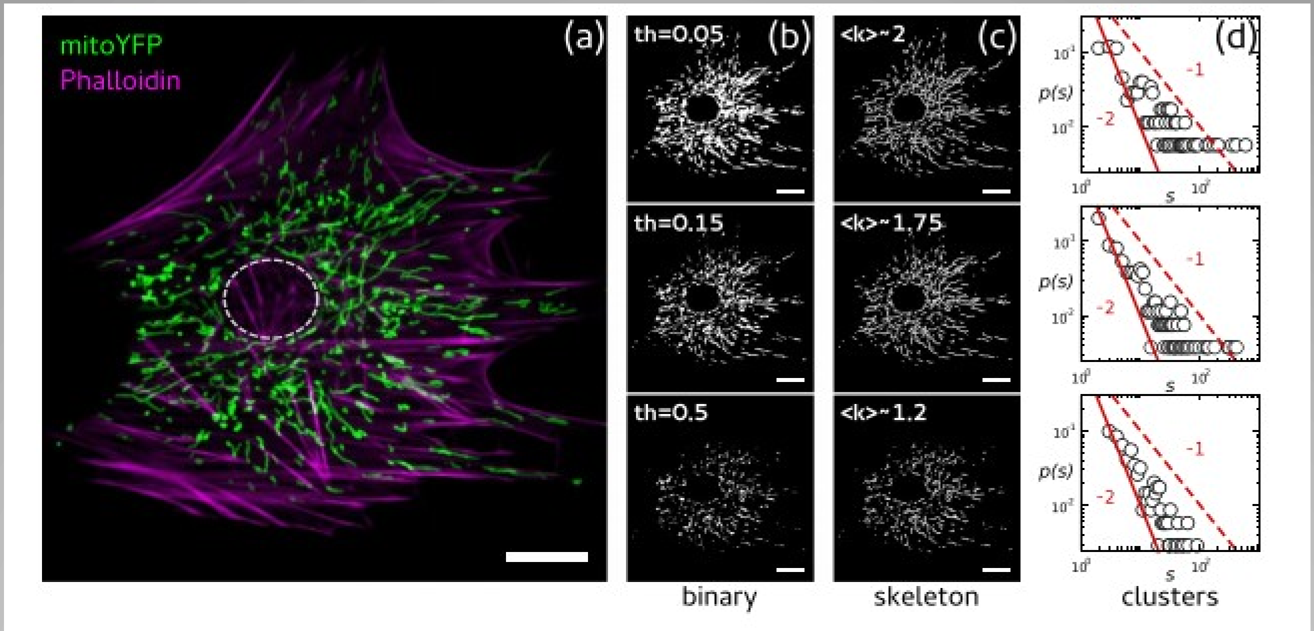


$$\langle s \rangle = \frac{\sum_s' N_s s^2}{\sum_s' N_s s}$$

In which part of this phase diagram might real mitochondria be located?

EXPERIMENTS

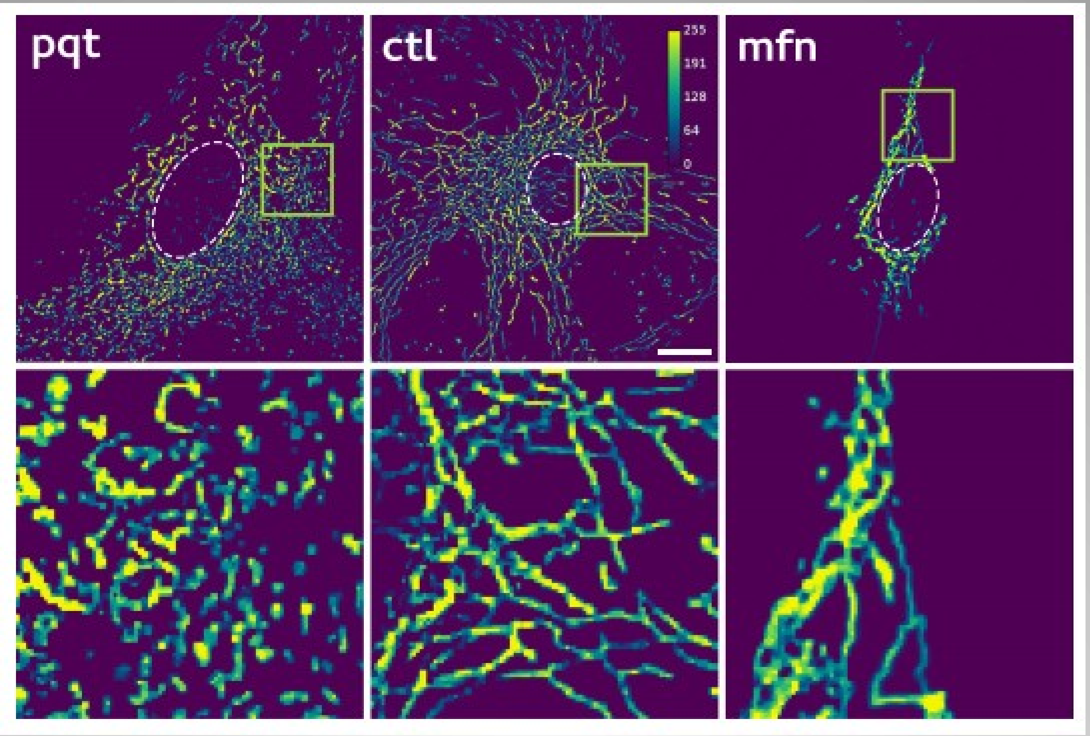
- **Imaging using confocal microscopy on genetically modified cells: mouse embryonic fribroblasts**



