Collective Behavior of Cells: Learning from Planar Cell Polarity

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Himakar

Nirupam

Kamleswar

Collective Behavior of Cells: Learning from Planar Cell Polarity

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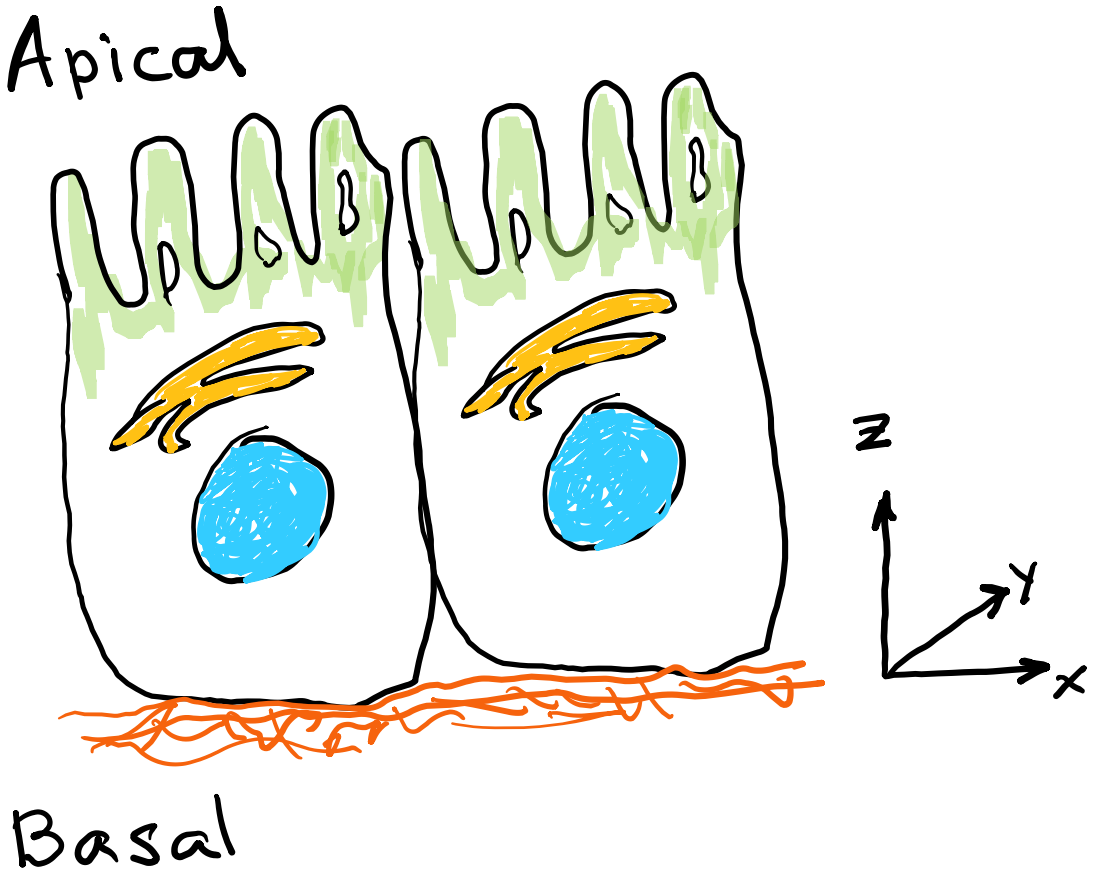
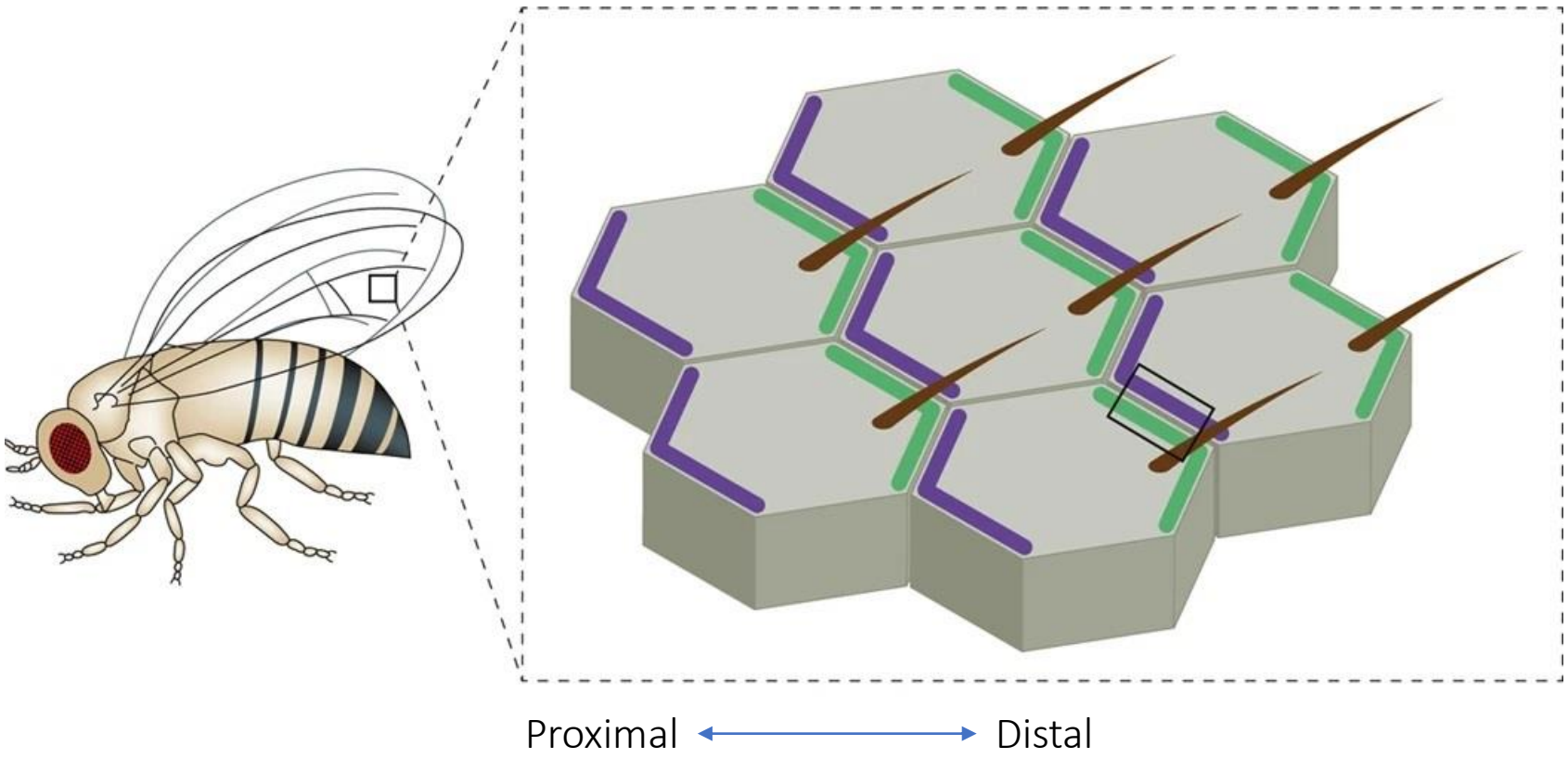
Polarity Of Epithelial Cells



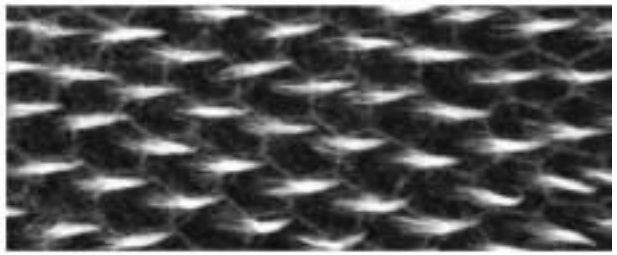
PCP: Coordinated polarization of thousands of epithelial cells along the plane orthogonal to apical-basal axis

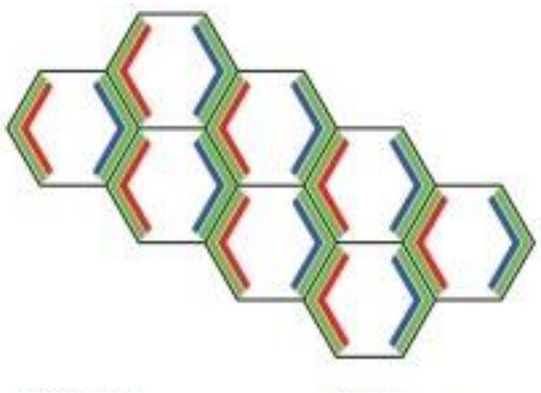
Compass In A Cell



PMID: 28293032

PCP In Fly Wing





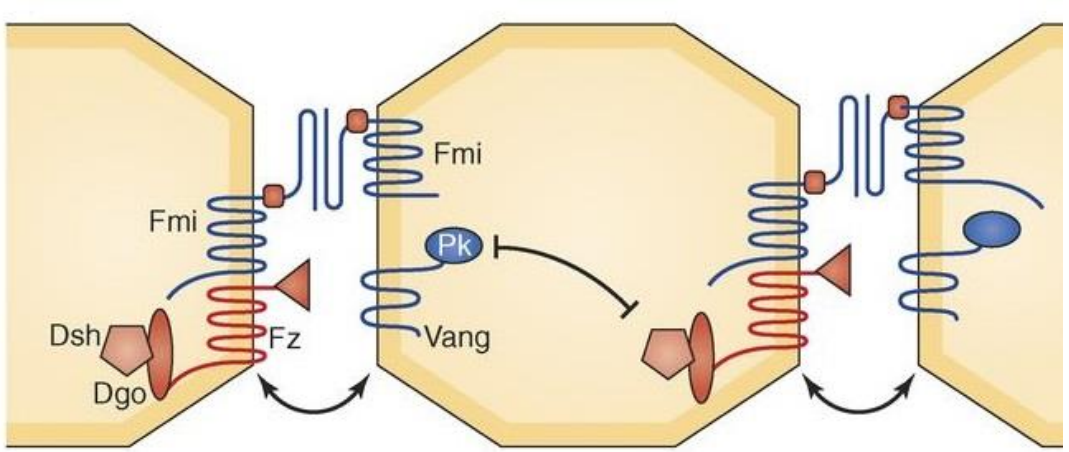
Proximal ⟷ Distal

Vang, Pk — Fz, Dsh, Dgo

PMID: 20066108

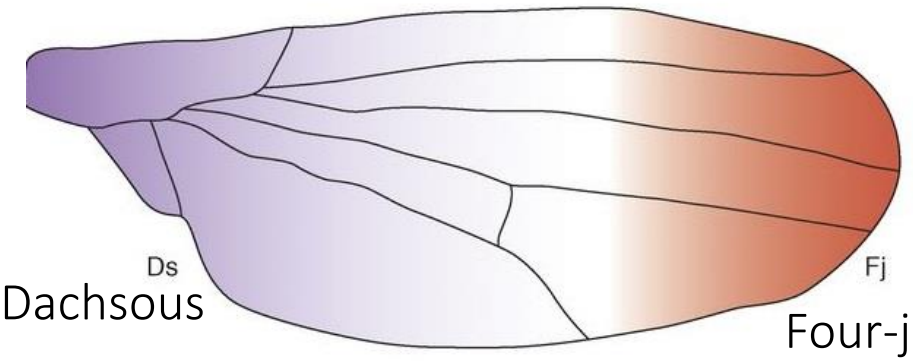
The Molecular Regulations Of PCP

Local



Proximal ⟷ Distal

Global



Proximal ⟷ Distal

PMID: 25349257

Mathematical Models

Mathematical Modeling of Pla
Cell Polarity to Understar
Domineering Nonautonomy

Keith Amonlirdviman,[1] Narmada A. Khare,[2] David R. P. Tree,[2]
Wei-Shen Chen,[2] Jeffrey D

Bulletin of Mathematical Biology (2010) 72: 645–680
DOI 10.1007/s11538-009-9464-0

