Single cell vs multiple cells

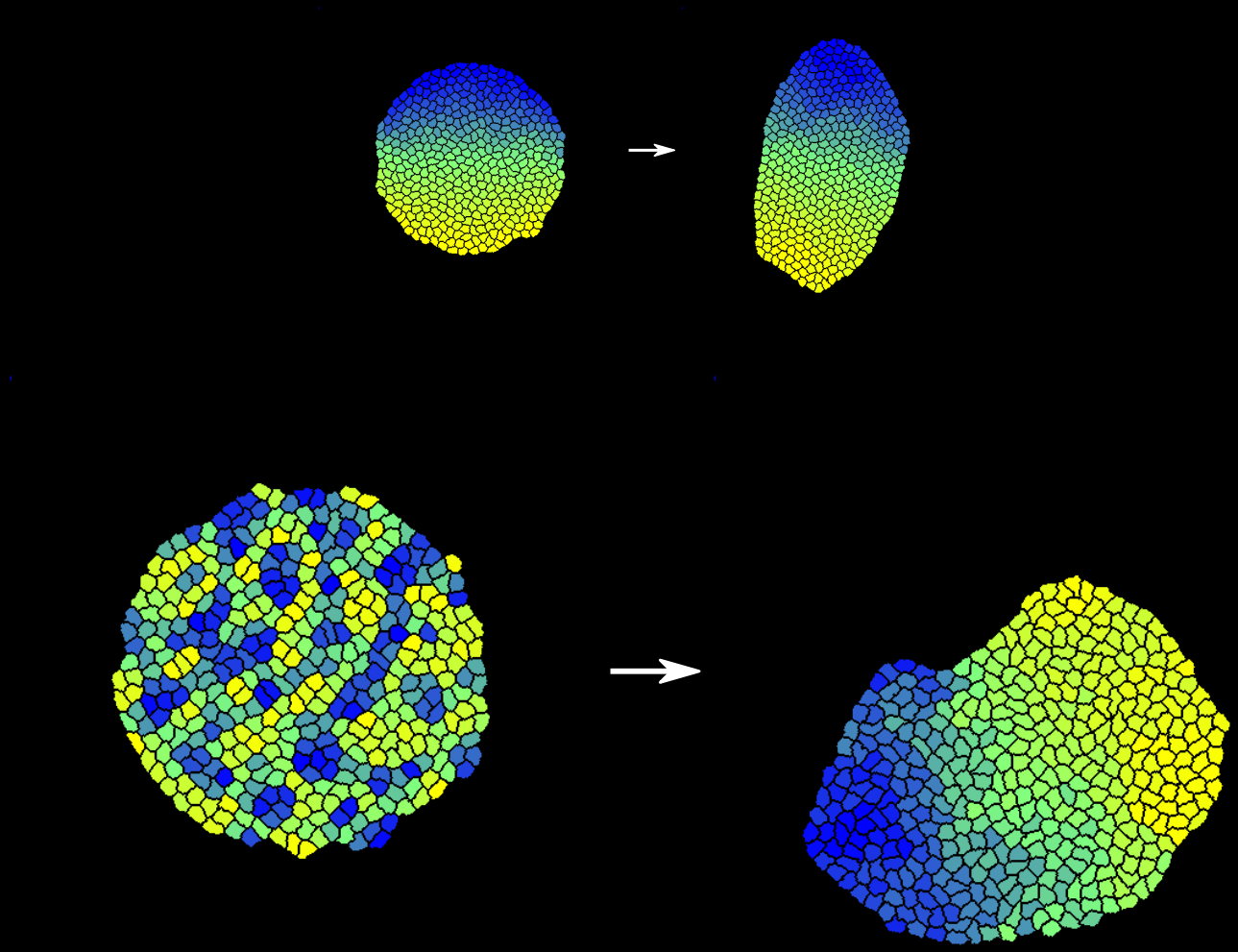
Perstime: how straight or wiggly

Few cells, no adhesion: random walk

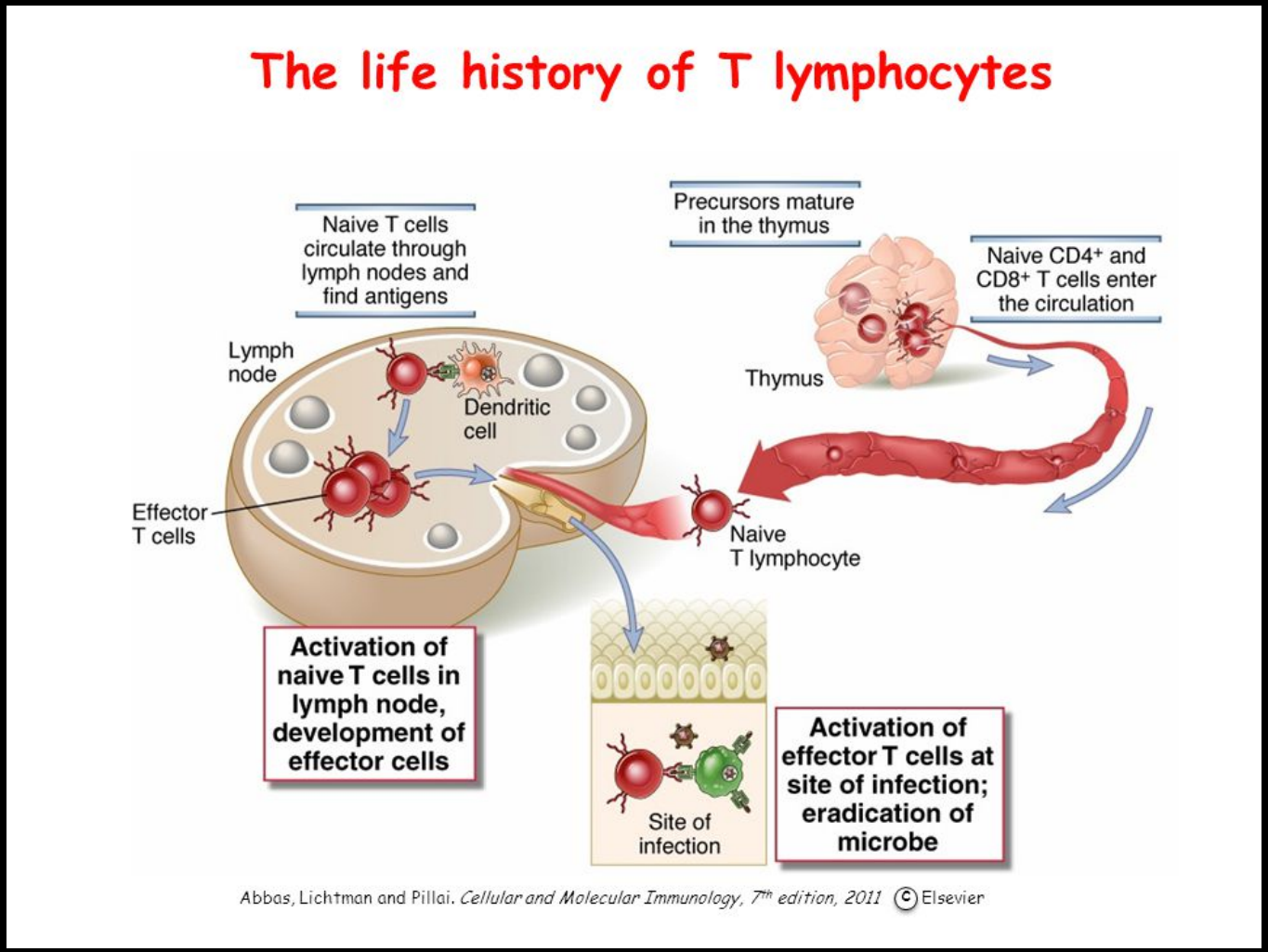
More cells and/or adhesion: streaming

Using active migration with adhesion

Get closer to minimal energy configuration: break through local optima.



T cells need to be activated



T cell migration

Lymph nodes are very packed

