A Discrete Model of Drosophila Eggshell Patterning

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A Discrete Model of *Drosophila* Eggshell Patterning Reveals Cell-Autonomous and Juxtacrine Effects

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Network Modelling

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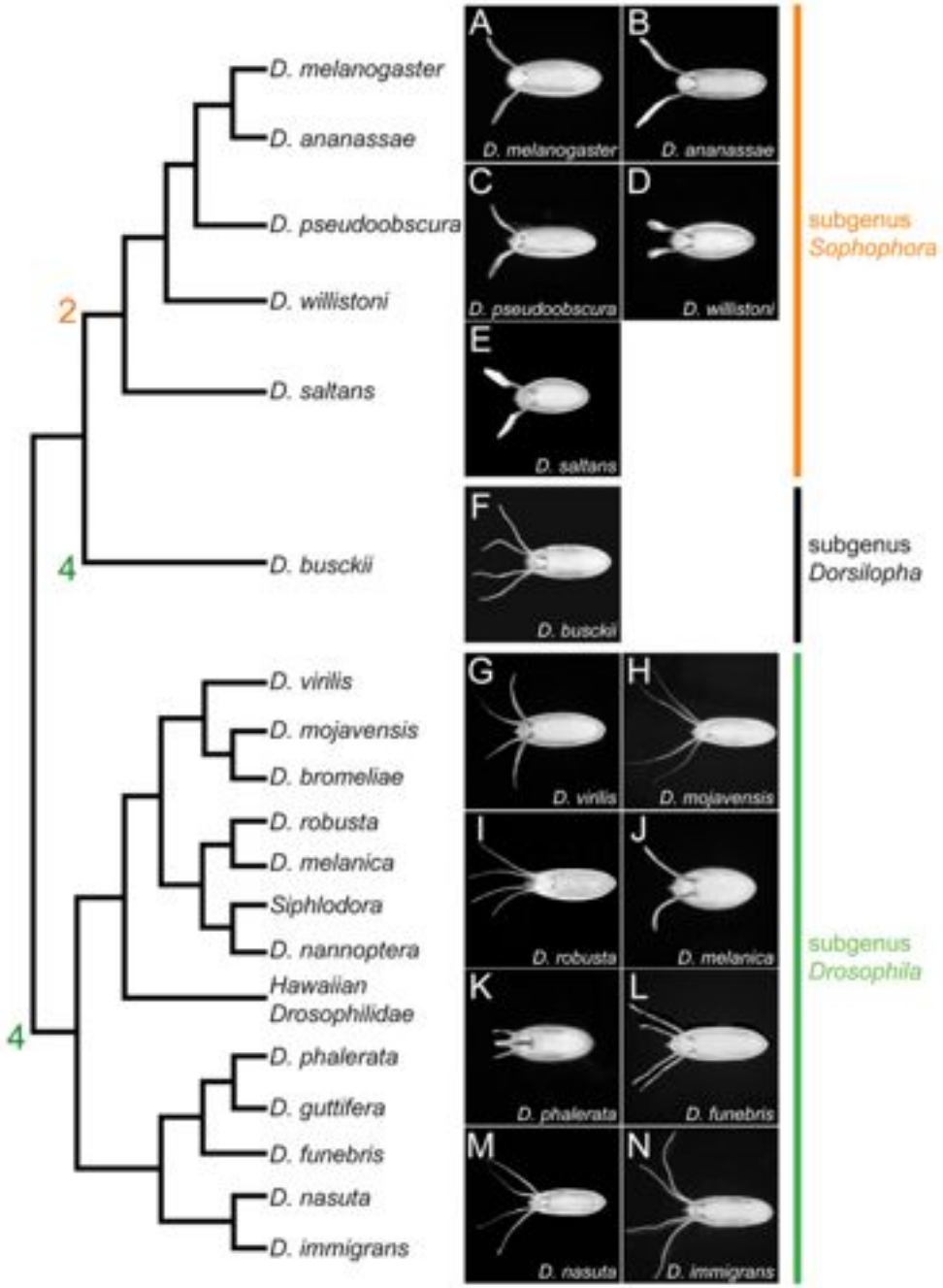
CoLoMoTo meeting
Lausanne 17-18 April 2014