ORIGINAL ARTICLE

Modelling and Analysis of Planar Cell Polarity

S. Schamberg*, P. Houston, N.A.M. Monk, M.R. Owen

Hazelwood and Hancock *BMC Developmental Biology* 2013, **13**:20
http://www.biomedcentral.com/1471-213X/13/20

BMC
Developmental B

RESEARCH ARTICLE

Open Access

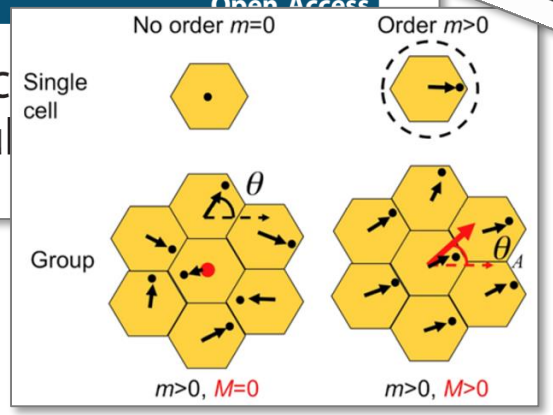
Functional modelling of planar c
approach for identifying molecul

Lee D Hazelwood[1*] and John M Hancock[2,3]

RESEARCH ARTICLE

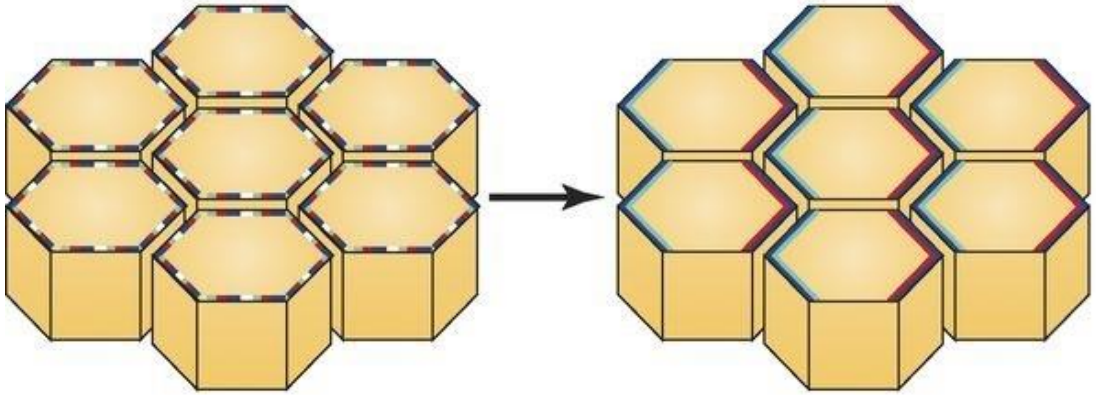
Establishment and Mai
Epithelial Cell Polarity by
Cadherin Bridges: A Computer Mo

Jean-François Le Garrec, Philippe Lopez, and Michel Kerszberg*



PMID: 20107923, 23672397, 15662015, 16258926

PCP As Phase Transition



Homogeneous/Disordered Non-Homogeneous/Ordered

Key Features:

It is a collective phenomenon.

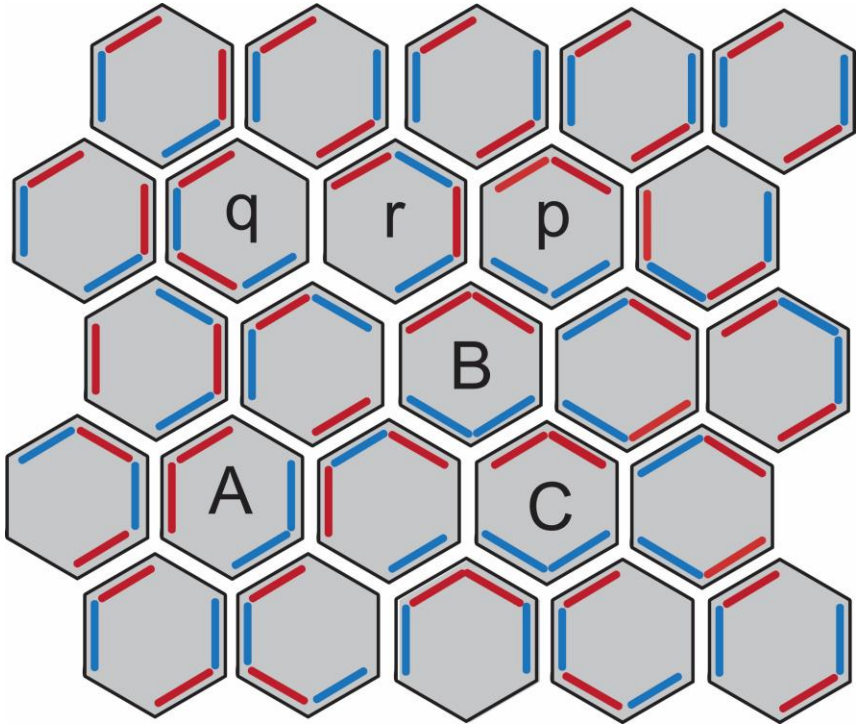
- involves both local and global interactions

It is *like* phase transition.

- possibly has critical threshold

PMID: 25349257

The PCP Model

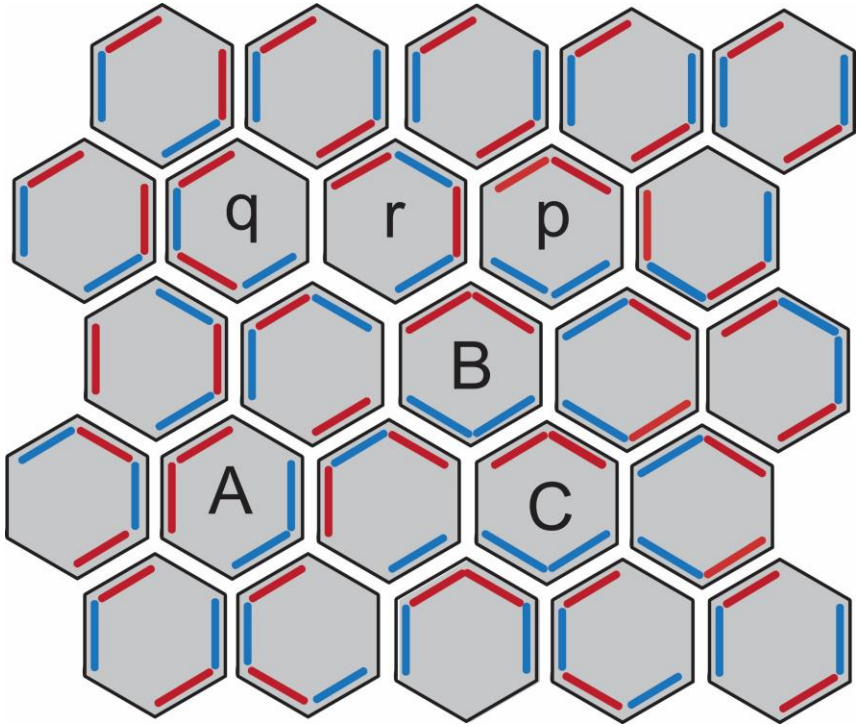


: Spin -1 = Protein complex 1

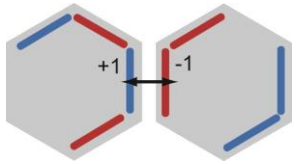
: Spin +1 = Protein complex 2

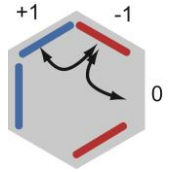
PhysRevE.100.032408

The PCP Model



$$h = m_1 \sum_{\substack{\text{all n} \\ \text{pairs}}} S_{\alpha,p} \times S_{\beta,q} + m_2 \sum_{\alpha=1}^{N} \sum_{\substack{all\ 6 \\ pairs}} S_{\alpha,a} \times S_{\alpha,b}$$