Beltman *et al.* 2007

Lymph node structure causes realistic migration

Beltman *et al.* 2007

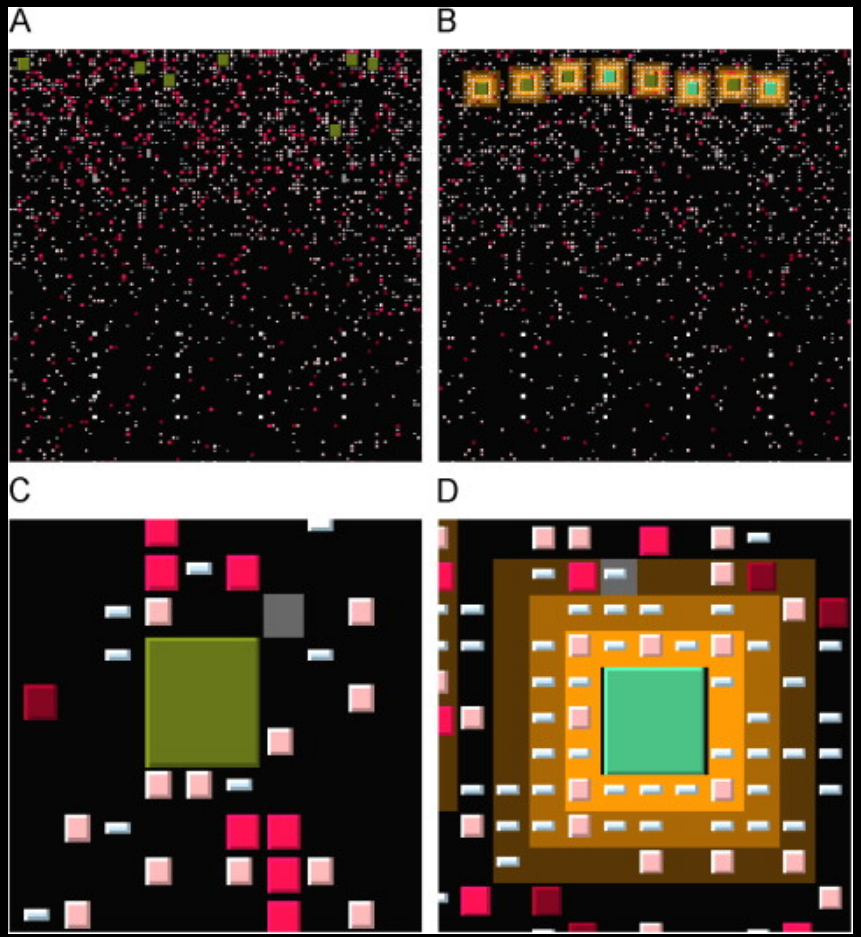
A T cell's perspective

Beltman *et al.* 2007

Another application in immunology

Before immune response is mounted, fraction of antigen-specific T cells is $10^{-5}, 10^{-6}$

How does an antigen-presenting cell "find" the right T cell? It's the T cells that move. Chemotaxis?