Oogenesis in *Drosophila melanogaster*

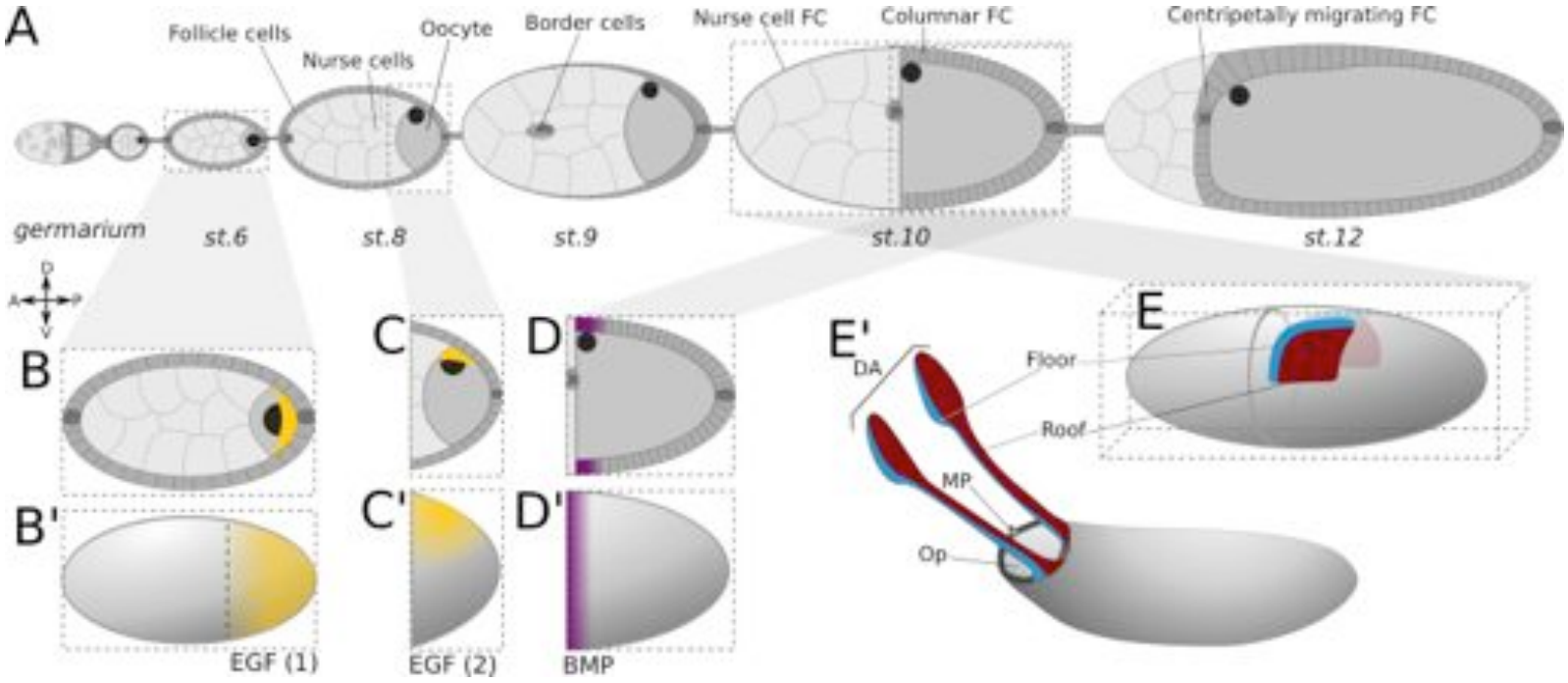
Wu *et al.*, Semin Cell Dev Biol. 2008 June ; 19(3): 271–282.

DA in related species



Kagesawa *et al.*, 2008

Oogenesis in *Drosophila melanogaster*



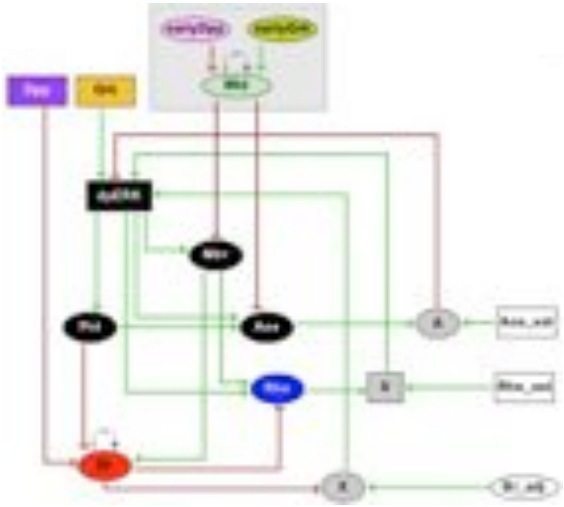
What defines the broad domain (roof cells) and the rhomboid domain (floor cells)?

- Grk and Dpp signals
- Intra-cellular regulatory network
- Juxtacrine signal
- Grk signal extinction (vitelline membrane formation)

A hierarchical, discrete modelling framework

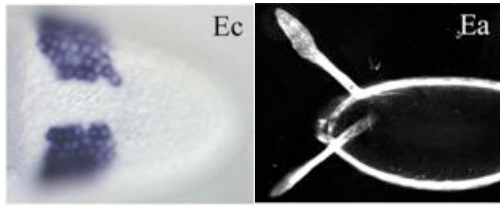
- Cellular model (logical regulatory graph)

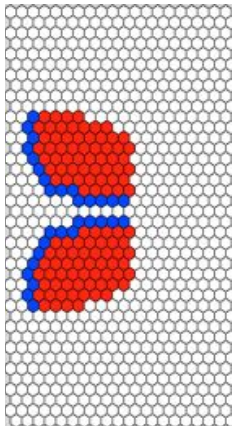
  GINsim



- Epithelial model (cellular automaton)