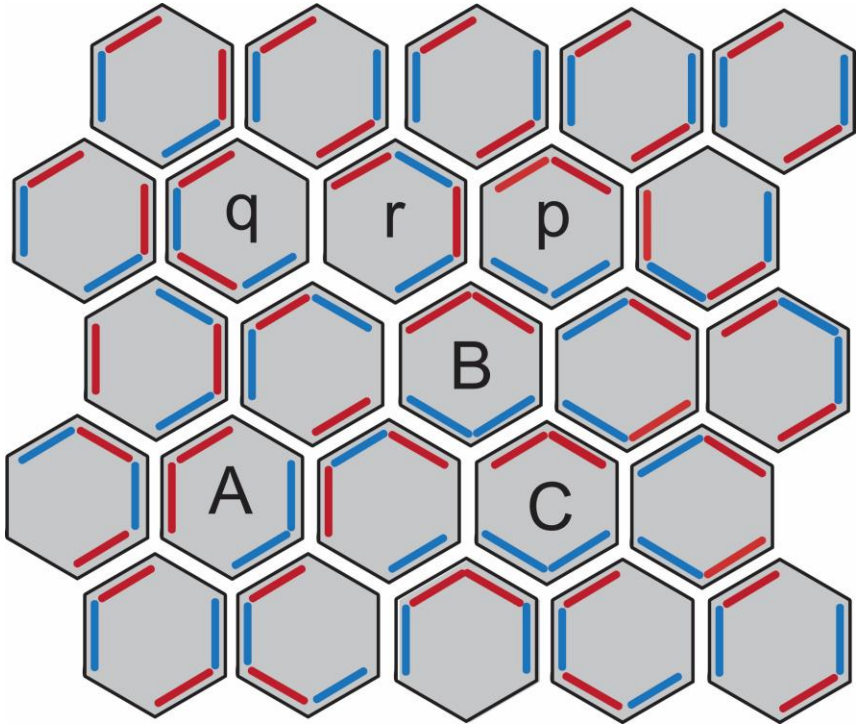




$$m_1 > 0 \quad m_2 < 0$$

PhysRevE.100.032408

The PCP Model



Randomly pick a cell

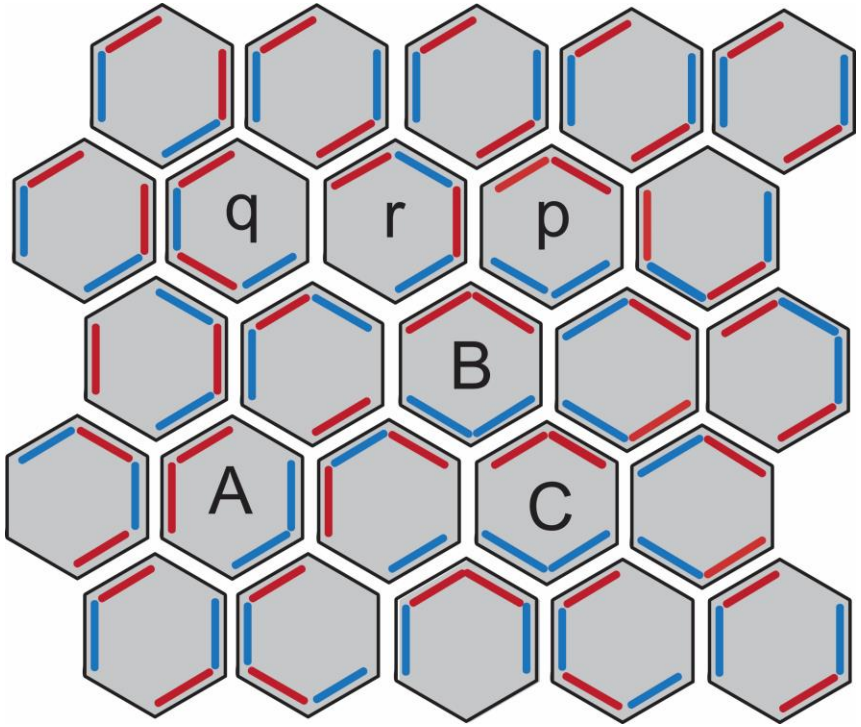
Randomly pick any two edges

Swap the spins

Calculate Δh

Accept the swap with $P = min(e^{-\Delta h}, 1)$

Aligned Cells & Clusters

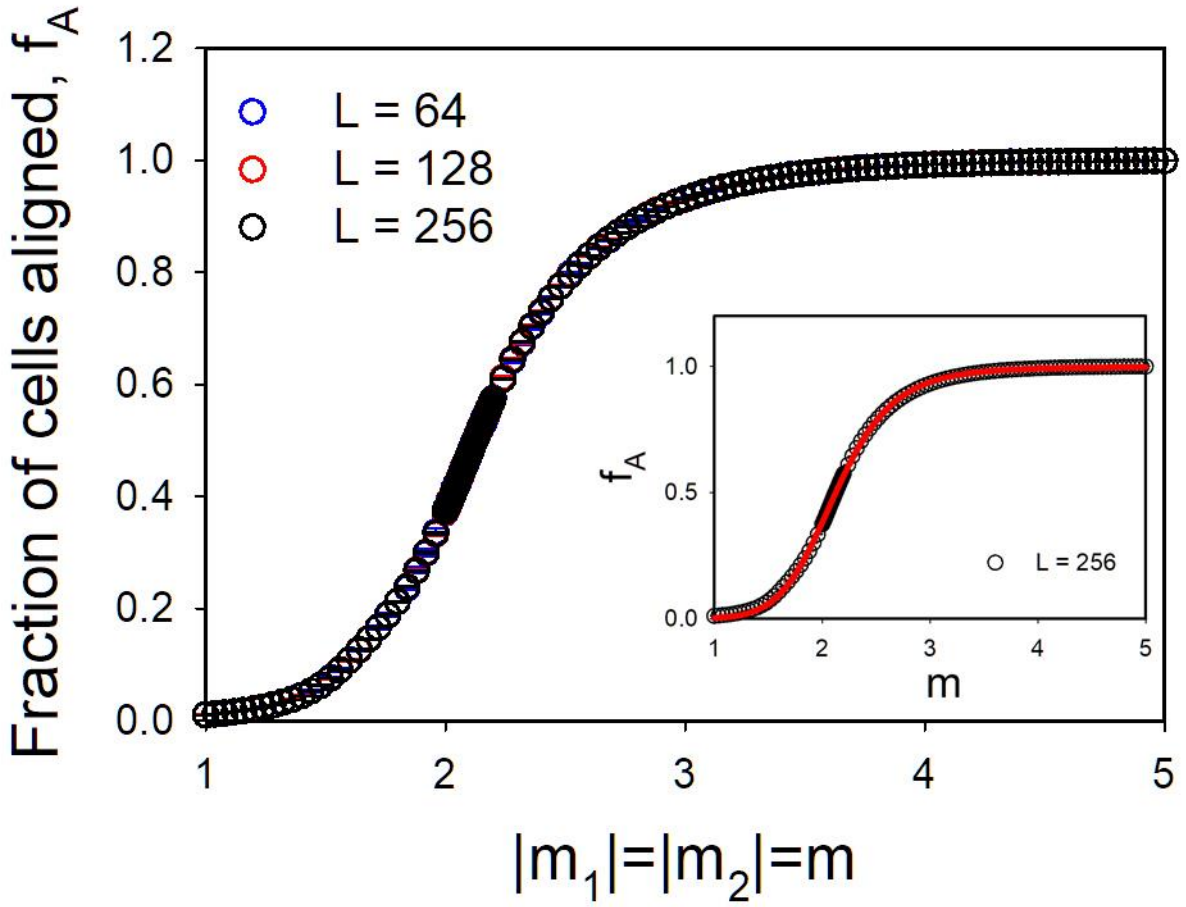


A, B & C: **Aligned** cells

A is a **Cluster** aligned cells of *s* =1

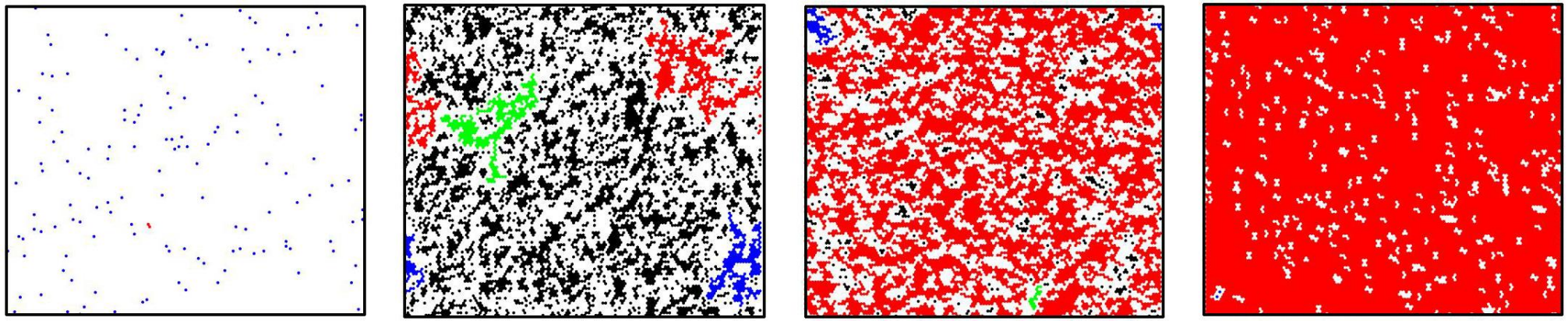
BC is a **Cluster** of *s* =2

Cooperativity in Alignment



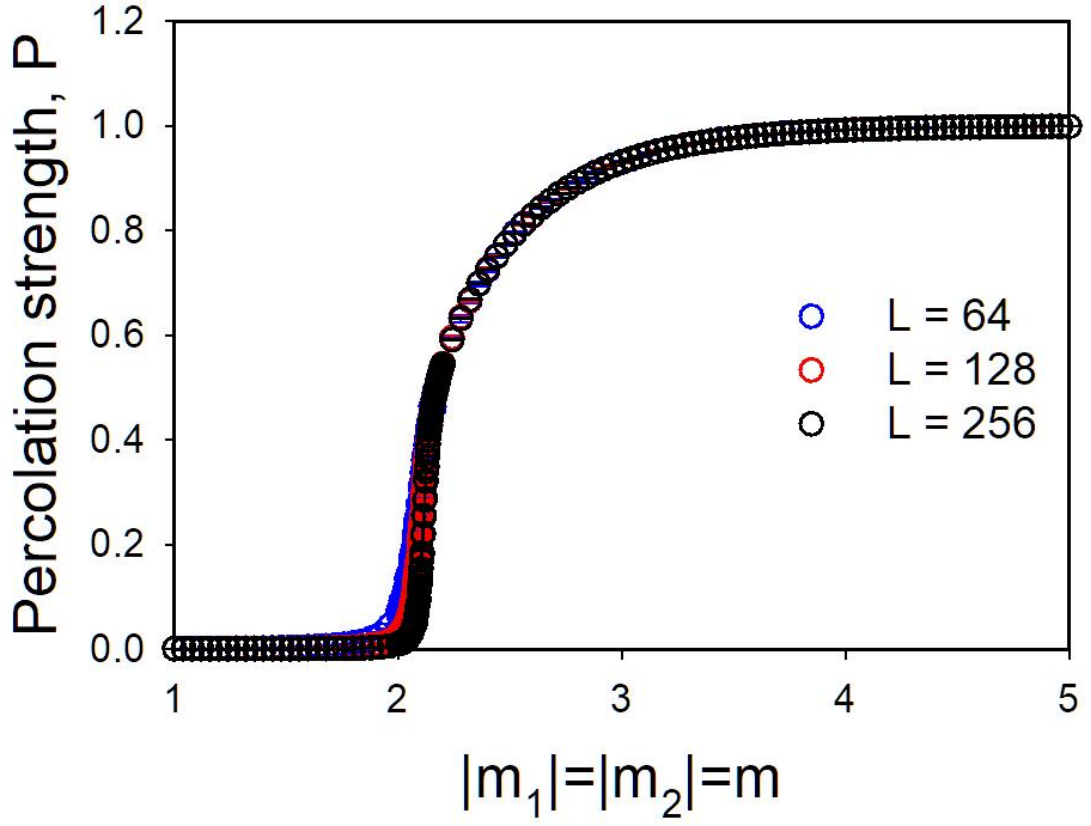
$$f_U = \frac{m^b}{c^b + m^b}$$

Emergence of Clusters of Aligned Cells



$|m_1|=|m_2| = 1$ $|m_1|=|m_2| = 2$ $|m_1|=|m_2| = 2.2$ $|m_1|=|m_2| = 3$

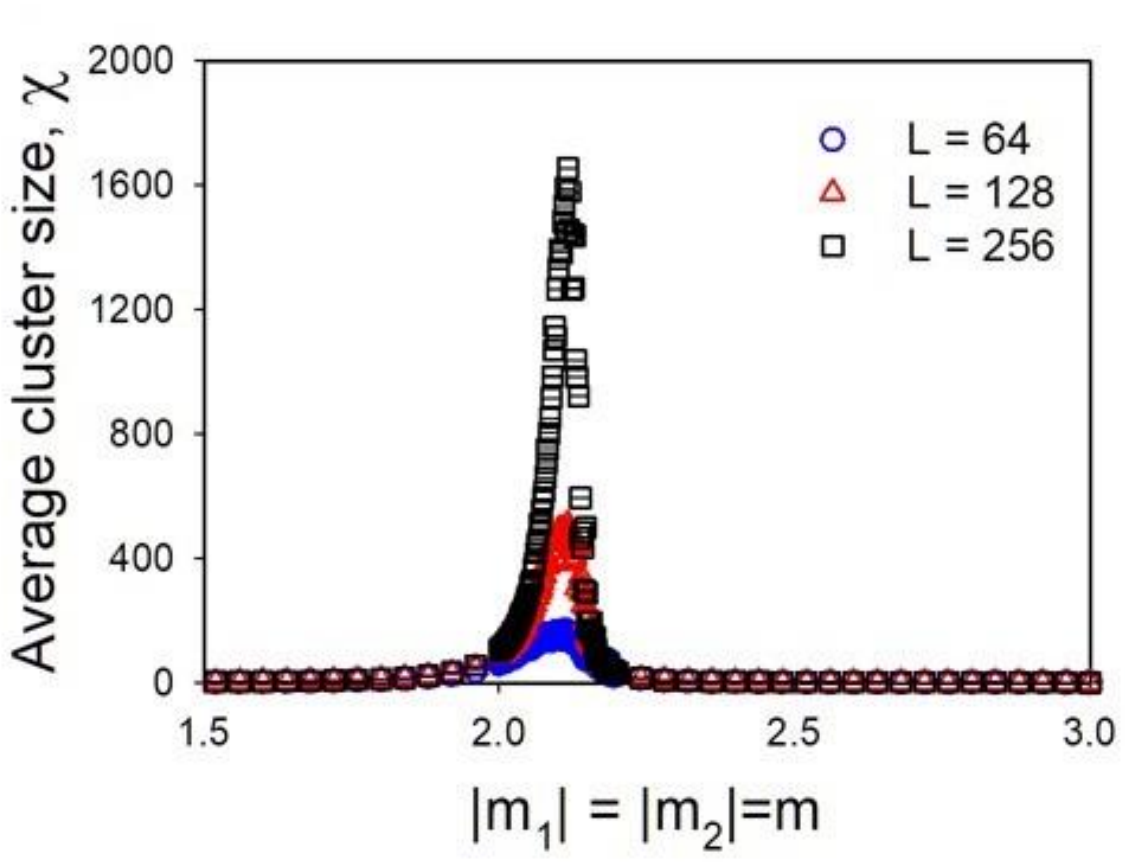
Percolation of Cell Clusters



$$P = \frac{C}{L \times L}$$

P: Relative size of the largest cluster

Percolation of Cell Clusters



$$\chi = \frac{\sum_s n_s . s^2}{\sum_s n_s . s}$$

χ: Avg. size of the other cluster

Universality: Getting Rid of the Clutter

Scaling in random percolation:

$$P \sim (p - p_c)^{\beta}$$

$$\chi \sim |p - p_c|^{-\gamma}$$

Finite-size scaling ansatz:

$$P = L^{-\beta/\nu} F[(p - p_c)L^{1/\nu}]$$

$$\chi = L^{\gamma/\nu} G[(p - p_c)L^{1/\nu}]$$

p: occupancy probability

Universality: Getting Rid of the Clutter

Finite-size scaling ansatz:

$$P = L^{-\beta/\nu} F[(p - p_c)L^{1/\nu}]$$

$$\chi = L^{\gamma/\nu} G[(p - p_c)L^{1/\nu}]$$

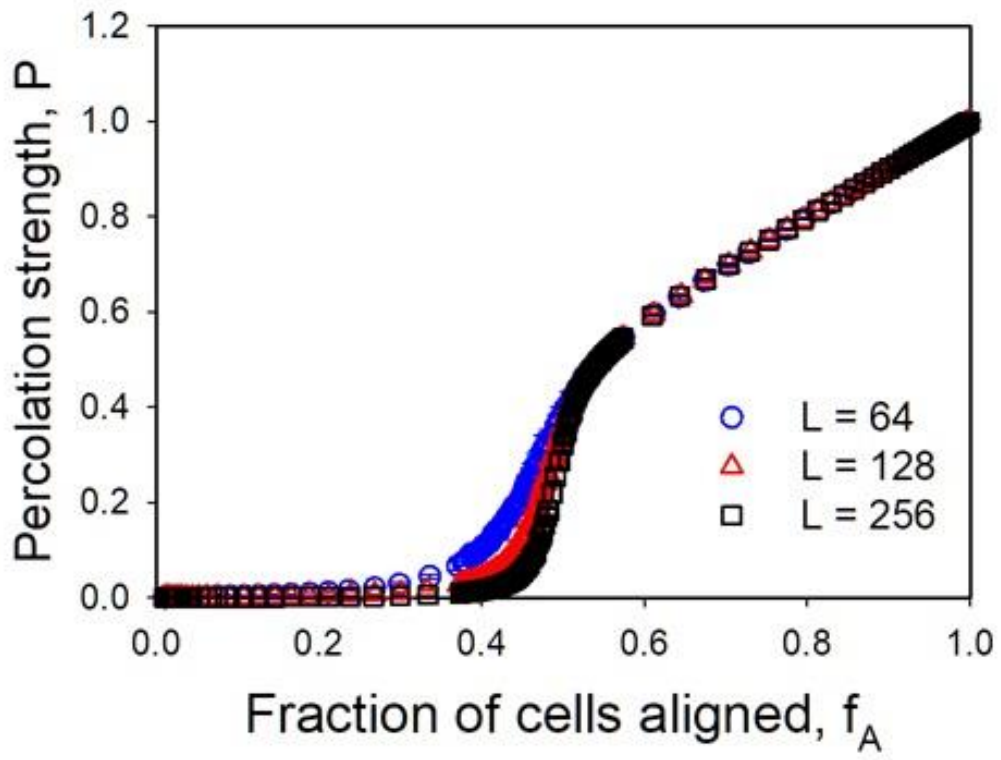
p: occupancy probability

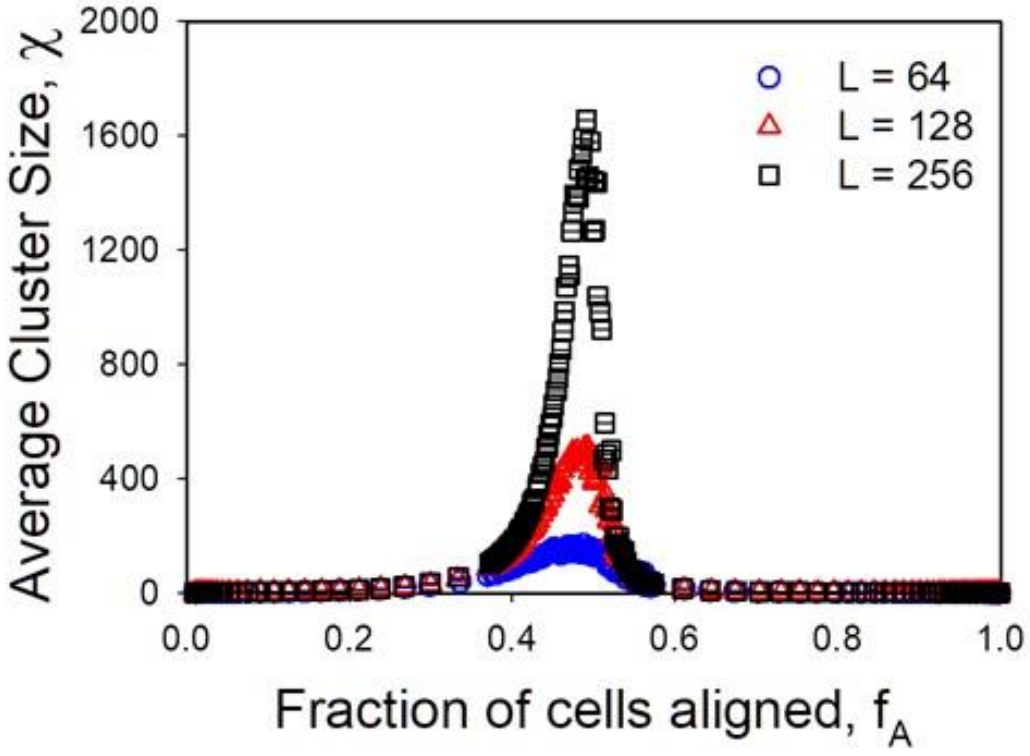
$$P = L^{-\beta/\nu} F[(f_A - f_{Ac})L^{1/\nu}]$$

$$\chi = L^{\gamma/\nu} G[(f_A - f_{Ac})L^{1/\nu}]$$

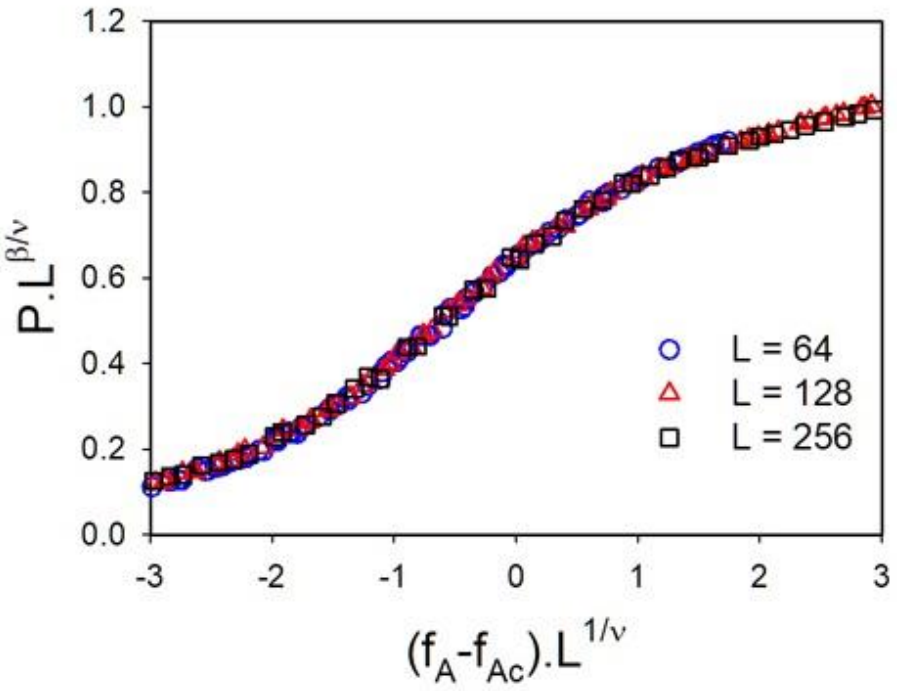
f_A: fraction of cells aligned

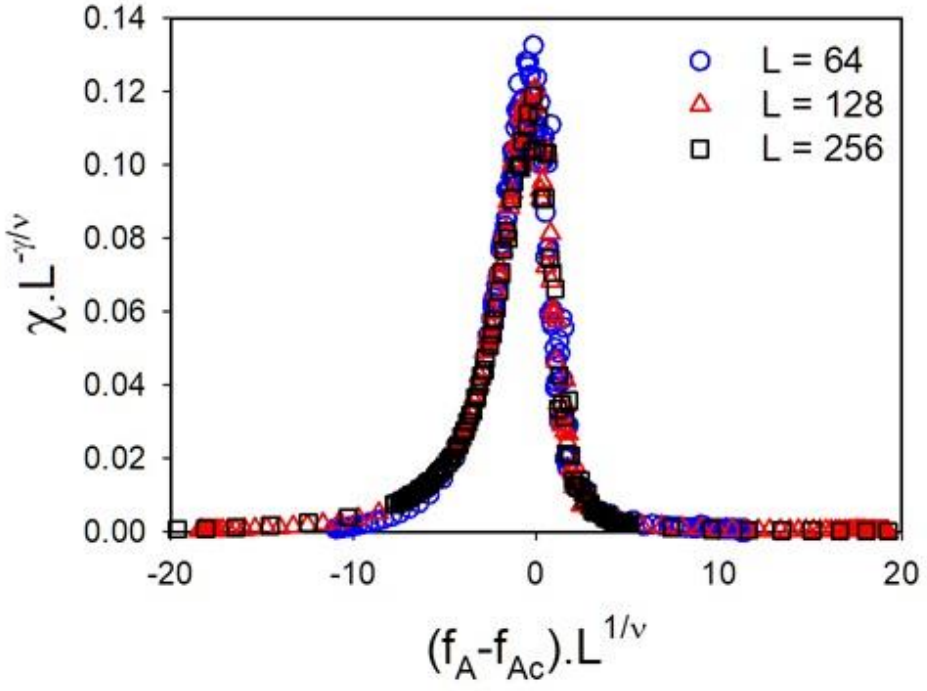
Behavior w.r.t f_A





PCP Model ≅ 2D Random Percolation



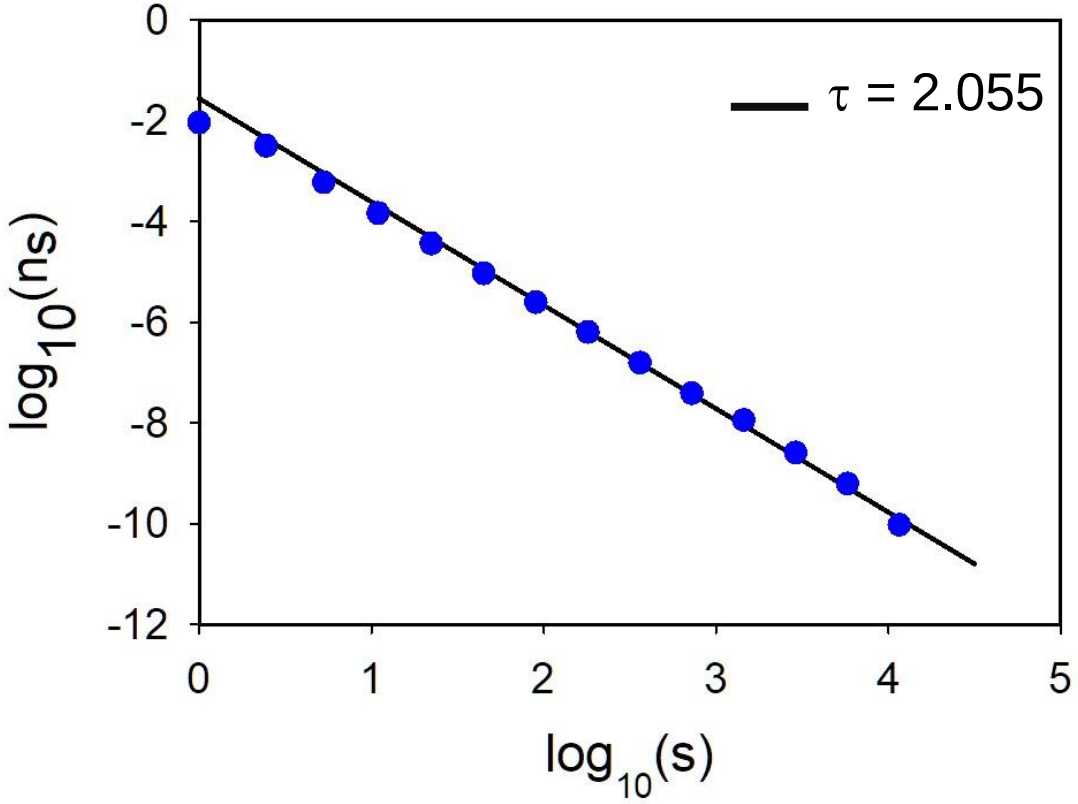


Critical index	PCP Model	2D Percolation
1/ν	0.75(8)	0.75
β/ν	0.125(15)	0.104
γ/ν	1.7208(5)	1.785