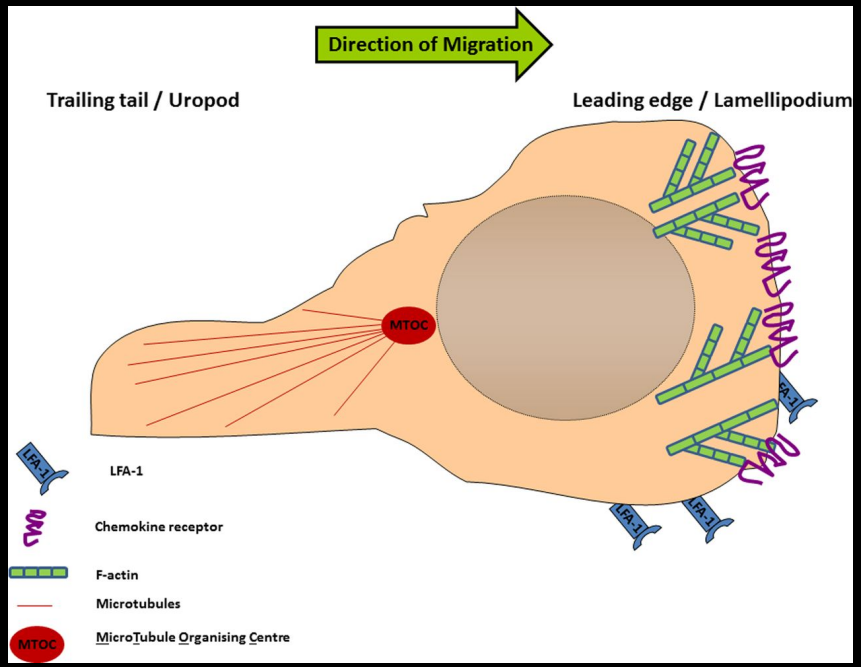


Model without chemotaxis

Chemotaxis does help

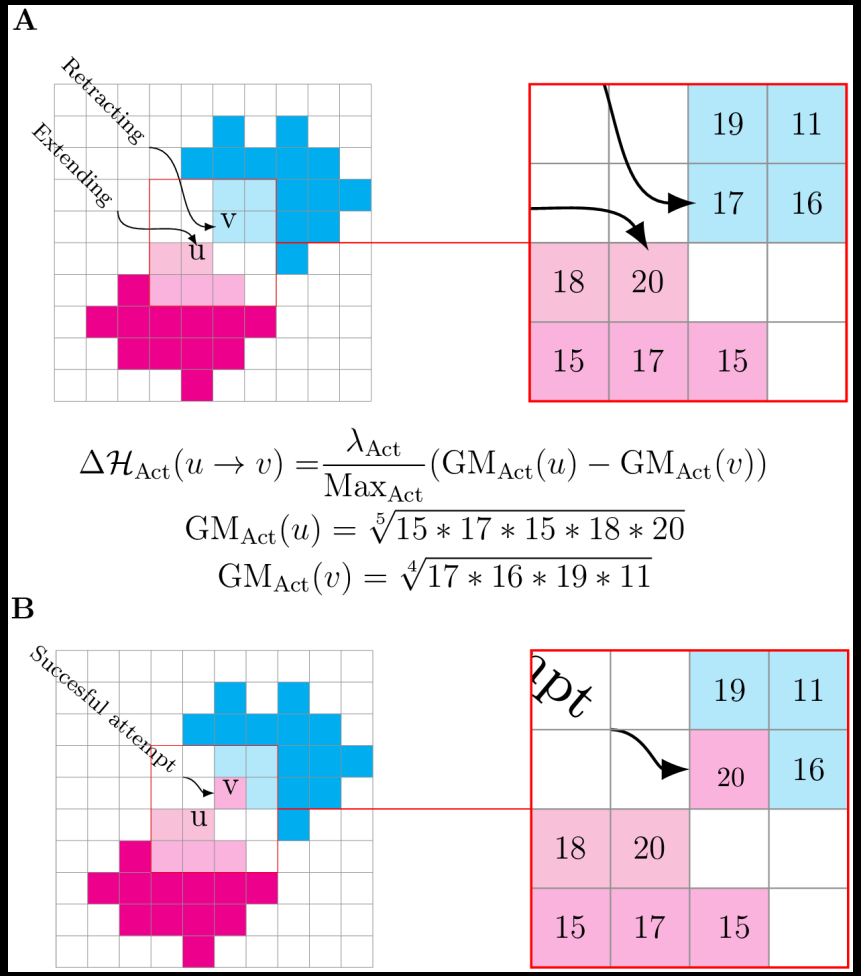
...so long as cells do not get crushed

Another way to implement cell migration



Niculescu *et al.*, 2015

Another way to implement cell migration



Niculescu *et al.*, 2015

two main modes

Amoeboid keratocyte-like

multiple modes of migration possible

Tissue context makes migration pattern

Amoeboid cells are better able to squeeze through tightly packed tissue

Endless forms most beautiful...

Cell growth, cell death: increase target volume or set to 0

Cell division or cleavage: Assign new ID to part of the cell

Chemotaxis: $\Delta H+ = \mu_{chem}(C_{neigh} - C_{target})$

Cortical tension: surface area constraint =
$H+ = \lambda_s(s - S)^2$

Cell elongation (various ways)

different J values along parts of membrane

elastic springs between cells

secretion of signalling molecules or ECM

Gene expression (influencing any cell property)