N. Zamponi, E. Zamponi, S.A. Cannas, O.V. Billoni, P. Helguera, D. R. Chialvo, Scientific Reports **8**, 363 (2018)

Morphology manipulation: treatments

- **Paraquat (pqt): promotes fission**
- **Mitofusin (mfn): promotes fusion**



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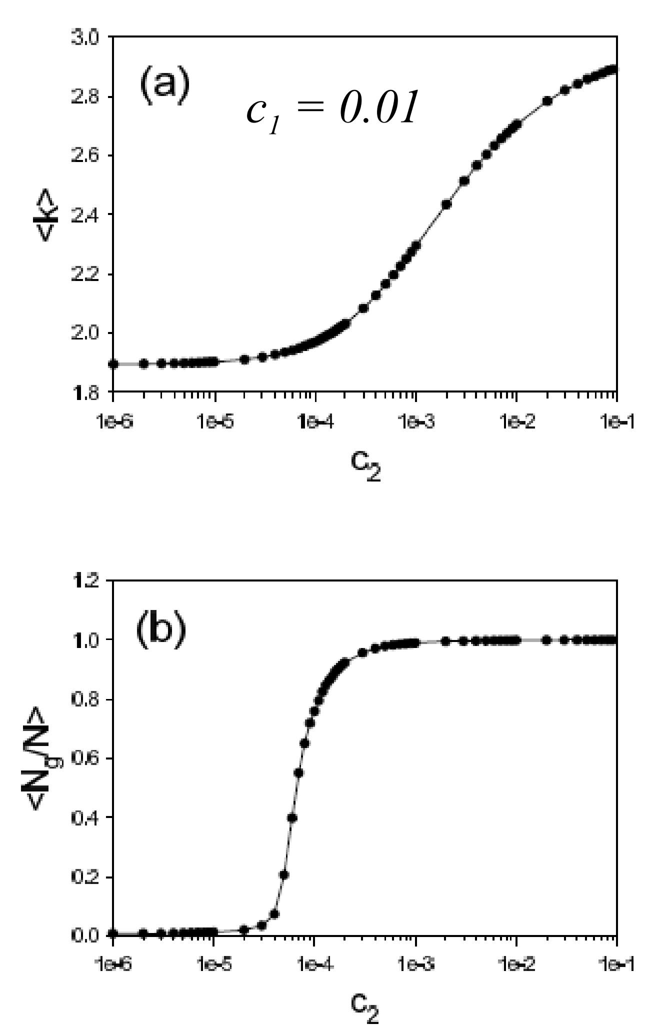
MEAN FIELD MODEL