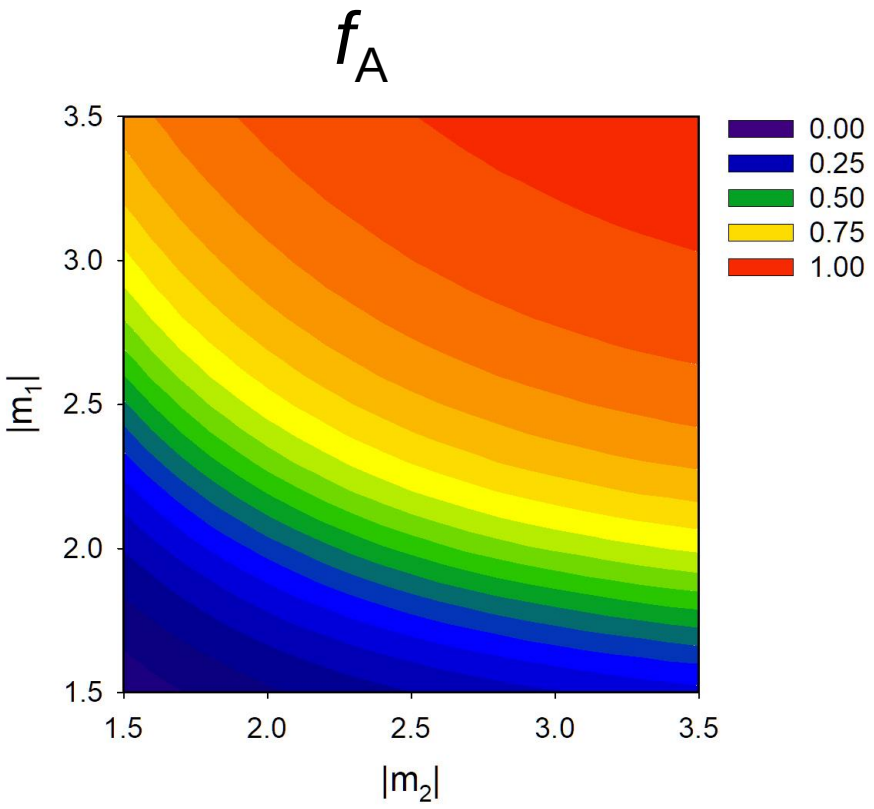
PhysRevE.100.032408

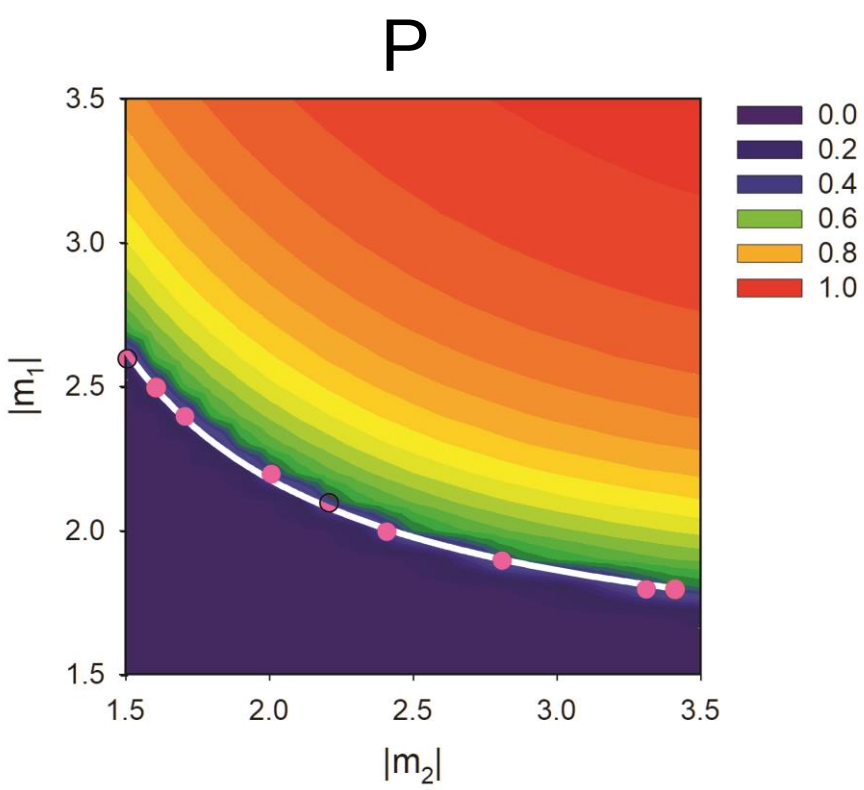
PCP Model ≅ 2D Random Percolation

$$n_s \sim s^{-\tau}$$



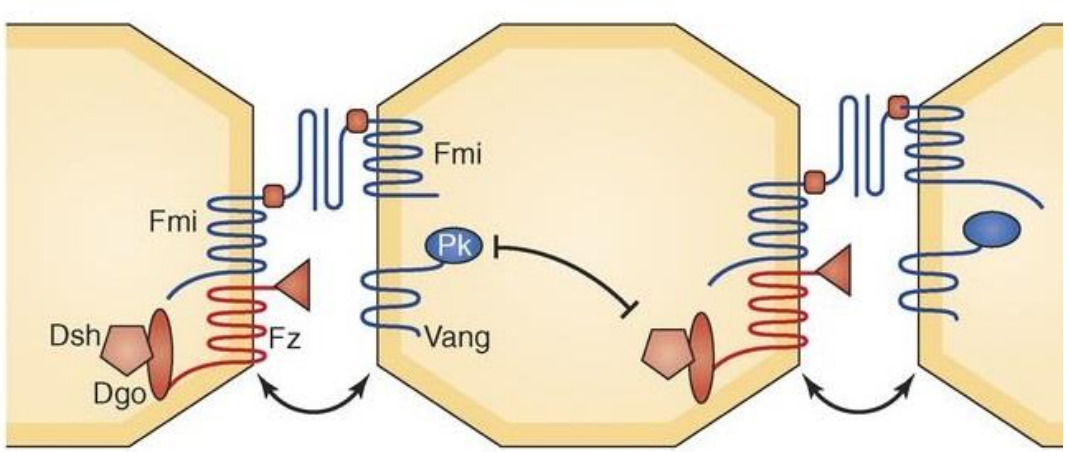
The Case of Unequal m_1, m_2





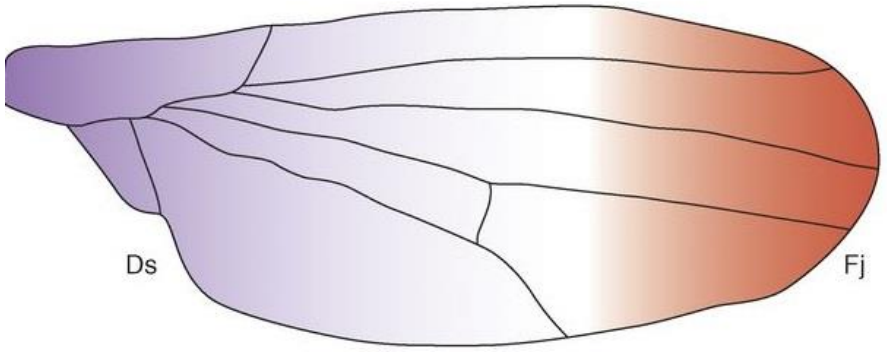
The Molecular Cues of PCP

Local



Proximal ⟷ Distal

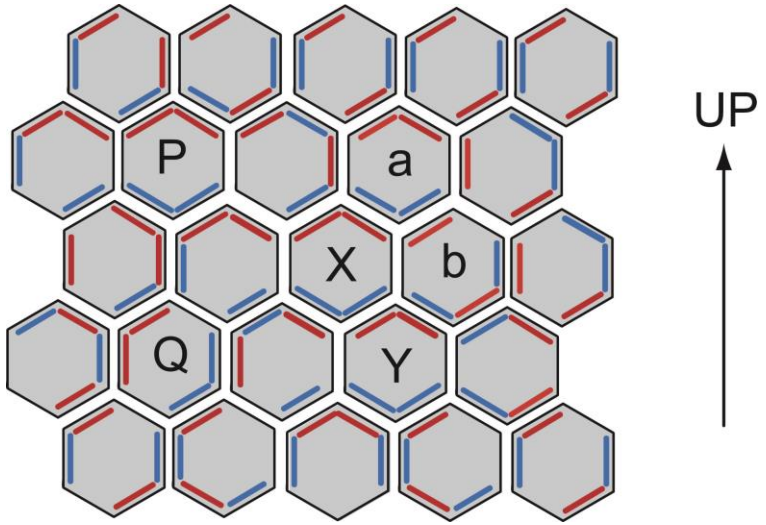
Global

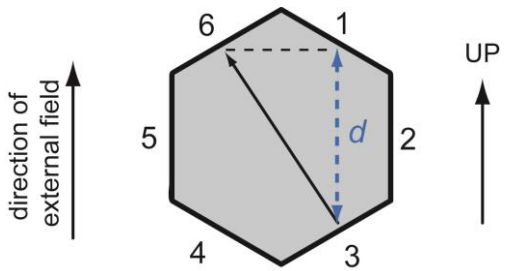


Proximal ⟷ Distal

PMID: 25349257

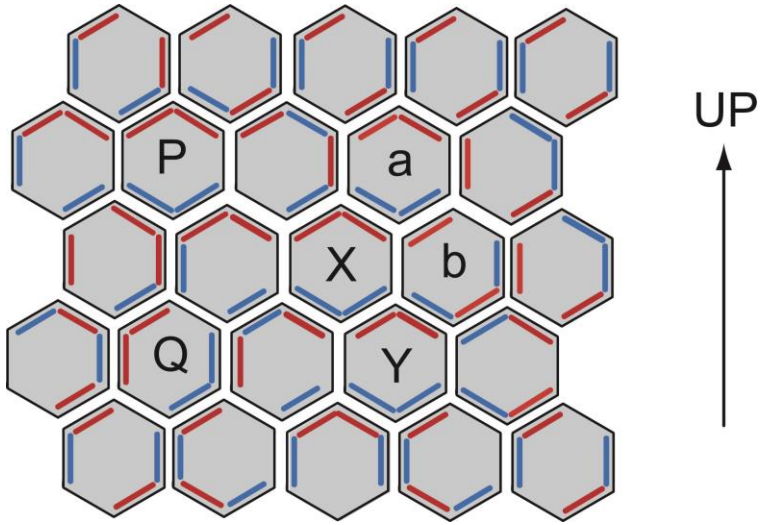
Directional model: External Field Specify Direction

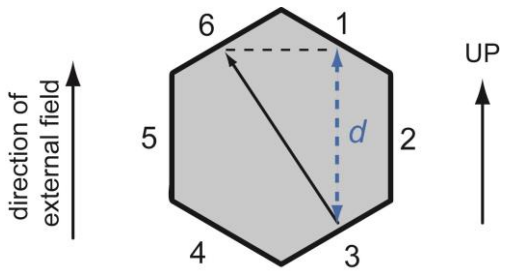




arXiv:2308.10508

Directional model: External Field Specify Direction





Cell-Cell & within cell interactions

$$h = m_1 \sum_{\substack{\text{all n} \\ \text{pairs}}} S_{\alpha,p} \times S_{\beta,q} + m_2 \sum_{\alpha=1}^{N} \sum_{\substack{all\ 6 \\ pairs}} S_{\alpha,a} \times S_{\alpha,b}$$