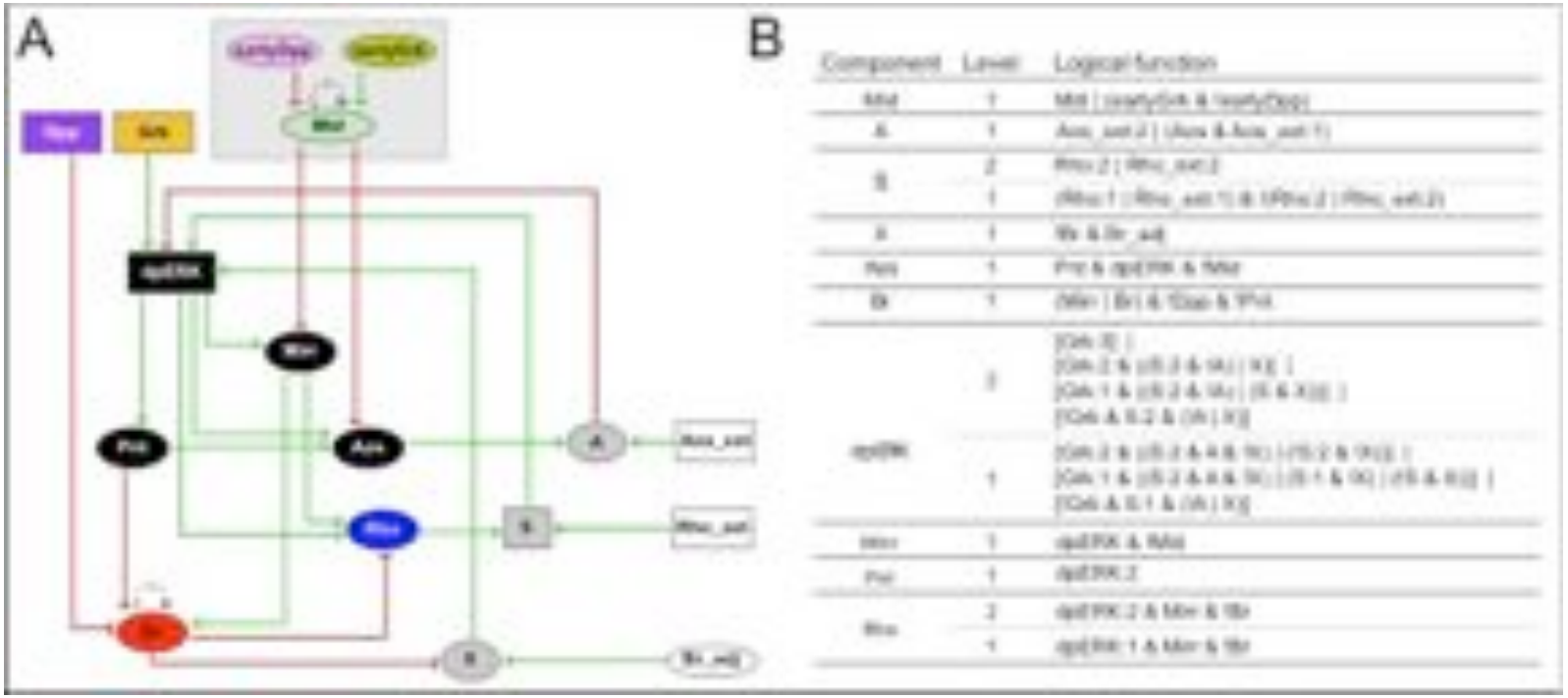
  Python prototype → EpiLog

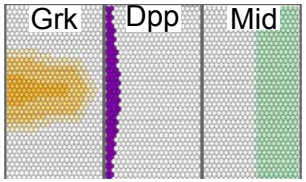




Shravage et al. (2007) Development 134:2261-71

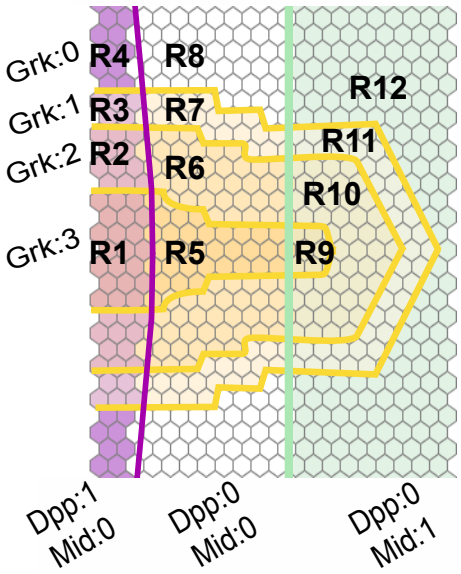
Patterning of the *Drosophila* eggshell
cellular model





Patterning of the *Drosophila* eggshell
cellular model

288 input combinations (levels of Dpp, Grk, Mid, Aos_ext, Br_adj and Rho_ext) → Attractors: 8 stable states (cellular fates), 4 cyclical attractors



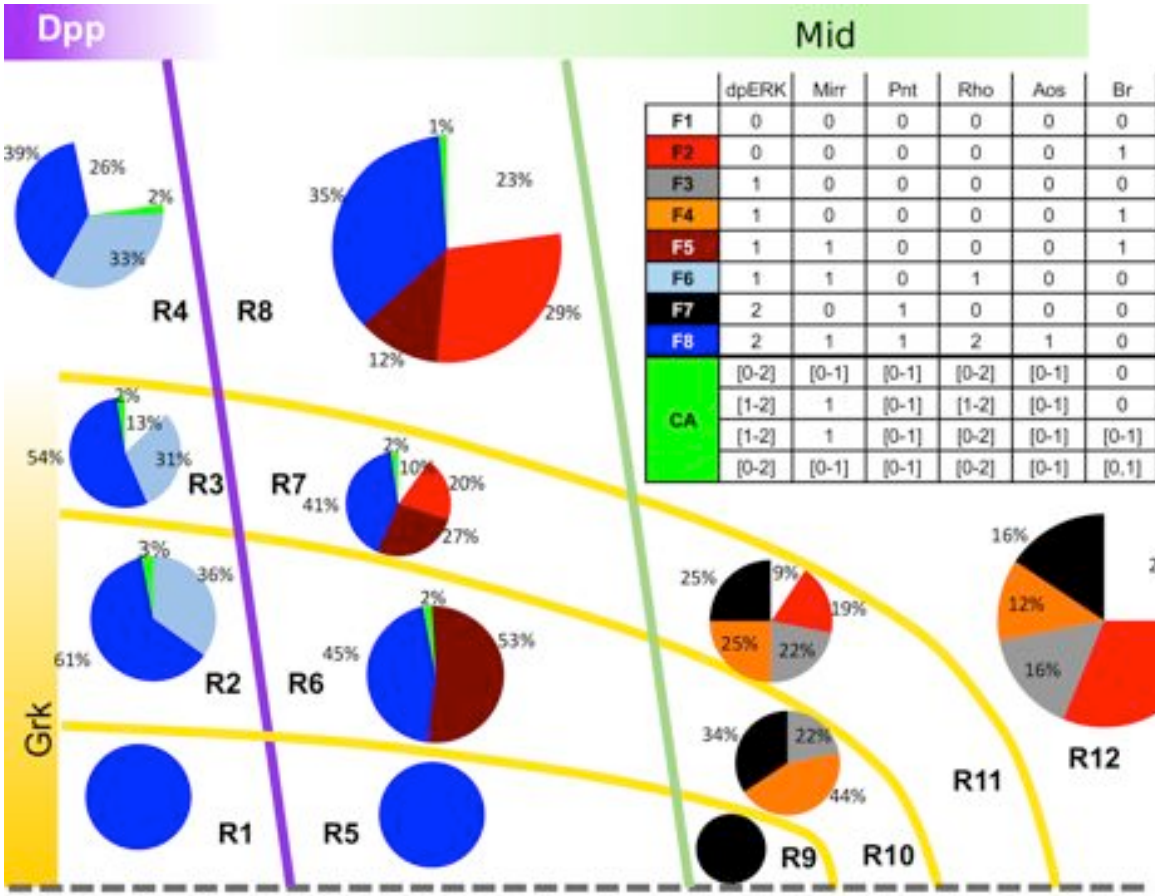
	dpERK	Mirr	Pnt	Rho	Aos	Br	Regions
F1	0	0	0	0	0	0	4, 7-8
F2	0	0	0	0	0	1	7-8
F3	1	0	0	0	0	0	10-12
F4	1	0	0	0	0	1	10-12
F5	1	1	0	0	0	1	6-8
F6	1	1	0	1	0	0	2-4
F7	2	0	1	0	0	0	9-12
F8	2	1	1	2	1	0	1-8
CA	[0-2]	[0-1]	[0-1]	[0-2]	[0-1]	0	4
	[1-2]	1	[0-1]	[1-2]	[0-1]	0	2-3
	[1-2]	1	[0-1]	[0-2]	[0-1]	[0-1]	6-7
	[0-2]	[0-1]	[0-1]	[0-2]	[0-1]	[0,1]	8