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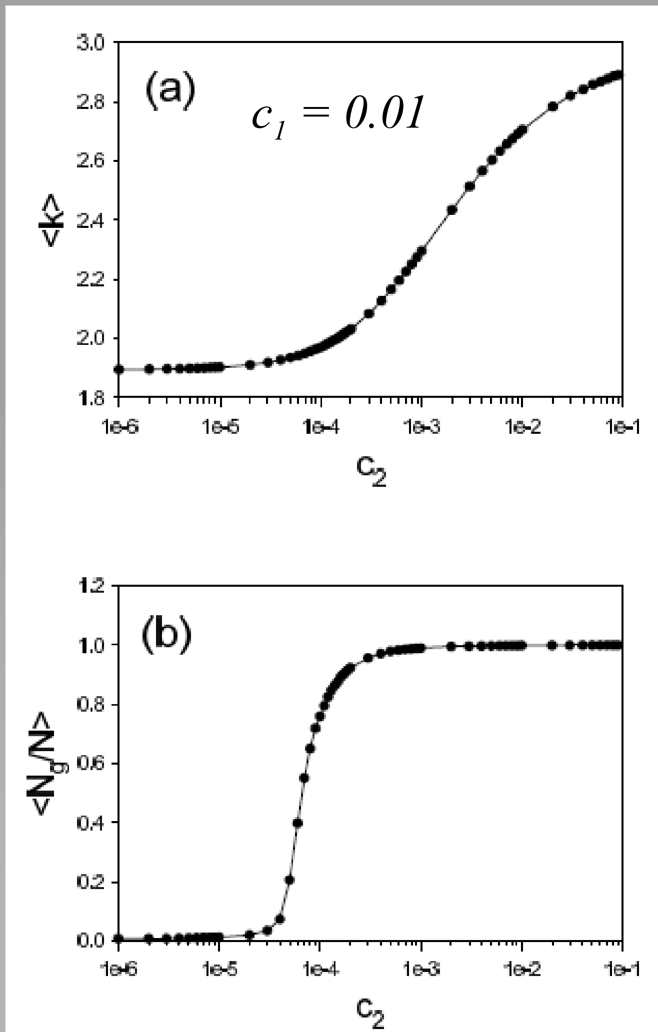
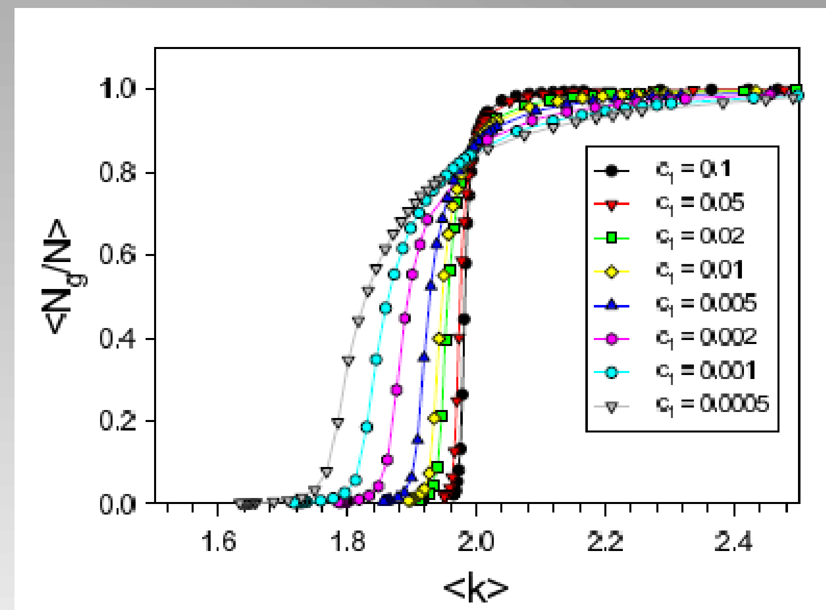
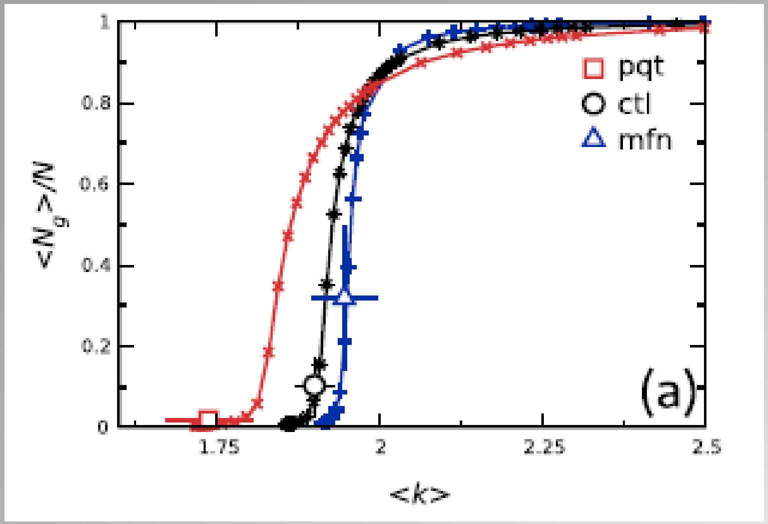
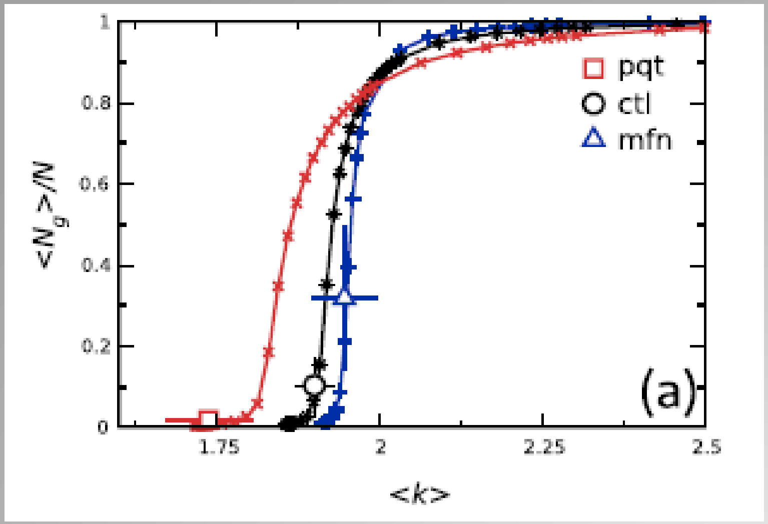
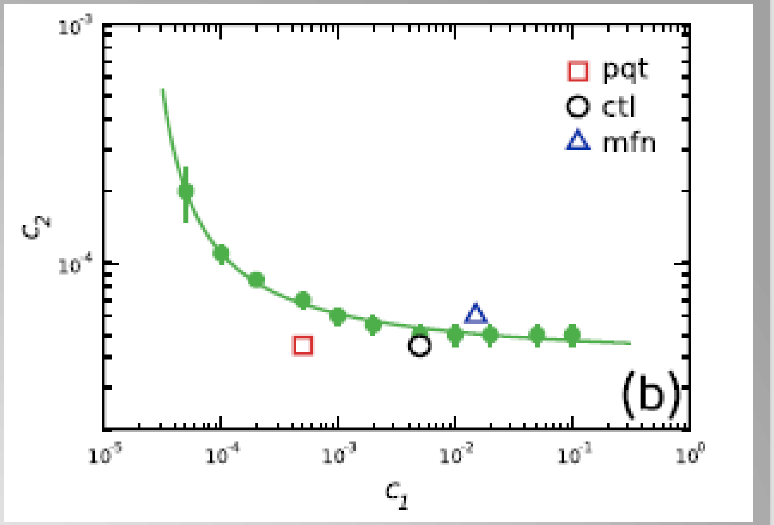