Platforms

CompuCell3D

Morpheus

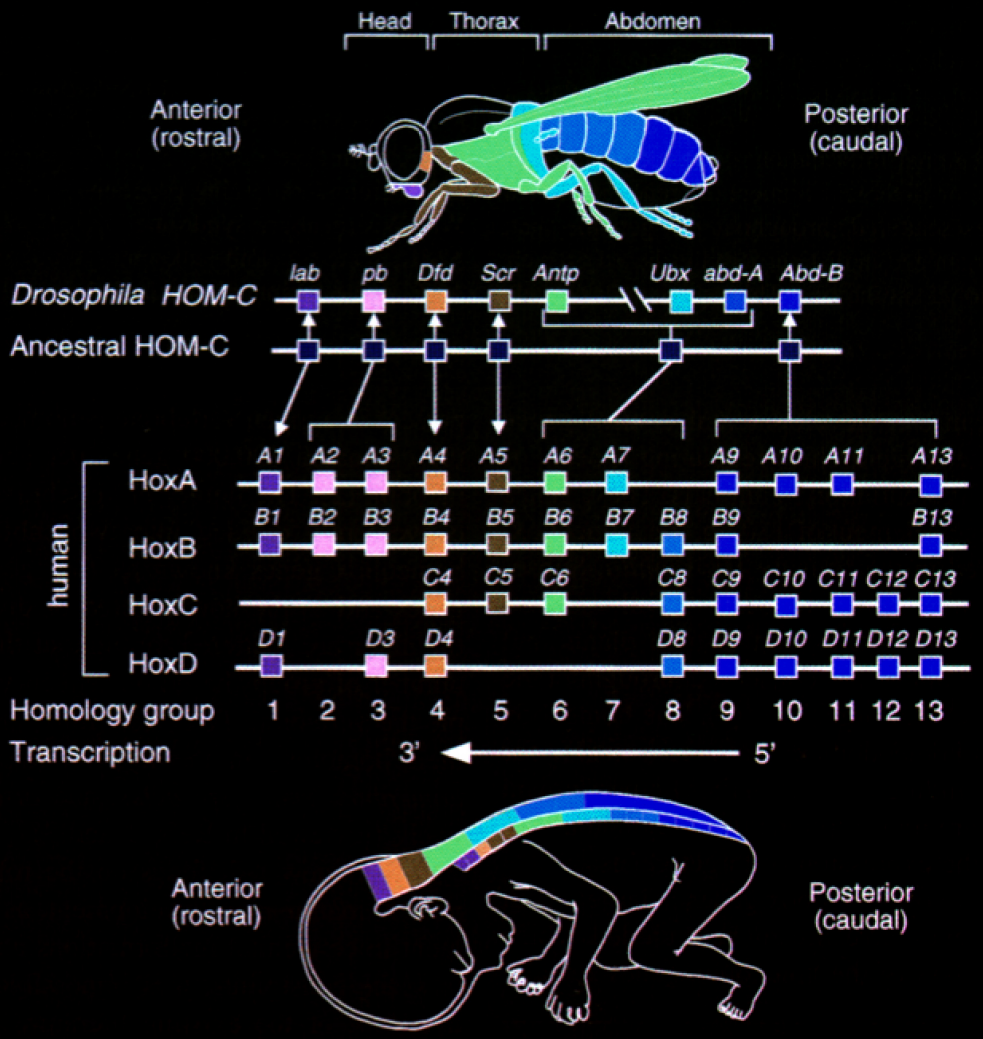
Tissue Simulator

Chaste

...have been, and are being, evolved

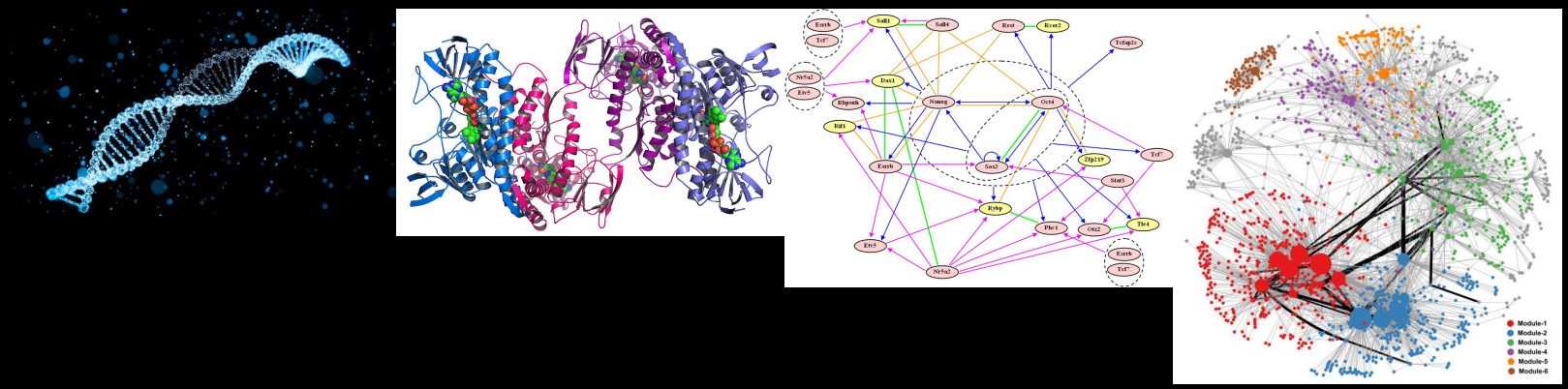
Ernst Mayr

The signature of evolution



The importance of the GP map

From the genotype to the phenotype:
a long and complex path



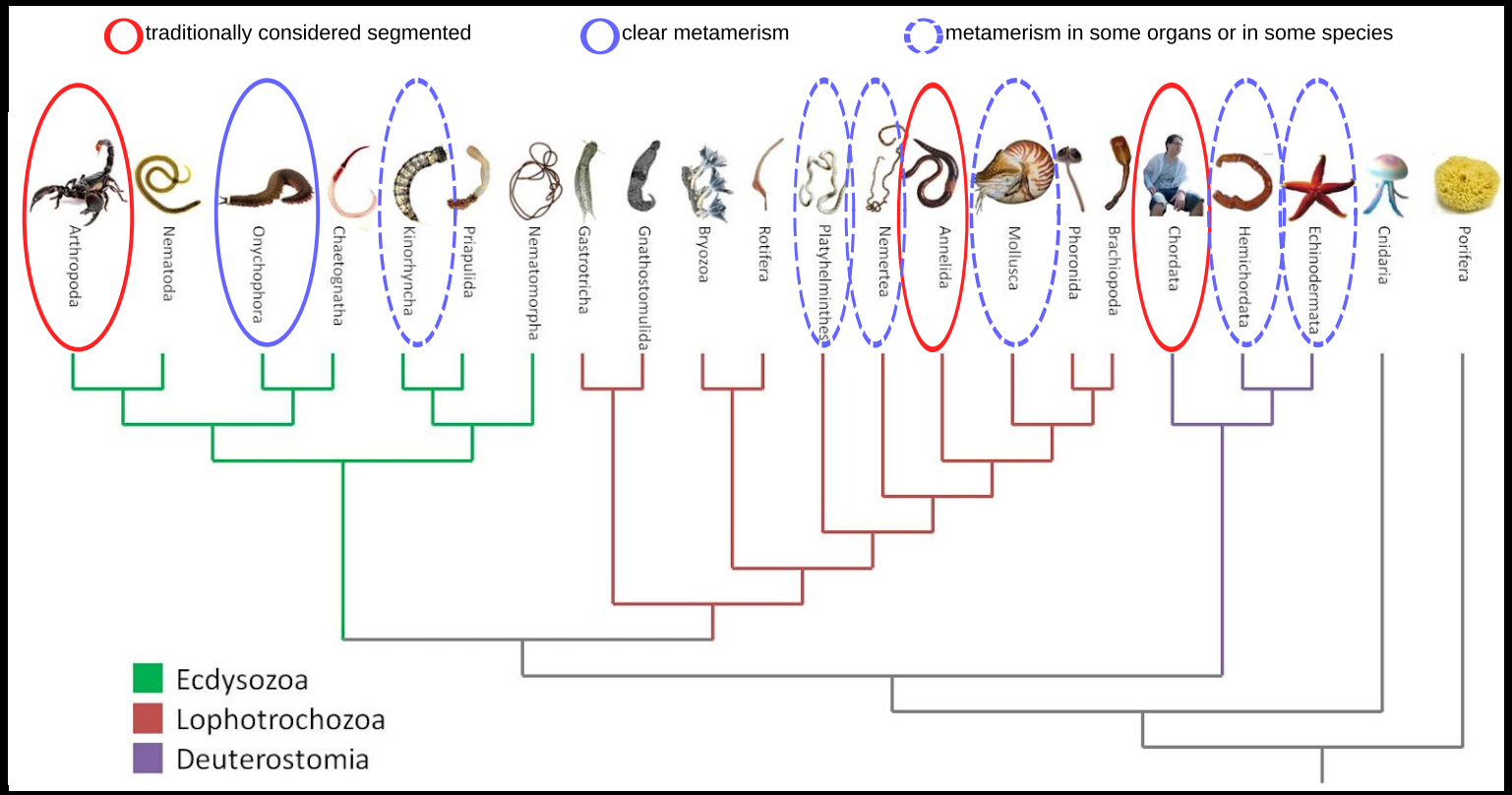
Feedback between different levels, also for development

The questions of Evo-Devo

Why do we see certain developmental mechanisms?
How do developmental mechanisms shape future evolution, and vice versa?