- **F1** undifferentiated state
- **F2**: roof
- **F8**: operculum and floor

(floor alone after Grk extinction)

Patterning of the *Drosophila* eggshell
cellular model

288 input combinations (levels of Dpp, Grk, Mid, Aos_ext, Br_adj and Rho_ext) → Attractors: 8 stable states (cellular fates), 4 cyclical attractors



	dpERK	Mirr	Pnt	Rho	Aos	Br	Regions
F1	0	0	0	0	0	0	4, 7-8
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F4	1	0	0	0	0	1	10-12
F5	1	1	0	0	0	1	6-8
F6	1	1	0	1	0	0	2-4
F7	2	0	1	0	0	0	9-12
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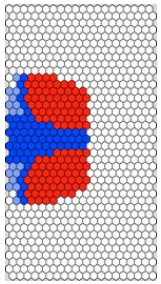
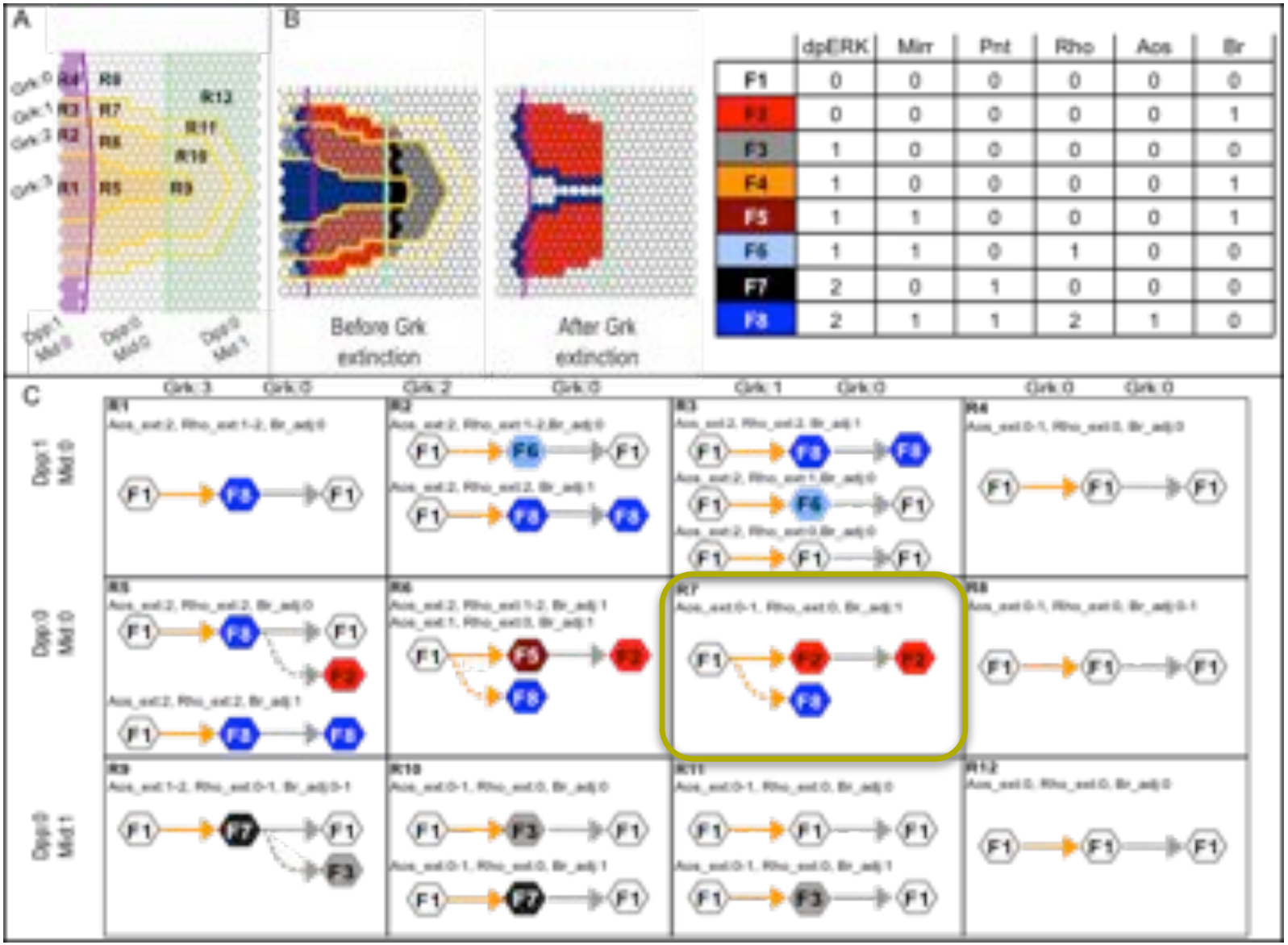
CA	[0-2]	[0-1]	[0-1]	[0-2]	[0-1]	0	4
	[1-2]	1	[0-1]	[1-2]	[0-1]	0	2-3
	[1-2]	1	[0-1]	[0-2]	[0-1]	[0-1]	6-7
	[0-2]	[0-1]	[0-1]	[0-2]	[0-1]	[0,1]	8