pqt
ctl
mfn
(a)
<N_g>/N
<k>
0
0.2
0.4
0.6
0.8
1
1.75
2
2.25
2.5





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QUESTIONS:

- Do the fusion/fission mechanism really generate criticality? Finite size scaling?

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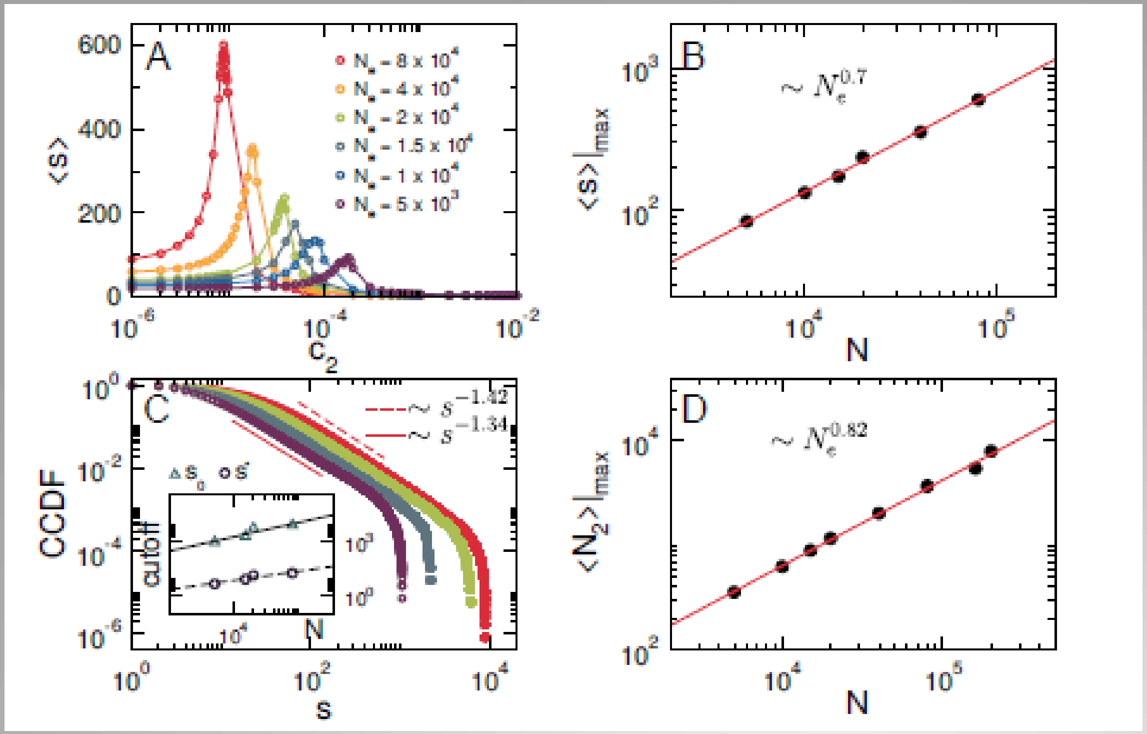
- Universality class?
- What happens in finite dimension?