Clades with segmentation

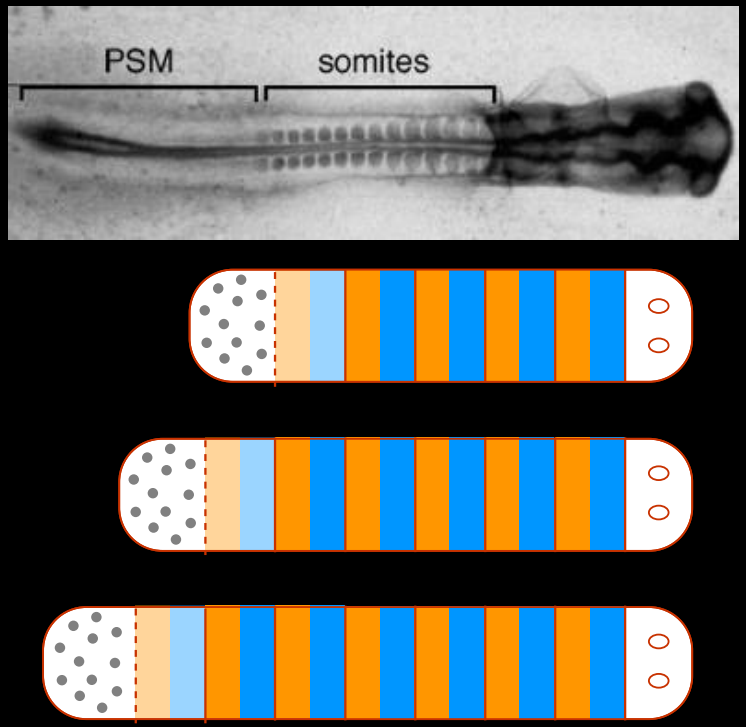
Segmentation across bilateria

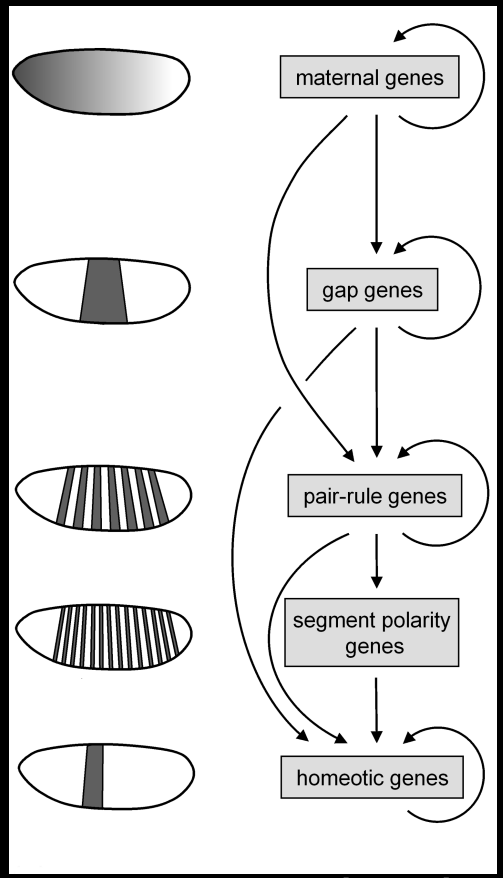


three overtly segmented clades, others partially or pseudosegmented.