18 combinations of values for the remaining inputs Aos_ext, Br_next, Rho_ext

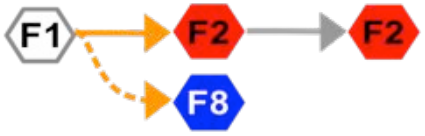
Patterning of the *Drosophila* eggshell
cellular model

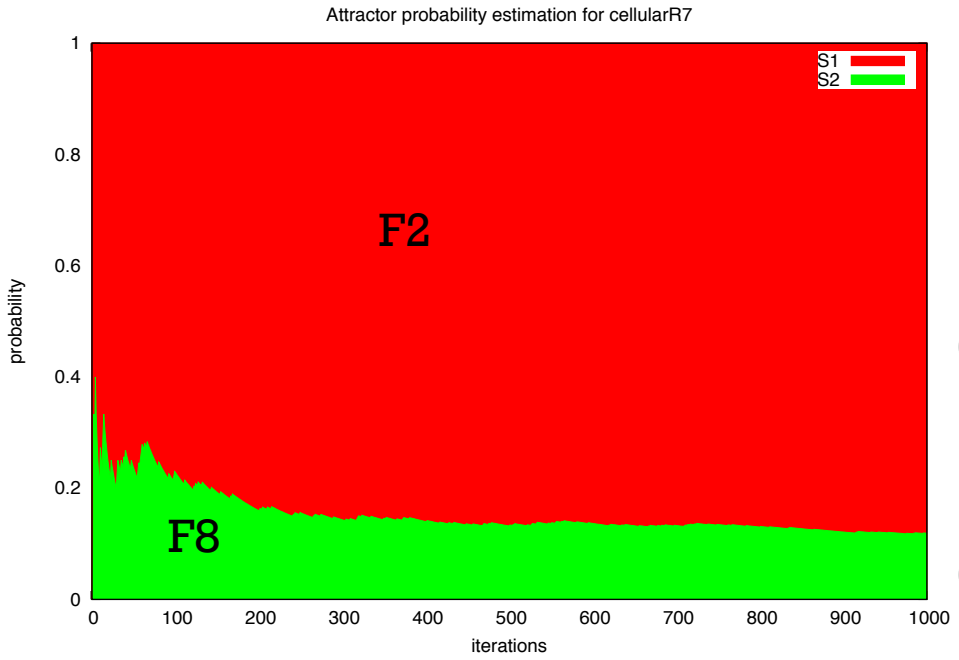


	dpERK	Mirr	Pnt	Rho	Aos	Br
F1	0	0	0	0	0	0
F2	0	0	0	0	0	1
F3	1	0	0	0	0	0
F4	1	0	0	0	0	1
F5	1	1	0	0	0	1
F6	1	1	0	1	0	0
F7	2	0	1	0	0	0
F8	2	1	1	2	1	0