Mean field model: finite size scaling

$c_1 = 0.01$



max $<s> \sim N^{\gamma/= d}$

max $<N_2> \sim N^{df/d}$

$n_s \sim s^{-\tau} exp(-s/s^*)$

$CCDF(s) = \Sigma_{s' \geq s}\, n_{s'}$

$CCDF \sim s^{-(\tau-1)} exp(-s/s^*)$

N. Zamponi, E. Zamponi, S.A. Cannas, D. R. Chialvo, Scientific Reports **12**, 17074 (2022)

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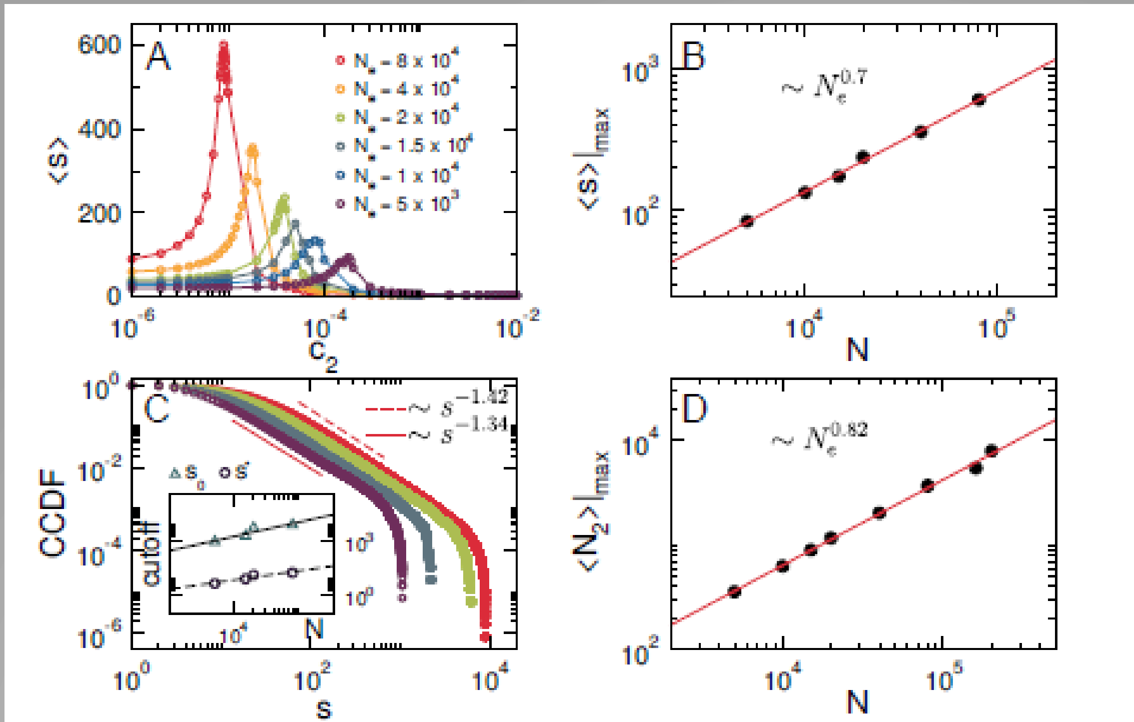

max $<s> \sim N^{\gamma/\nu d}$

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$n_s \sim s^{-\tau} \exp(-s/s^*)$