Interaction with external field

$$\Delta g = m_3 \left(d_a S_{\alpha,a} + d_b S_{\alpha,b} \right)$$

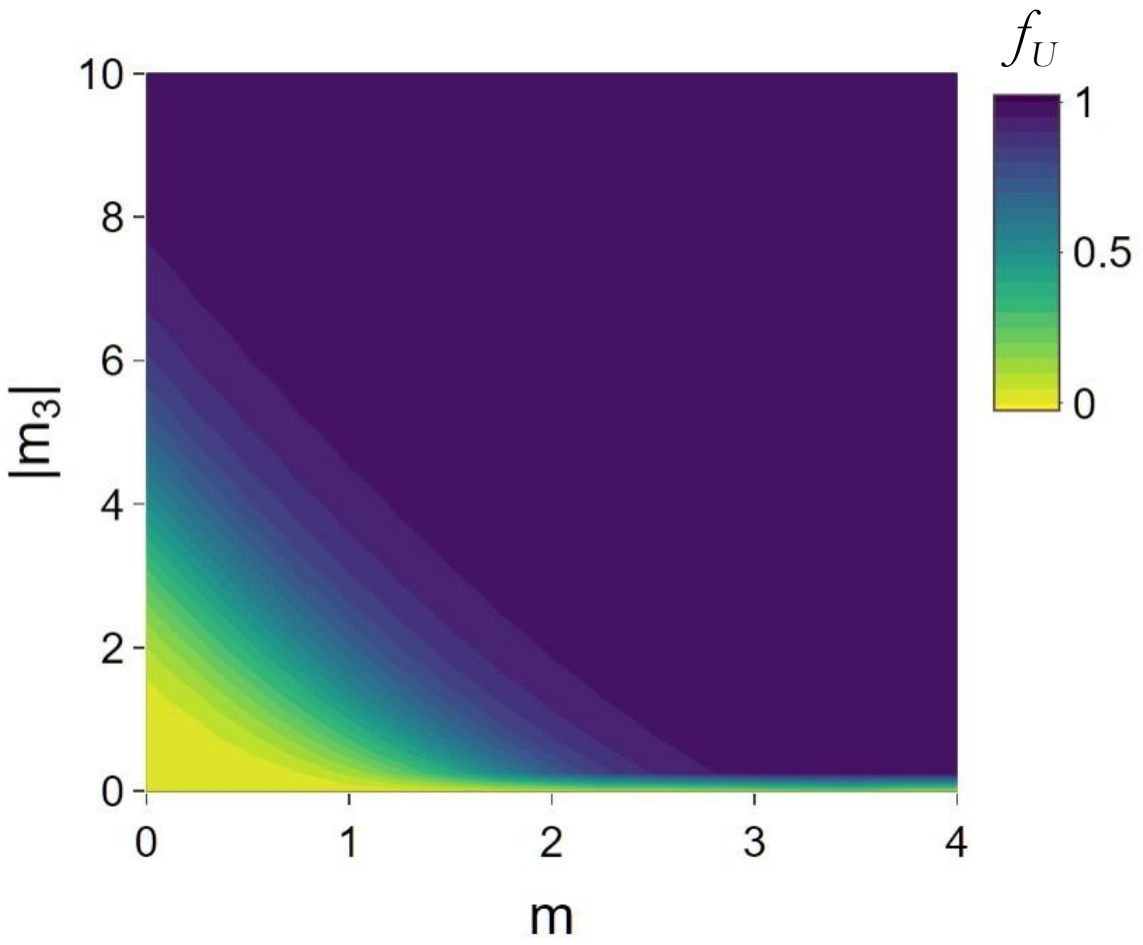
Total change in energy

$$\Delta \varepsilon = \Delta h + \Delta g$$

$$m_1 > 0 \qquad m_2, m_3 < 0 \qquad |d_a| = |d_b| = d$$

arXiv:2308.10508

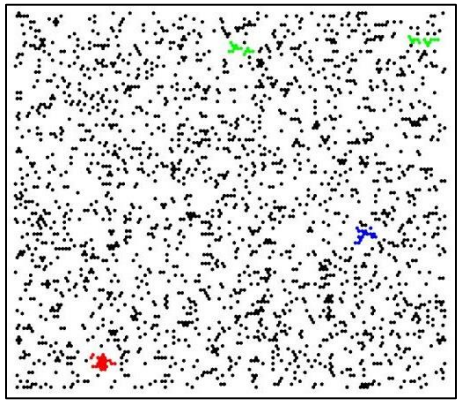
Alignment of Cells in Right Direction



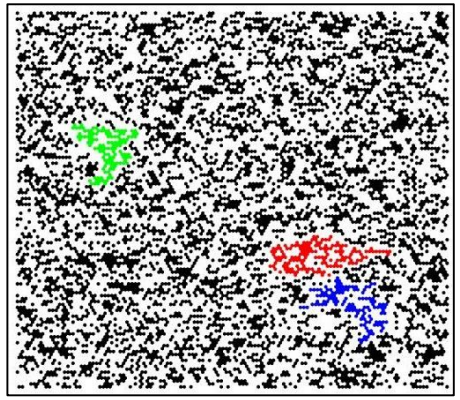
$|m_1| = |m_2| = m$

Emergence of Clusters of Aligned Cells

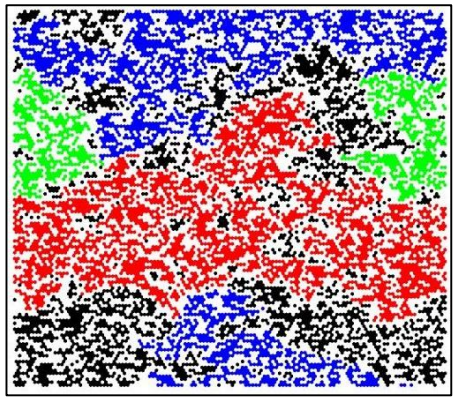
$|m_3| = 1$



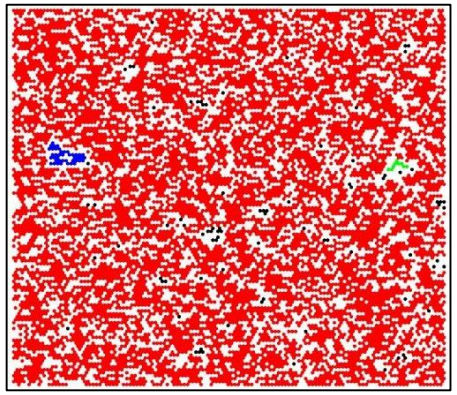
$|m_3| = 2$



$|m_3| = 2.5$

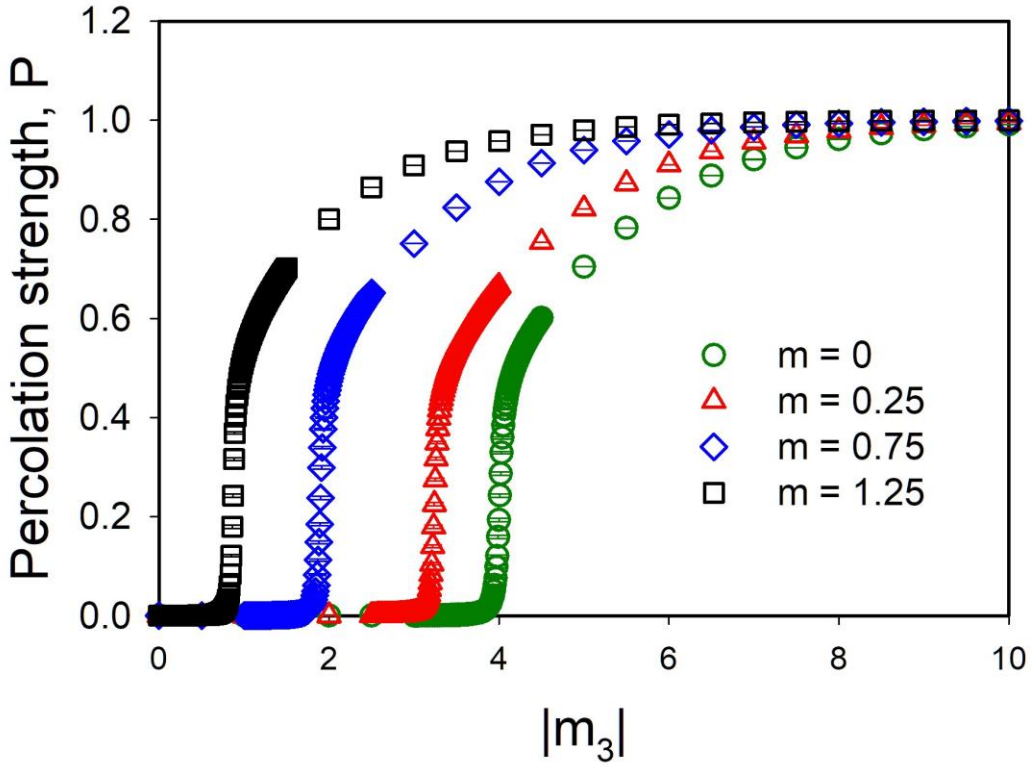


$|m_3| = 3$



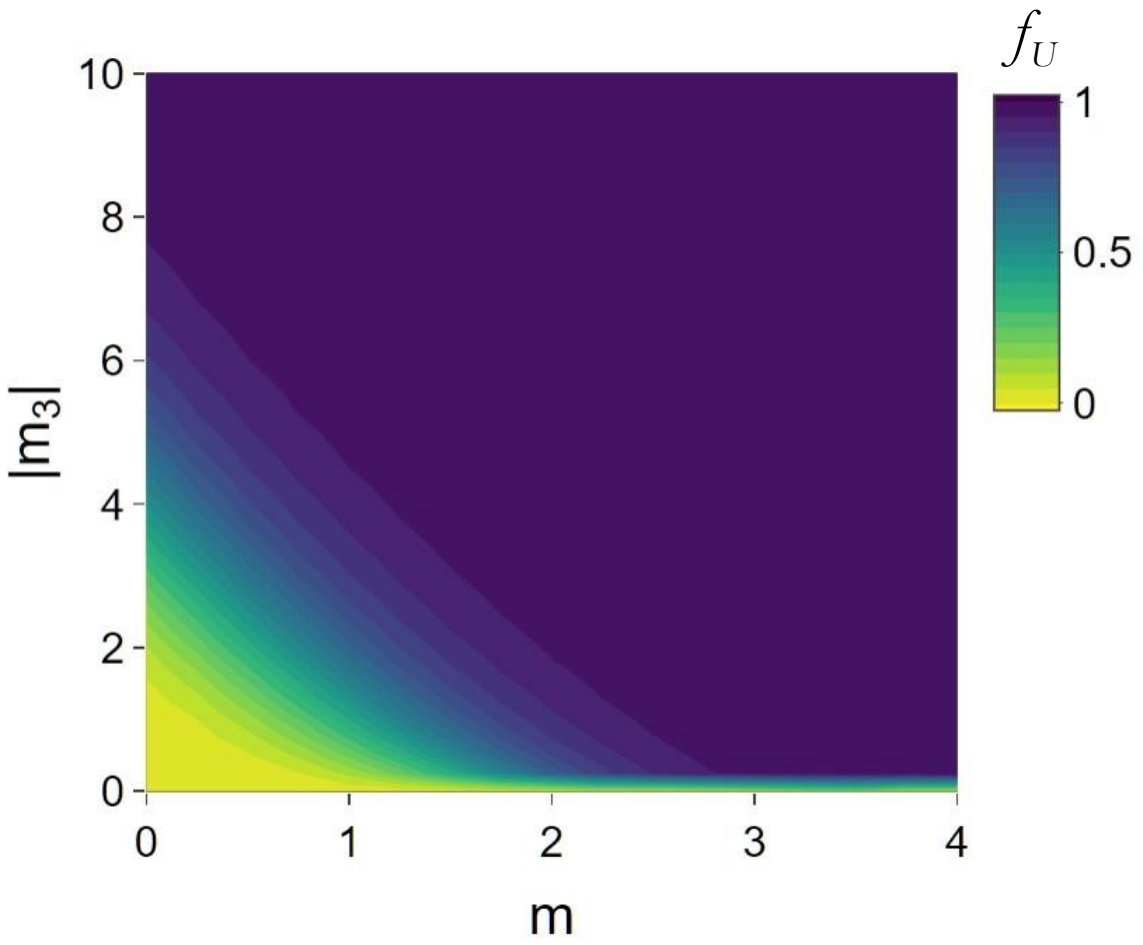
$|m_1| = |m_2| = m = 0.5$

Percolation of Cell Clusters



$|m_1| = |m_2| = m$

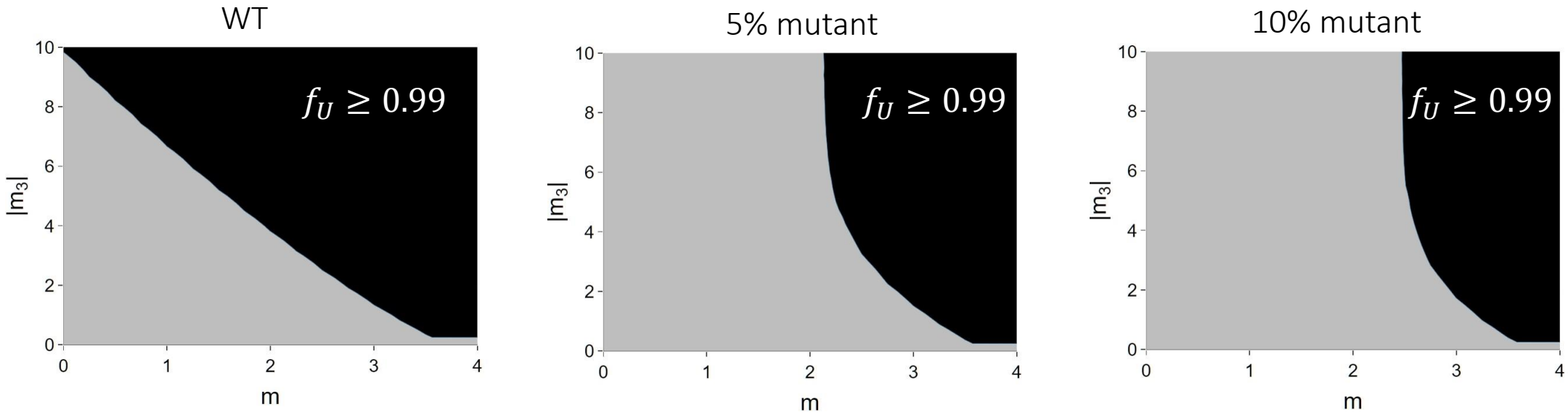
Alignment of Cells in Right Direction



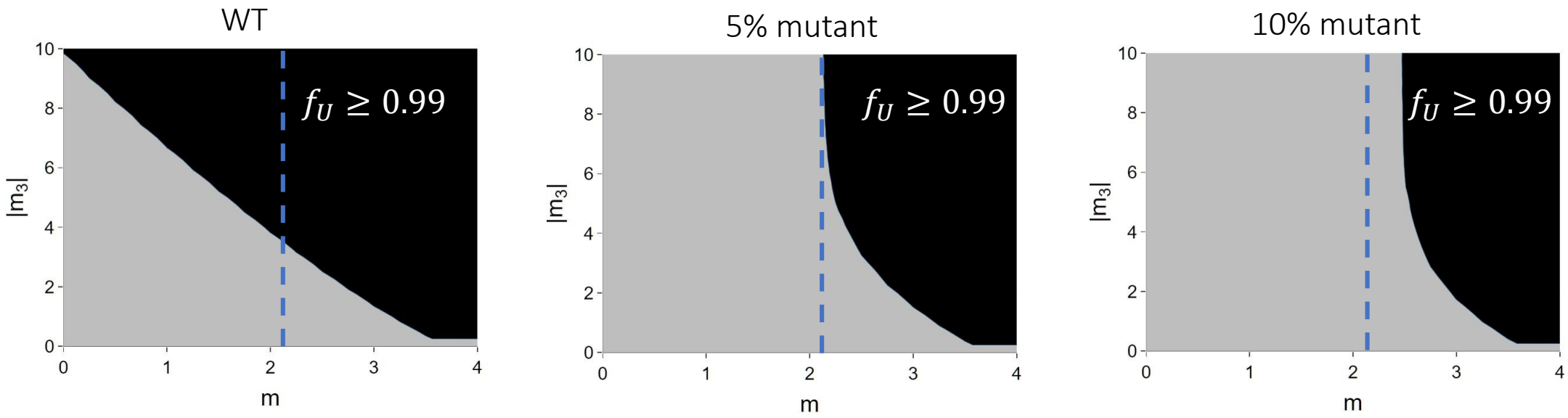