Patterning of the *Drosophila* eggshell
cellular model

R7
Aos_ext:0-1, Rho_ext:0, Br_adj:1

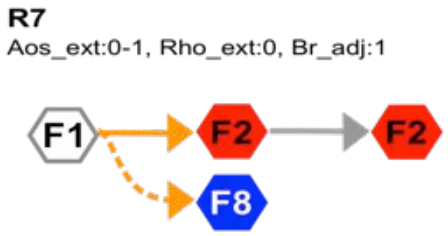


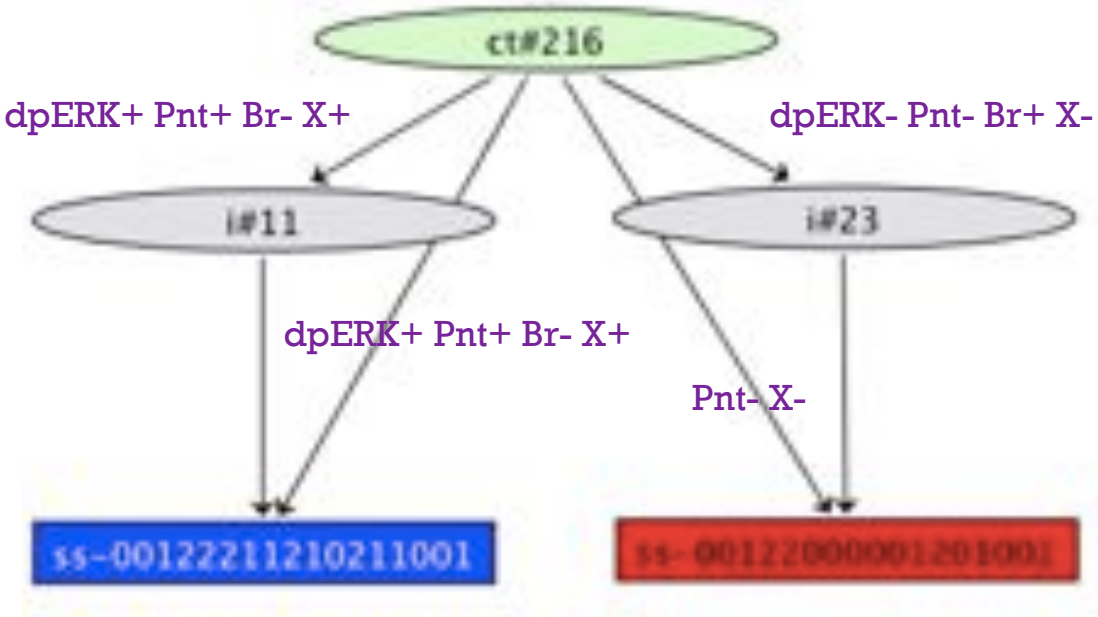


0.881

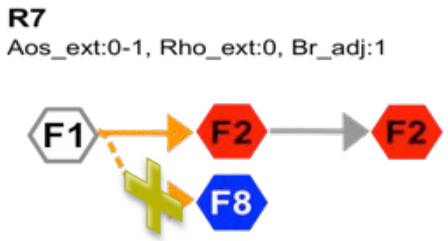
0.119

Patterning of the *Drosophila* eggshell
cellular model

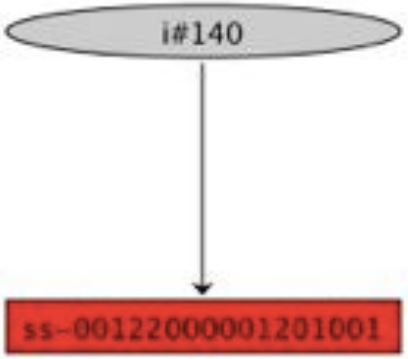




Patterning of the *Drosophila* eggshell
cellular model

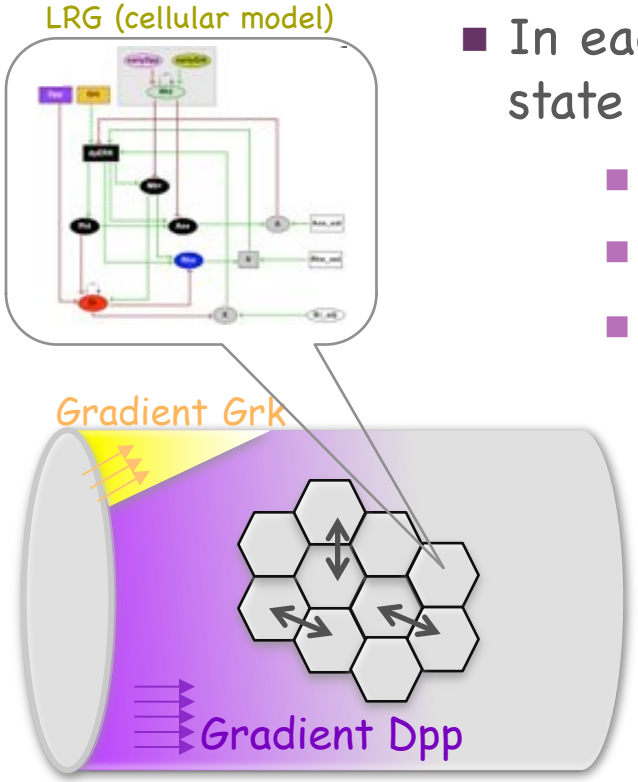


Introducing a lower priority to Pnt activity

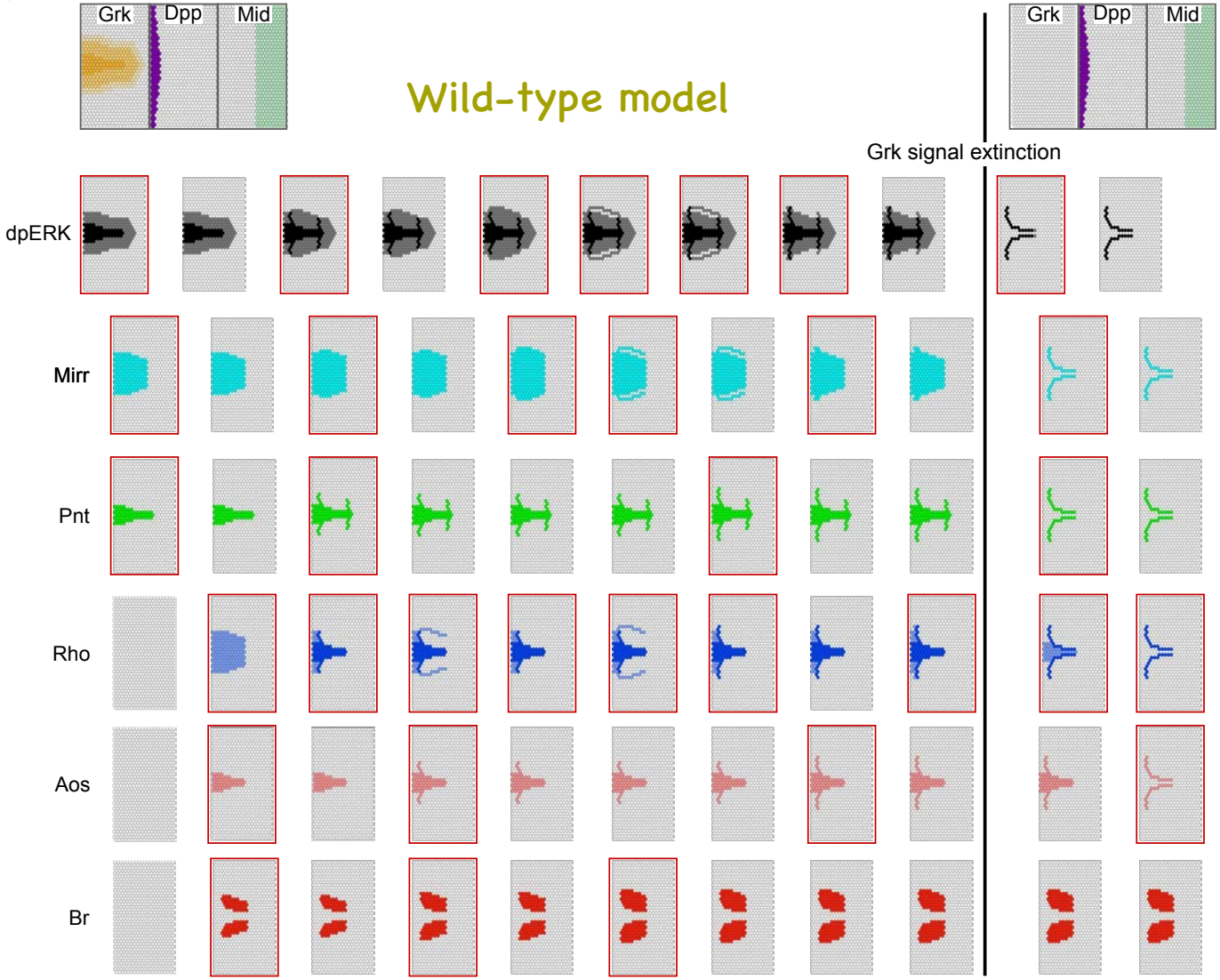


Patterning of the *Drosophila* eggshell
epithelial model