$\mathrm{CCDF}(s) = \Sigma_{s' \geq s}\, n_{s'}$

$CCDF \sim s^{-(\tau-1)} \exp(-s/s^*)$

$\tau = 2.38 \pm 0.04$ (MF standard perc.: 2.5)

$\gamma/\nu d = 0.70 \pm 0.01$ (MF standard perc.: 1/3)

$d_f/d = 0.82 \pm 0.01$ (MF standard perc.: 2/3)

$$CCDF(s) \approx 1 + \theta(s - s_0) s^{-\tau+1}\, e^{-s/s^*}$$

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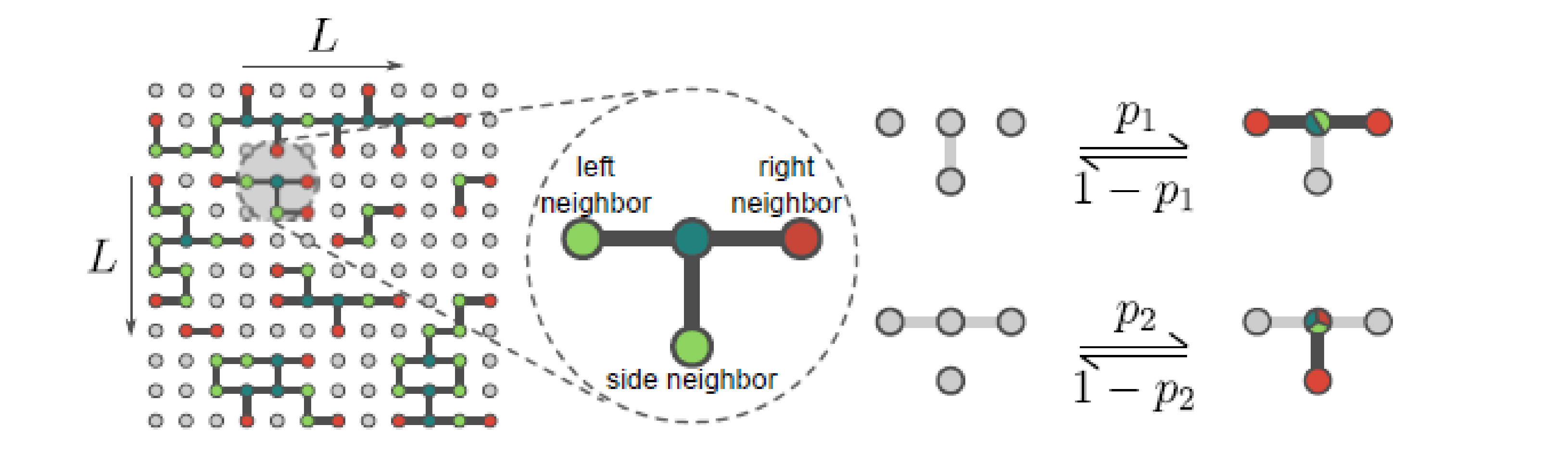
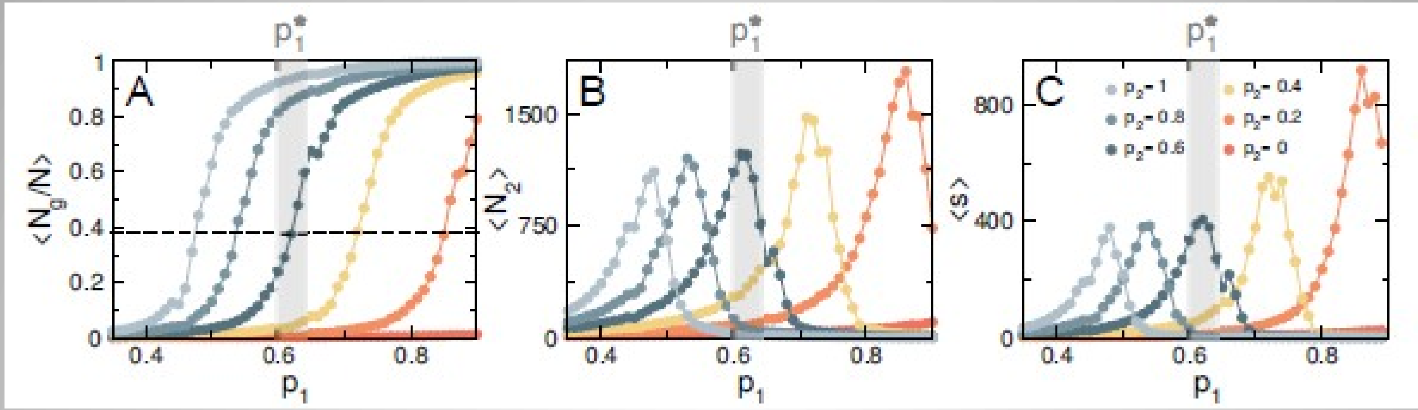
Spatially explicit model (2D)