$|m_1| = |m_2| = m$

Power of Collective Against Mutations

Mutated cells can not sense global cue



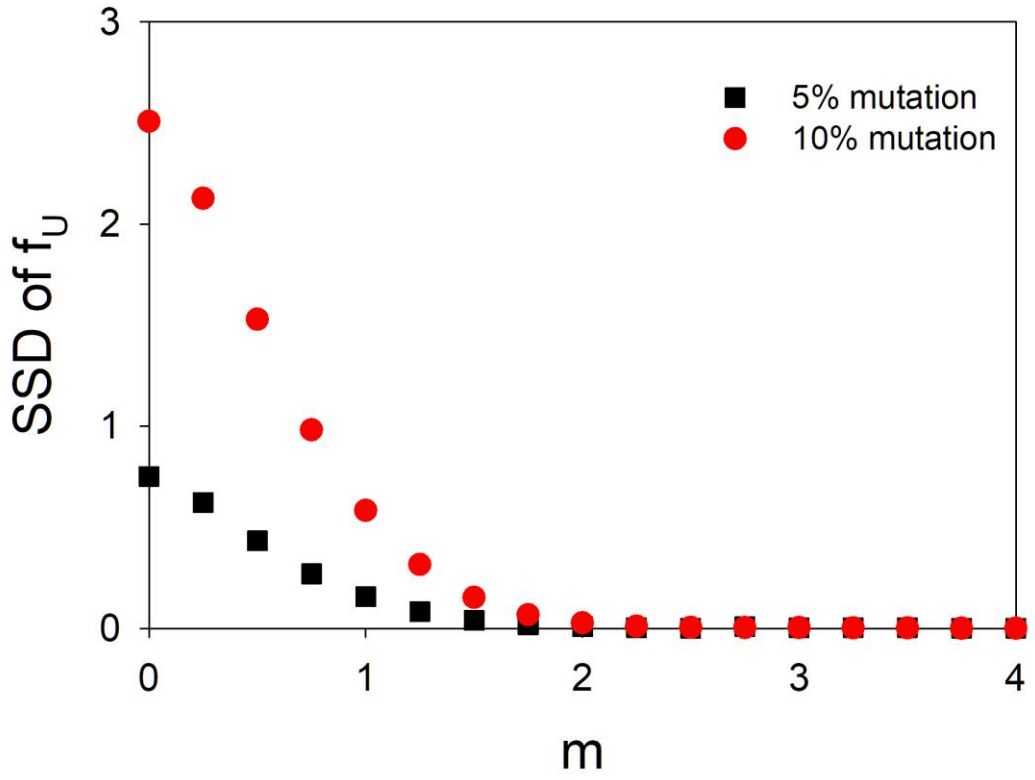
Role of Percolation Transition



Percolation threshold in absence of any directional cue,

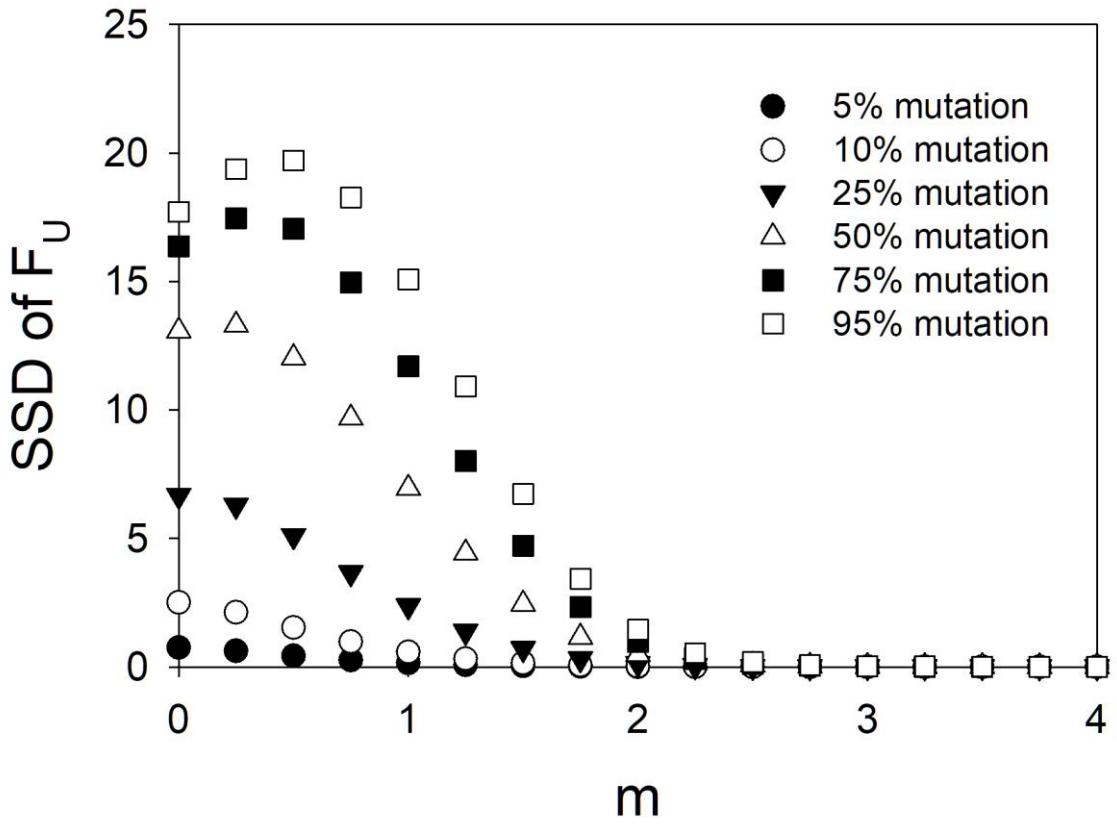
$|m_1| = |m_2| = m = 2.1254$

Role of Percolation Transition

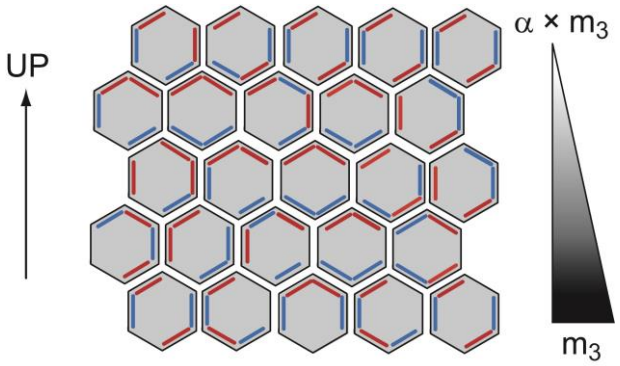


$$SSD_m = \sum_{|m_3|=0}^{10} \left(f_U^{WT,|m_3|} - f_U^{mut,|m_3|} \right)^2$$

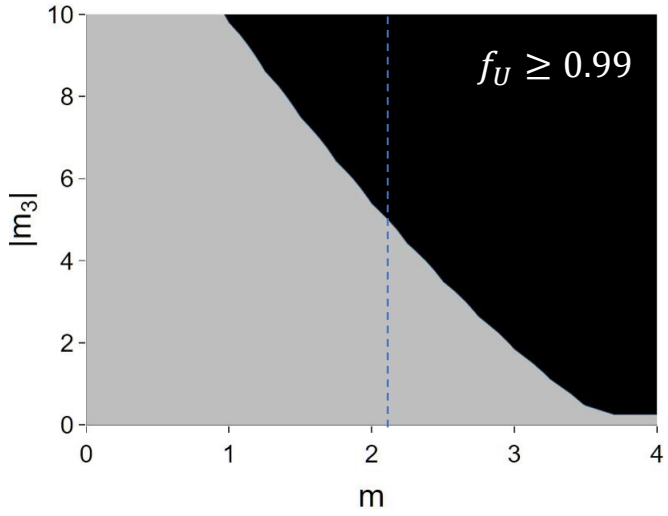
Cases of Extreme Mutations



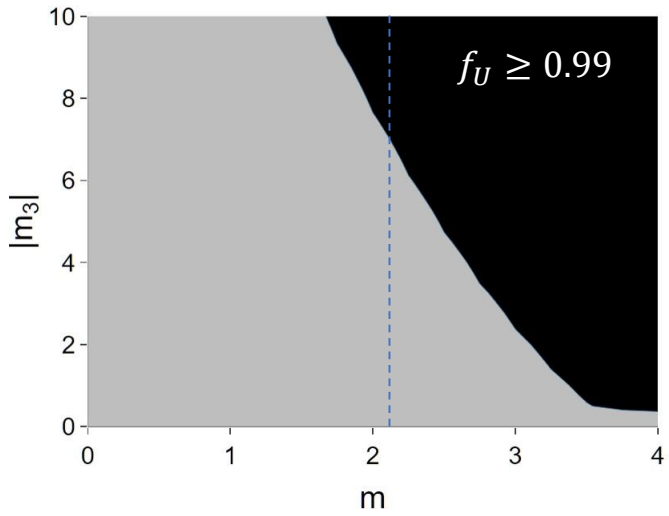
Robust With A Gradient Of Global Clue



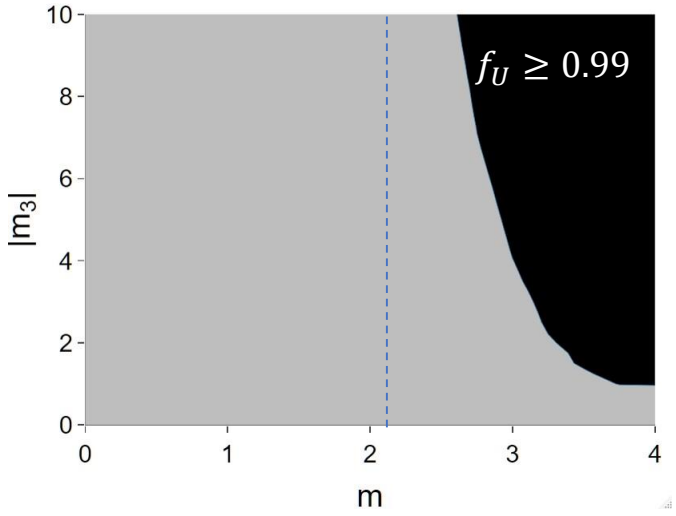
α = 0.5



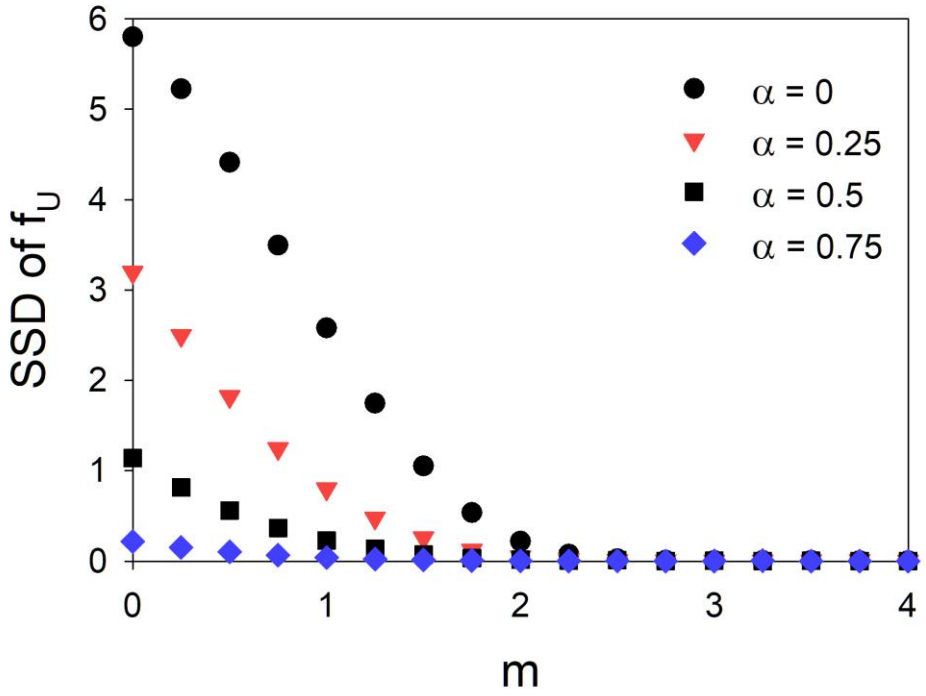
α = 0.25

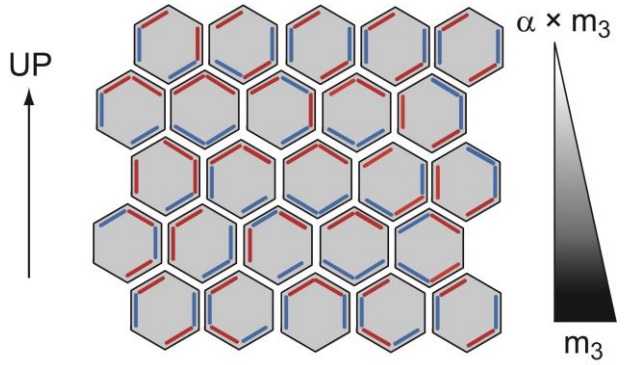


α = 0



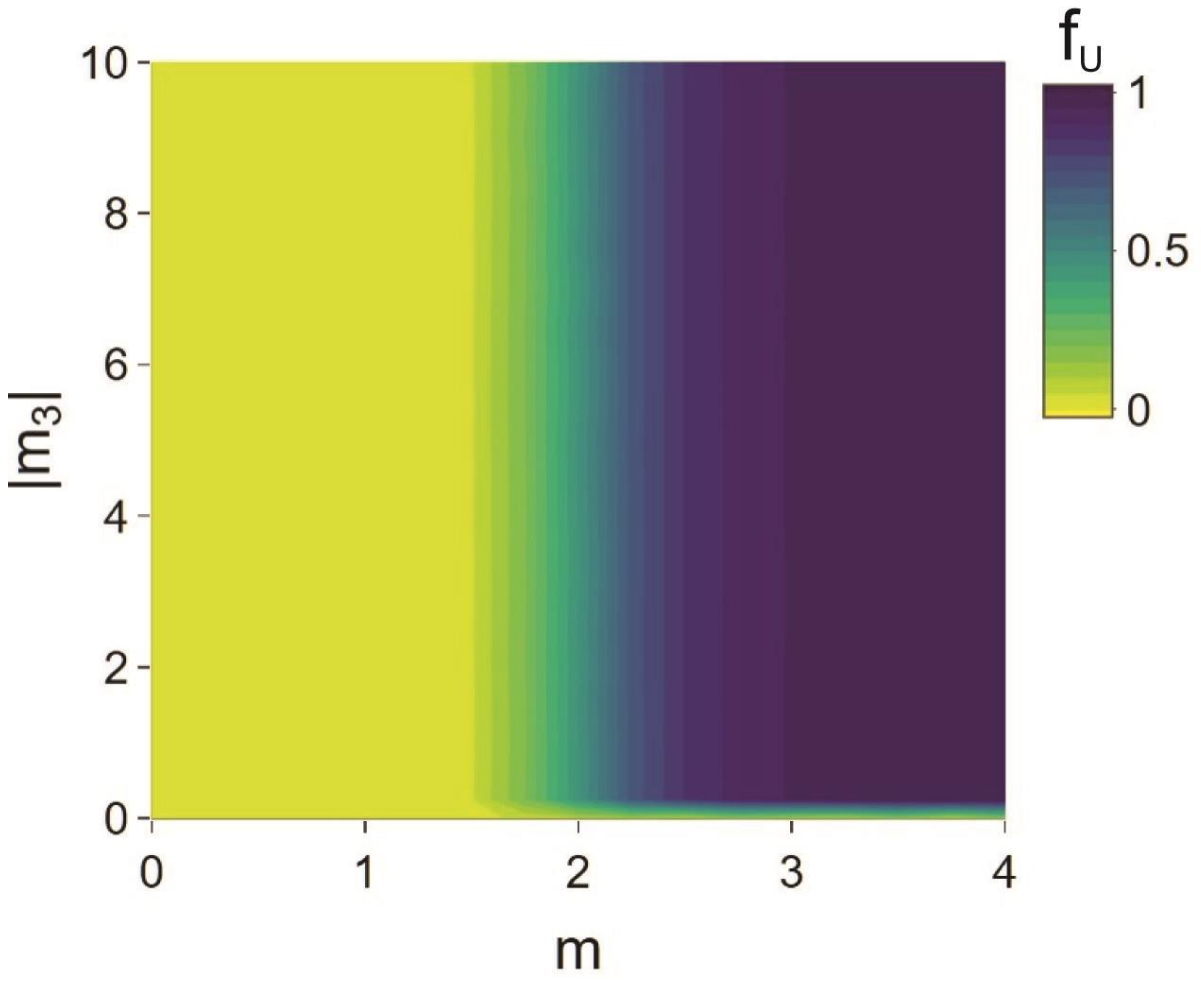
Robust With A Gradient Of Global Clue