Segmentation across bilateria

sequential vs hierarchical

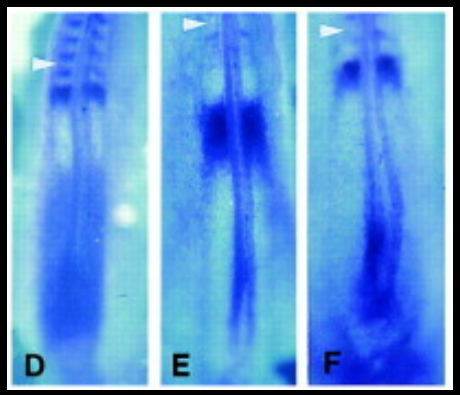


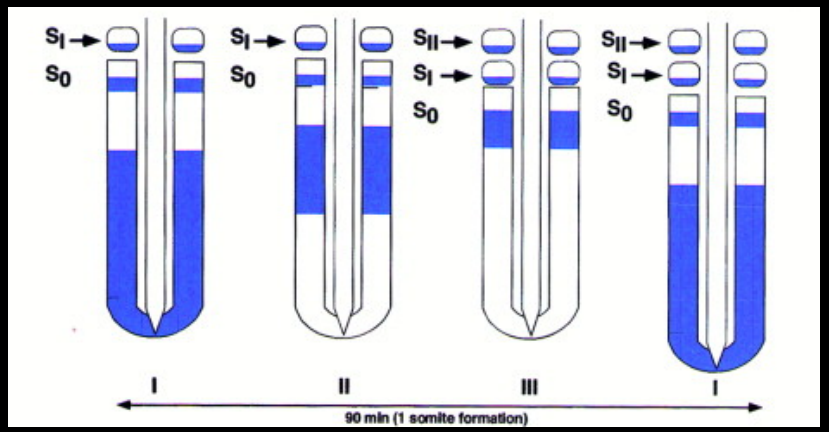


sequential is the more prevalent mechanism

Vertebrates: clock and wavefront mechanism

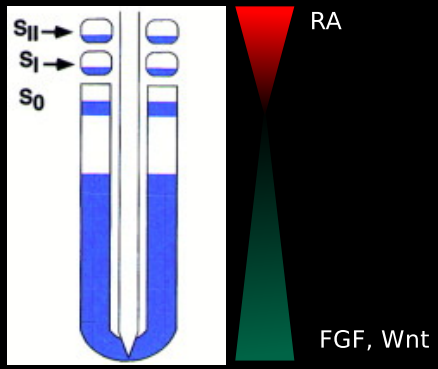
Clock





Palmeirim *et al.*, 1997

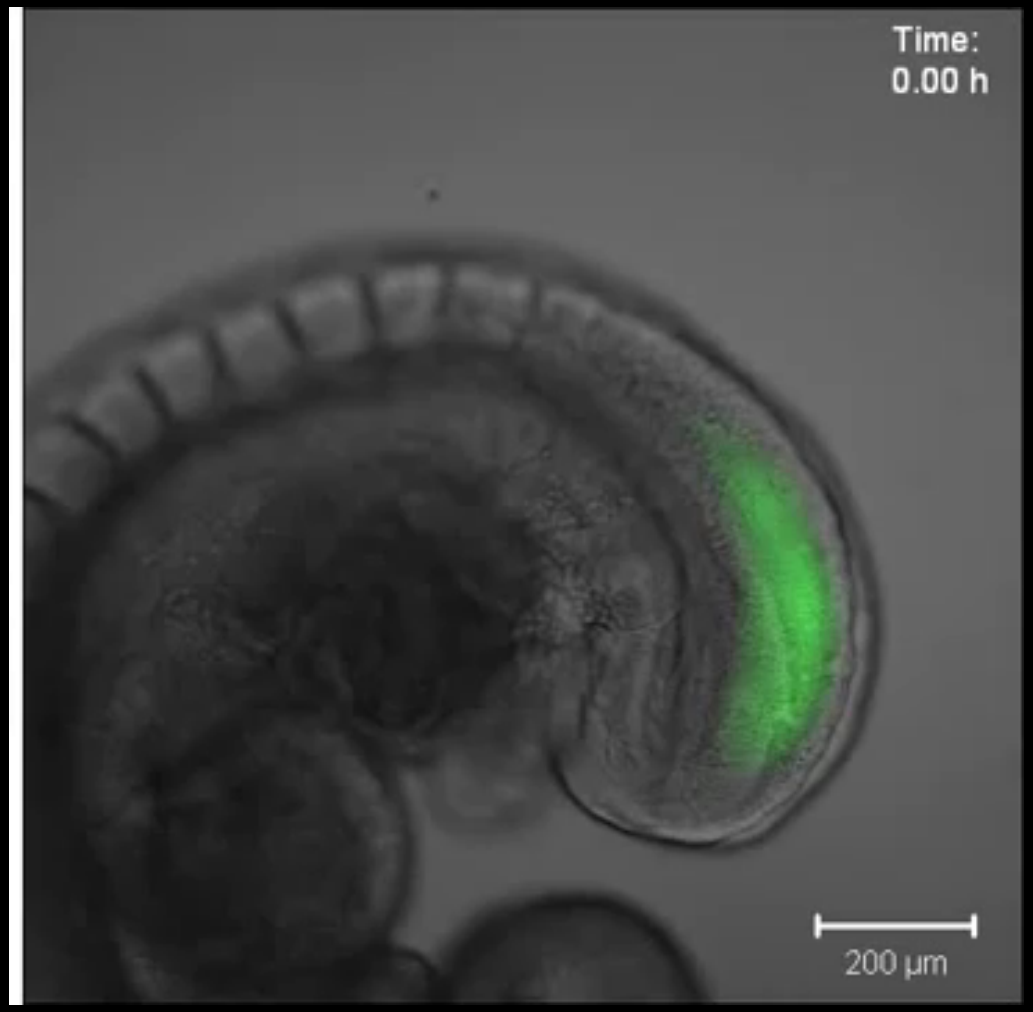
Wavefront



clock: gene expression oscillations

wavefront: morphogen gradient due to local production and global decay

Resulting GRN dynamics

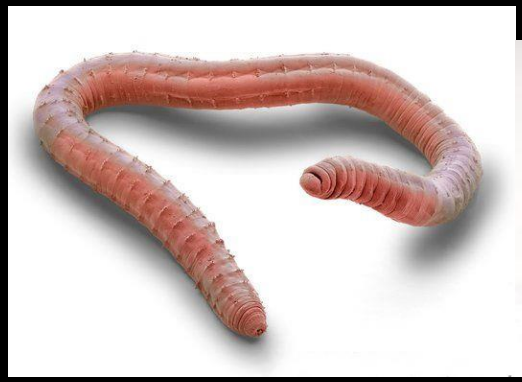


Segment development in insects

Choe et al., 2006

Evidence for a clock, nature of wavefront is unclear

What do we want to know?

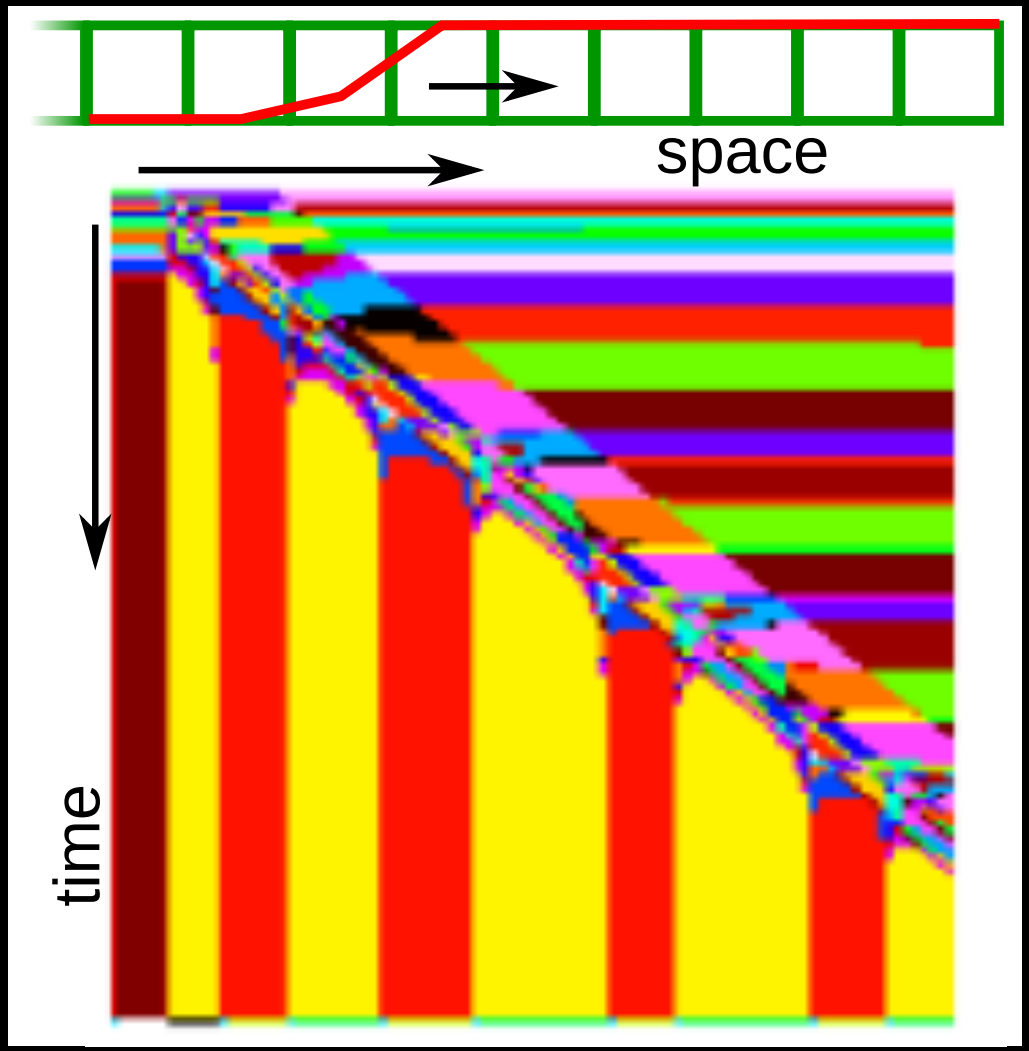


Why the clock-and-wavefront mechanism?

Can we understand the differences between vertebrates and insects?