- Cellular automaton; a grid of hexagonal cells
- Each cell has 6 neighbours (except along anterior and posterior borders)
- In each cell, the cellular model defines its state depending on
  - its proper components
  - signals from neighbouring cells
  - other external signals (Dpp, Grk, Mid)



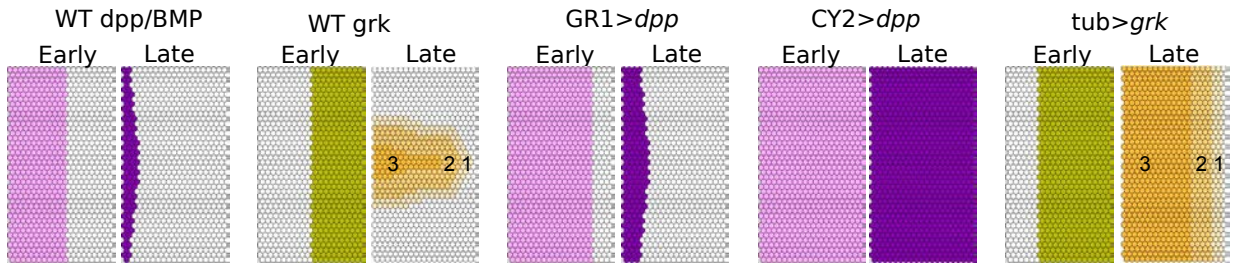
Patterning of the *Drosophila* eggshell
epithelial model



Patterning of the *Drosophila* eggshell
epithelial model

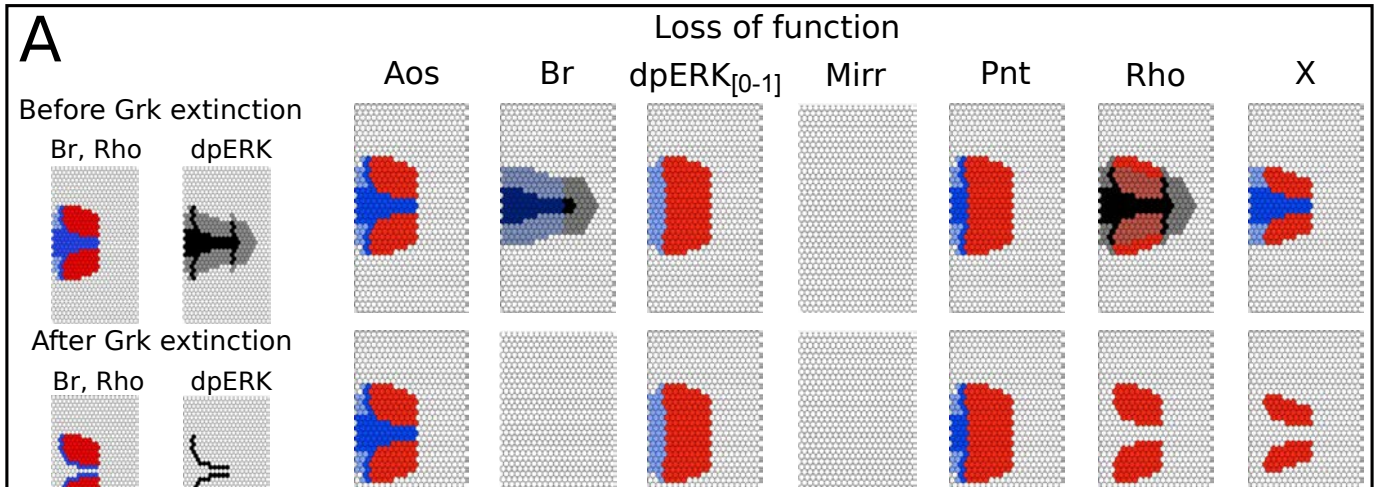
A

Perturbed inputs



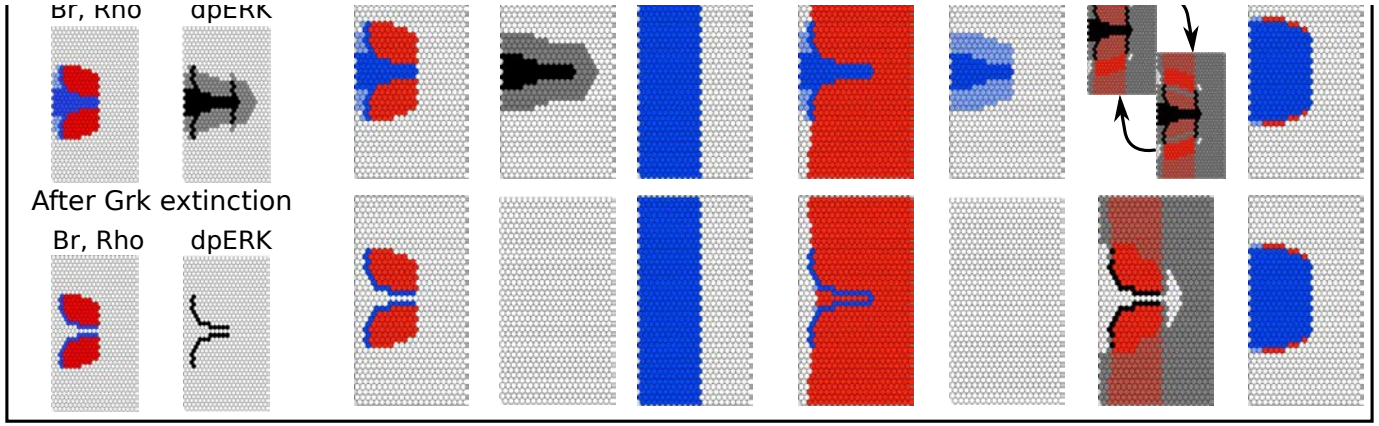
Patterning of the *Drosophila* eggshell
epithelial model