$$SSD_m = \sum_{|m_3|=0}^{10} \left(f_U^{WT,|m_3|} - f_U^{gradient,|m_3|} \right)^2$$

Transient Global Clue Is Sufficient



Thresholds in Other PCP Models

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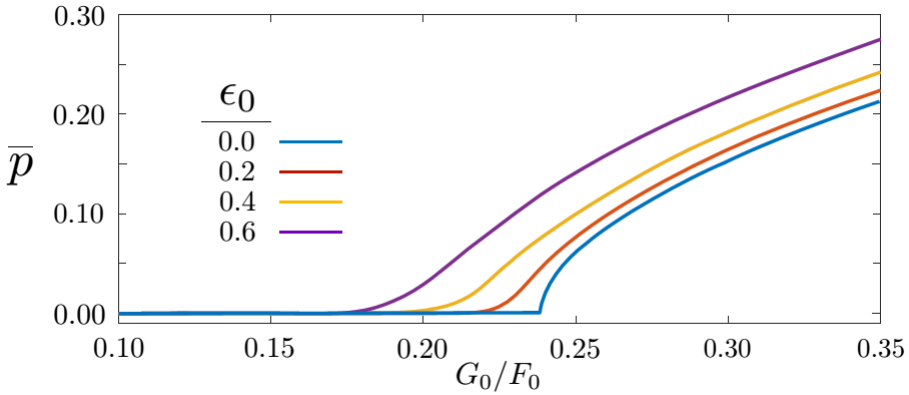
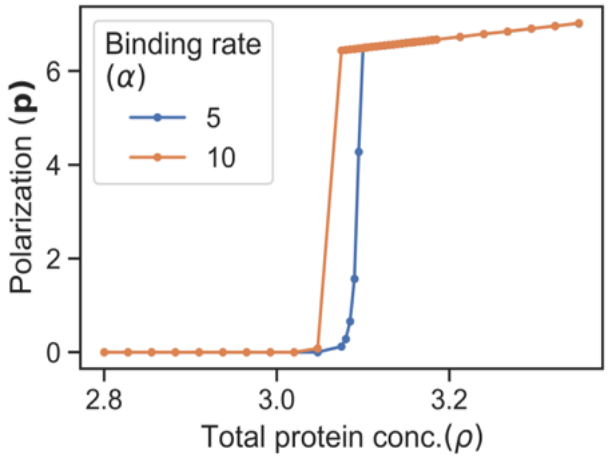


bioRxiv 2021.11.30.468750



Summary

PCP as a critical phenomenon: The toy model based only on elementary rules of fly wing PCP shows that this PCP is possibly a Percolation transition.

Universality & Simplicity: Even though this model is energy-based and involves several rules, it belongs to the class of simple 2D random percolation.

Percolation makes PCP robust: Local interactions beyond a critical threshold makes the system robust to failure.

Percolation allow weak global cue: Beyond the percolation threshold of local interactions, a weak global cue (possibly too week to detect) is good enough for collective alignment.