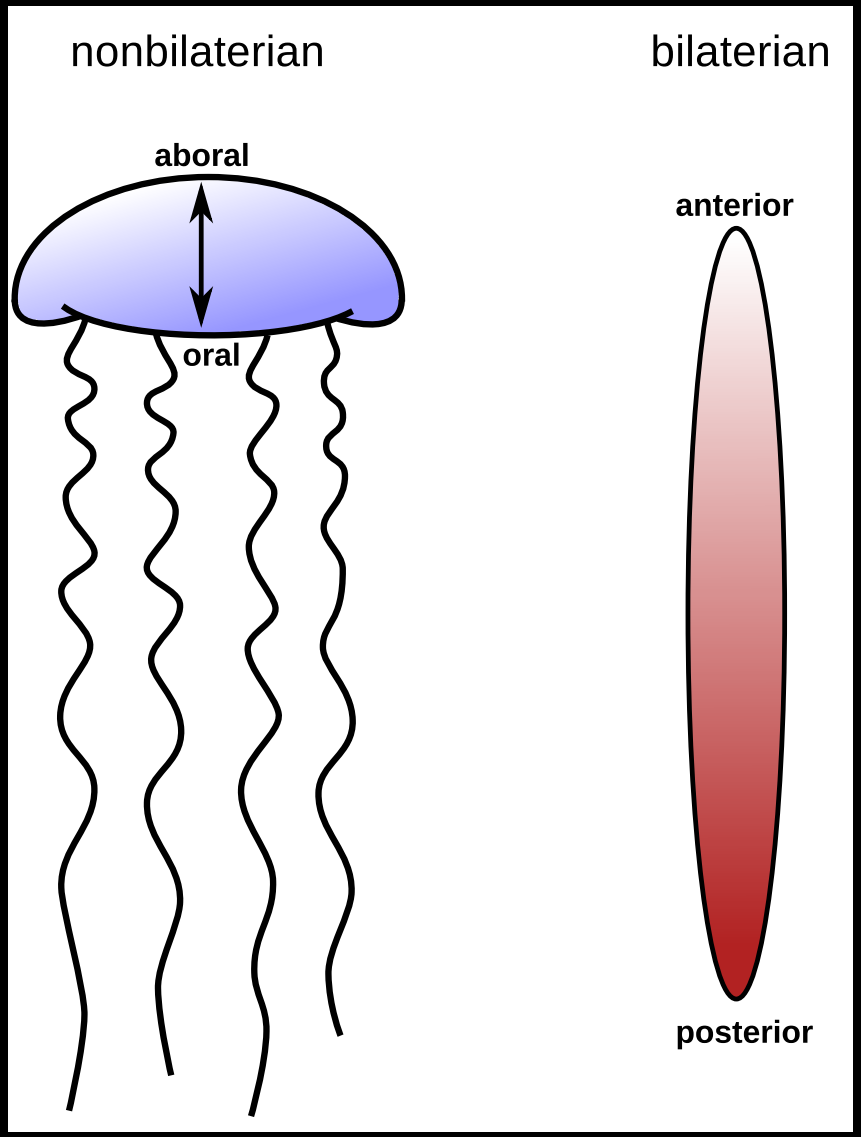
evolutionary origins of segmentation: what shaped the tree?