N = 10^{4}

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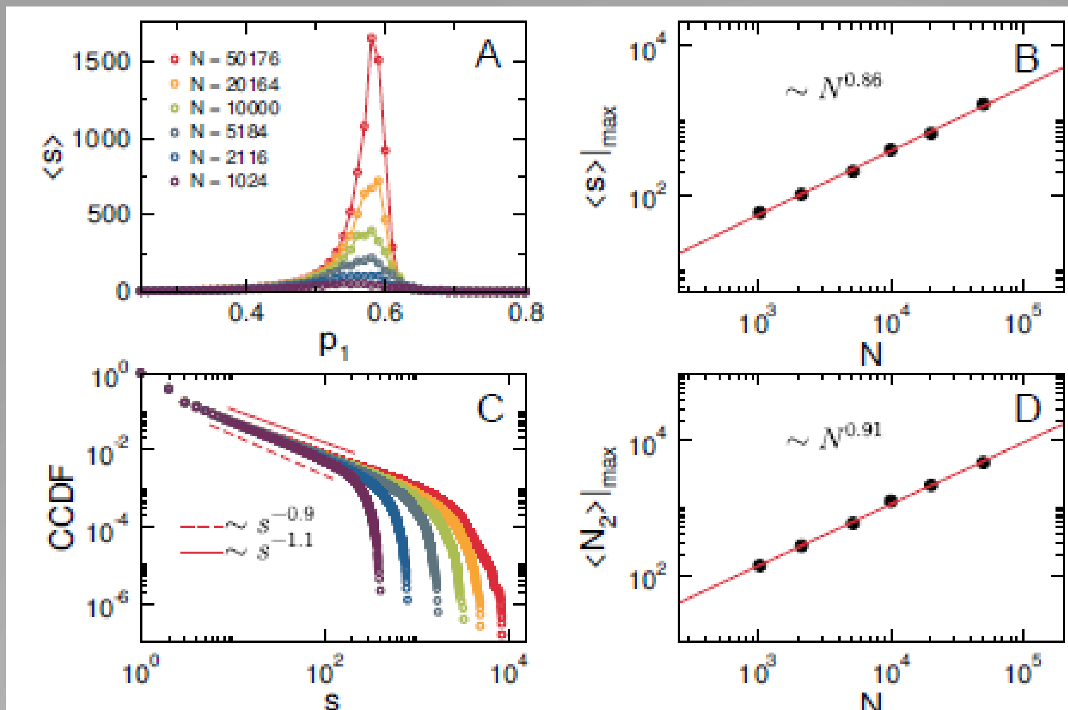
Spatially explicit model: finite size scaling

$p_2 = 0.7$



max $<s>$ ~ $N^{\gamma/= d}$

max $<N_2>$ ~ $N^{df/d}$

$n_s \sim s^{-\tau} \, exp(-s/s^*)$

$CCDF \sim s^{-(\tau-1)} \, exp(-s/s^*)$

$\tau = 2.0 \pm 0.1$ (2D standard perc.: 2.055)

$\gamma/\nu d = 0.86 \pm 0.02$ (2D standard perc.: 0.896)

$d_f/d = 0.91 \pm 0.02$ (2D standard perc.: 0.948)