LOF and GOF mutants

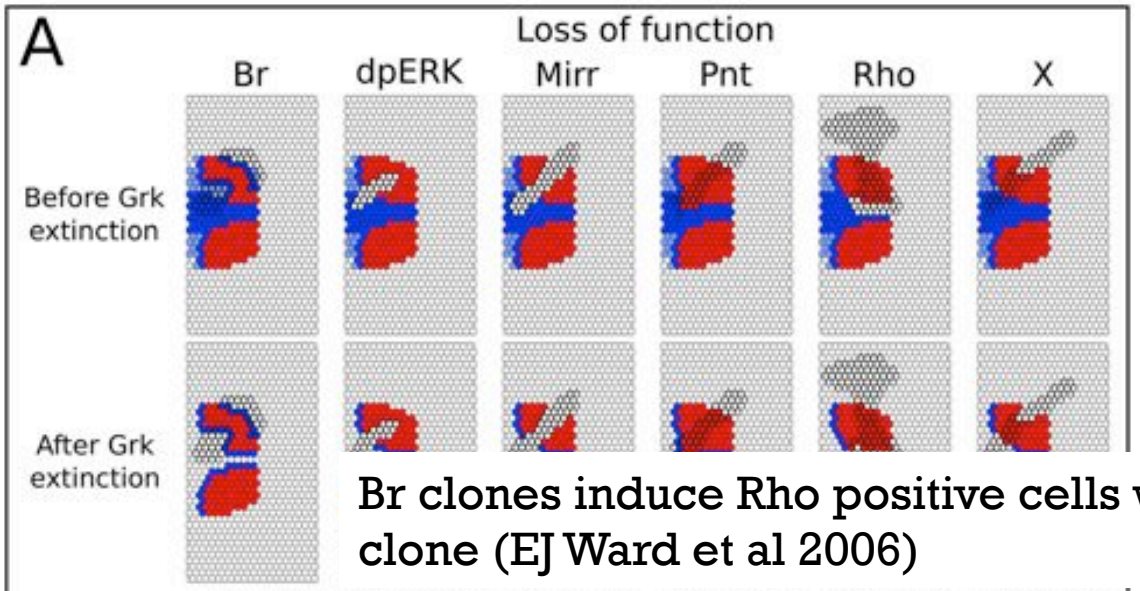


Aos GOF has a minimal effect (prediction)

Aos LOF has no visible effect on the Br domain, but prevents the splitting after Grk extinction (J-F Boisclair Lachance et al 2009)

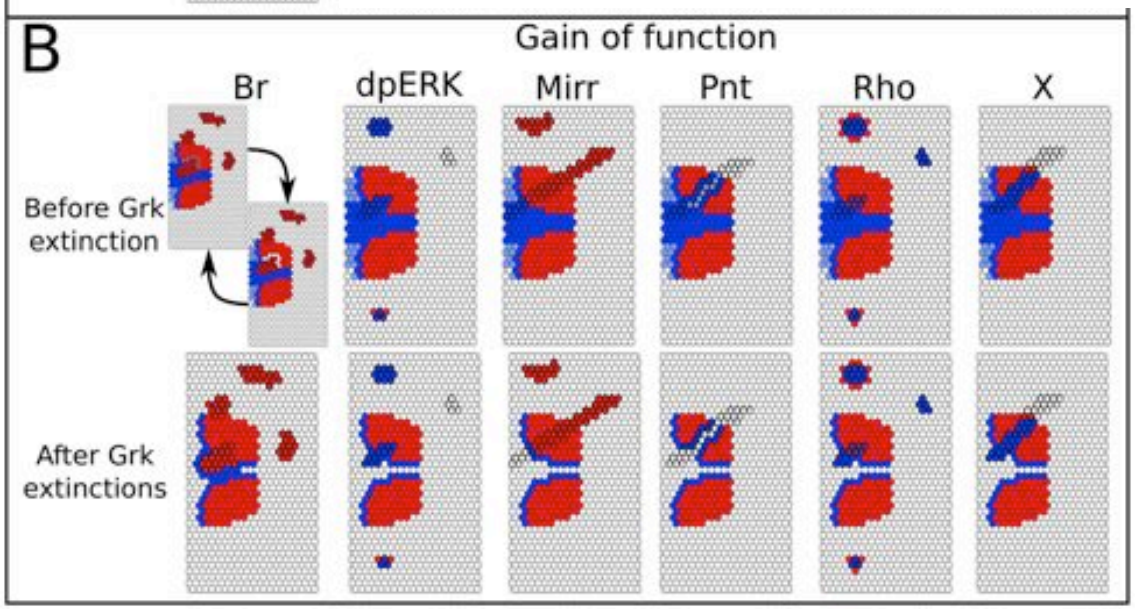


Patterning of the *Drosophila* eggshell
epithelial model



Clonal analysis

Br clones induce Rho positive cells within the clone (EJ Ward et al 2006)



Conclusions & prospects

- Molecular mechanisms responsible for the establishment of the floor pattern

⇒ Juxtacrine signal hypothesis

⇒ Candidate gene

- Role of Grk signal extinction
- Reconciliation of conflicting evidence (pattern of early and late Grk, Dpp)
- What about DA number variation in other species?
- Logical modelling applied to patterning in epithelia → EpiLog
- Updating schemes / robustness
- What format for this type of models?

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