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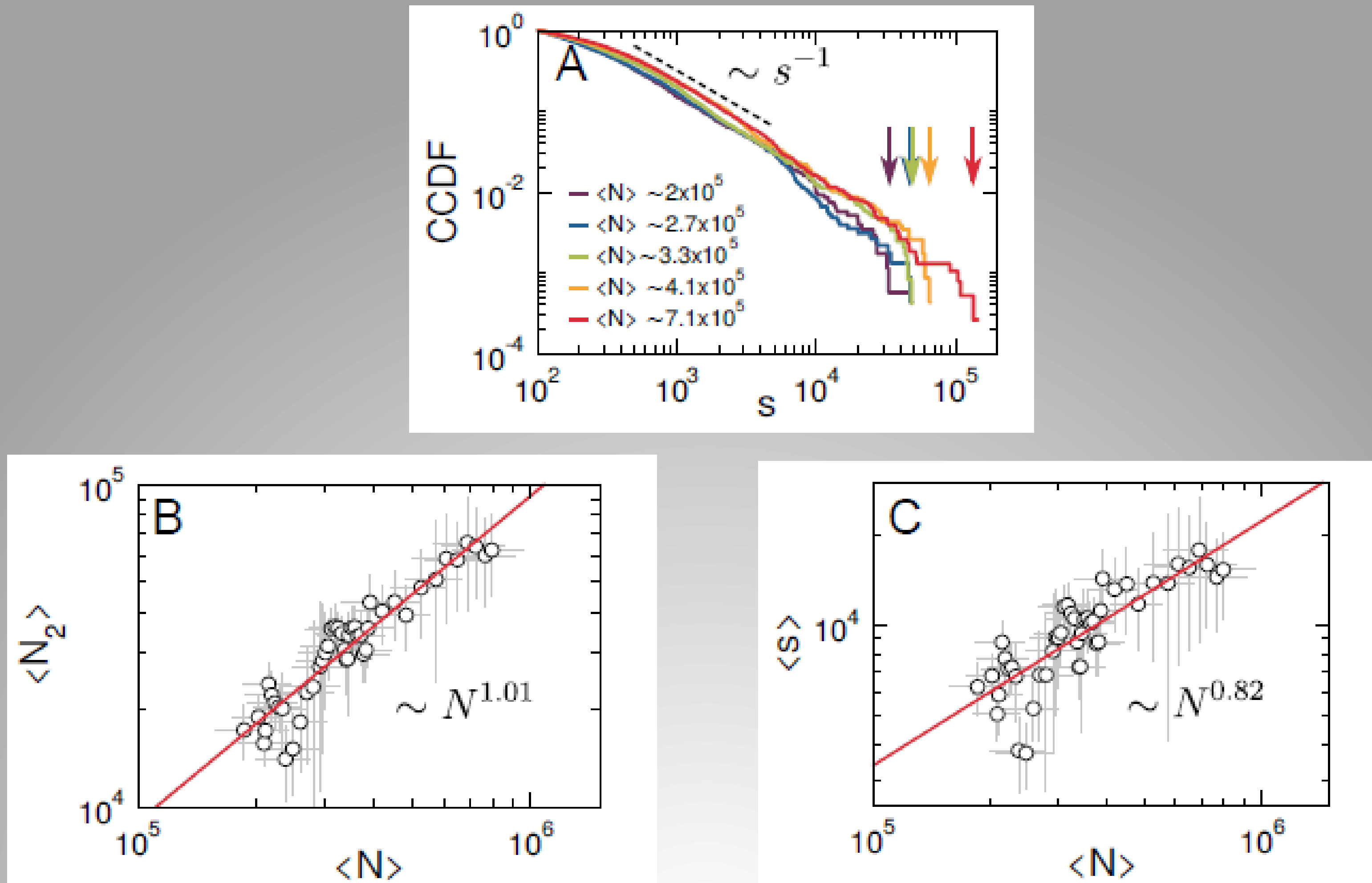
Real mitochondria: finite size scaling



N. Zamponi, E. Zamponi, S.A. Cannas, D. R. Chialvo, Scientific Reports **12**, 17074 (2022)

	τ	$\gamma/\nu d$	d_f/d
Mean field standard perc.	$5/2 = 2.5$	$1/3 \approx 0.33..$	$2/3 \approx 0.66..$
Mean field directed perc.	3	1/2	1/2
Mean field model	2.38 ± 0.04	0.7 ± 0.01	0.82 ± 0.01
3D standard perc.	2.15	0.67	0.84
2D standard perc.	$187/91 \approx 2.055$	$43/48 \approx 0.896$	$91/96 \approx 0.948$
2D directed perc.	≈ 2.66	≈ 1.07	≈ 0.60
2D model	2.0 ± 0.1	0.86 ± 0.02	0.91 ± 0.02
Experiments	2.01 ± 0.01	0.82 ± 0.08	1.01 ± 0.06

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Conclusions

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- Moving away from criticality leads mitochondria (and therefore the cell) to a pathological state.
- Mitochondrial critical point belongs to the standard percolation universality class.

N. Zamponi, E. Zamponi, S.A. Cannas, O.V. Billoni, P. Helguera, D. R. Chialvo, *Mitochondrial network complexity emerges from fission/fusion dynamics,* Scientific Reports **8**, 363 (2018)

N. Zamponi, E. Zamponi, S.A. Cannas, D. R. Chialvo, *Universal dynamics of mitochondrial networks: a finite-size scaling analysis,* Scientific Reports **12**, 17074 (2022)

Happy Birthday Constantino!