The likelihood of evolving sequential segmentation

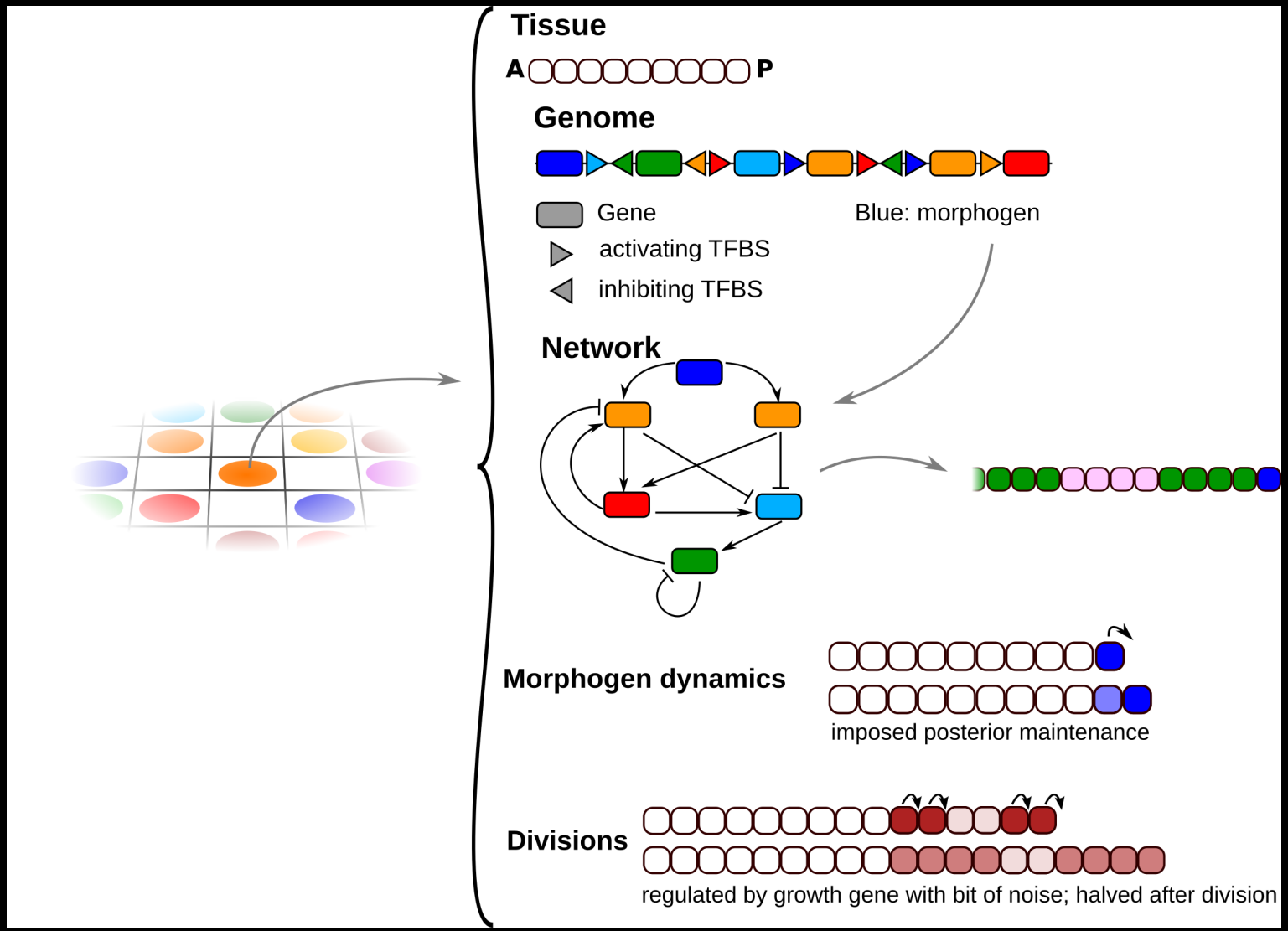


adapted from Ten Tusscher and Hogeweg, 2011

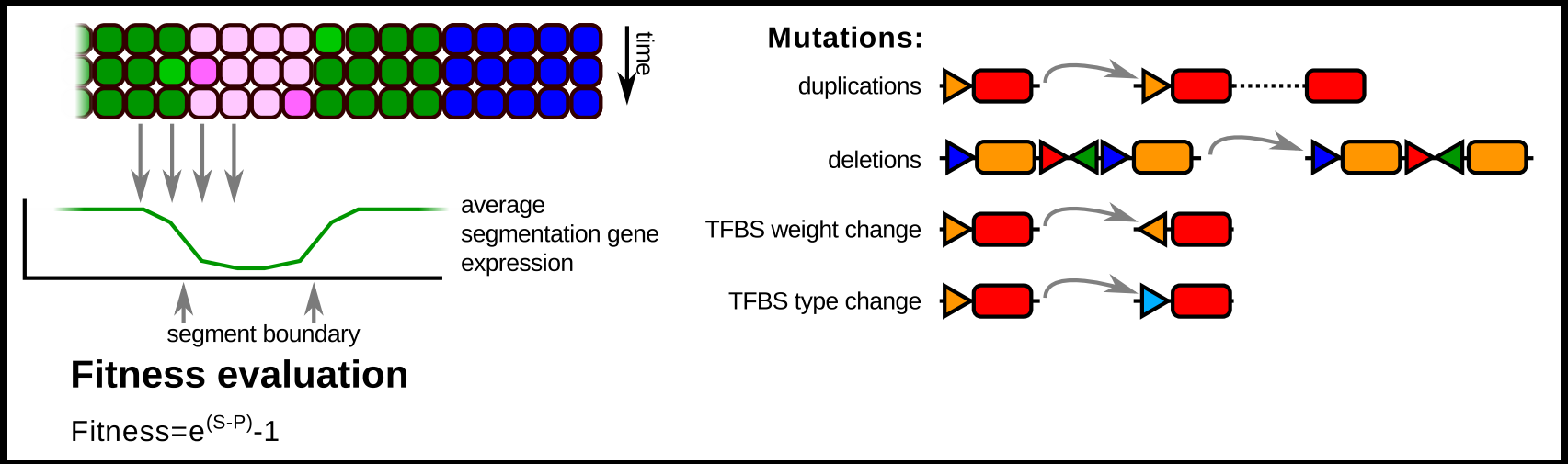
The likelihood of evolving sequential segmentation



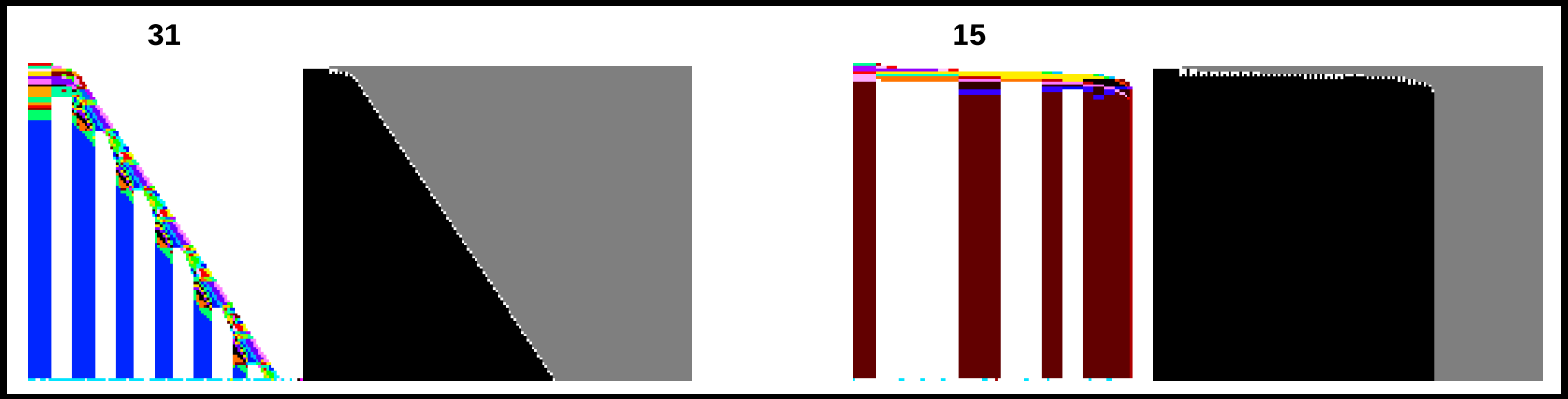
Model of evolving and developing individuals



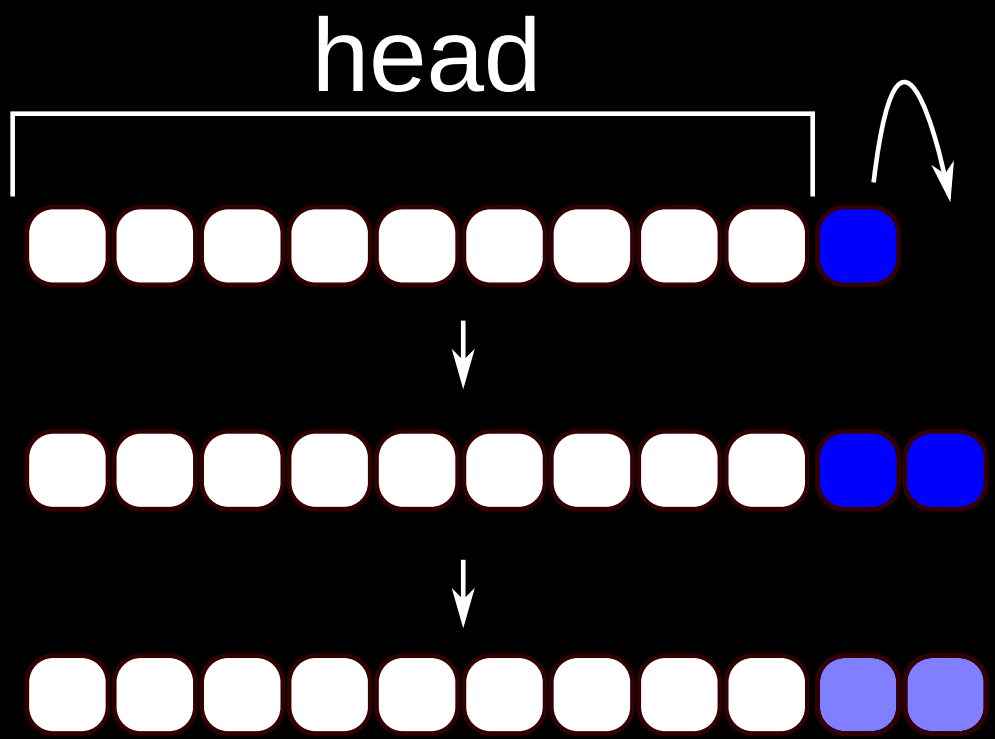
Selection and mutation



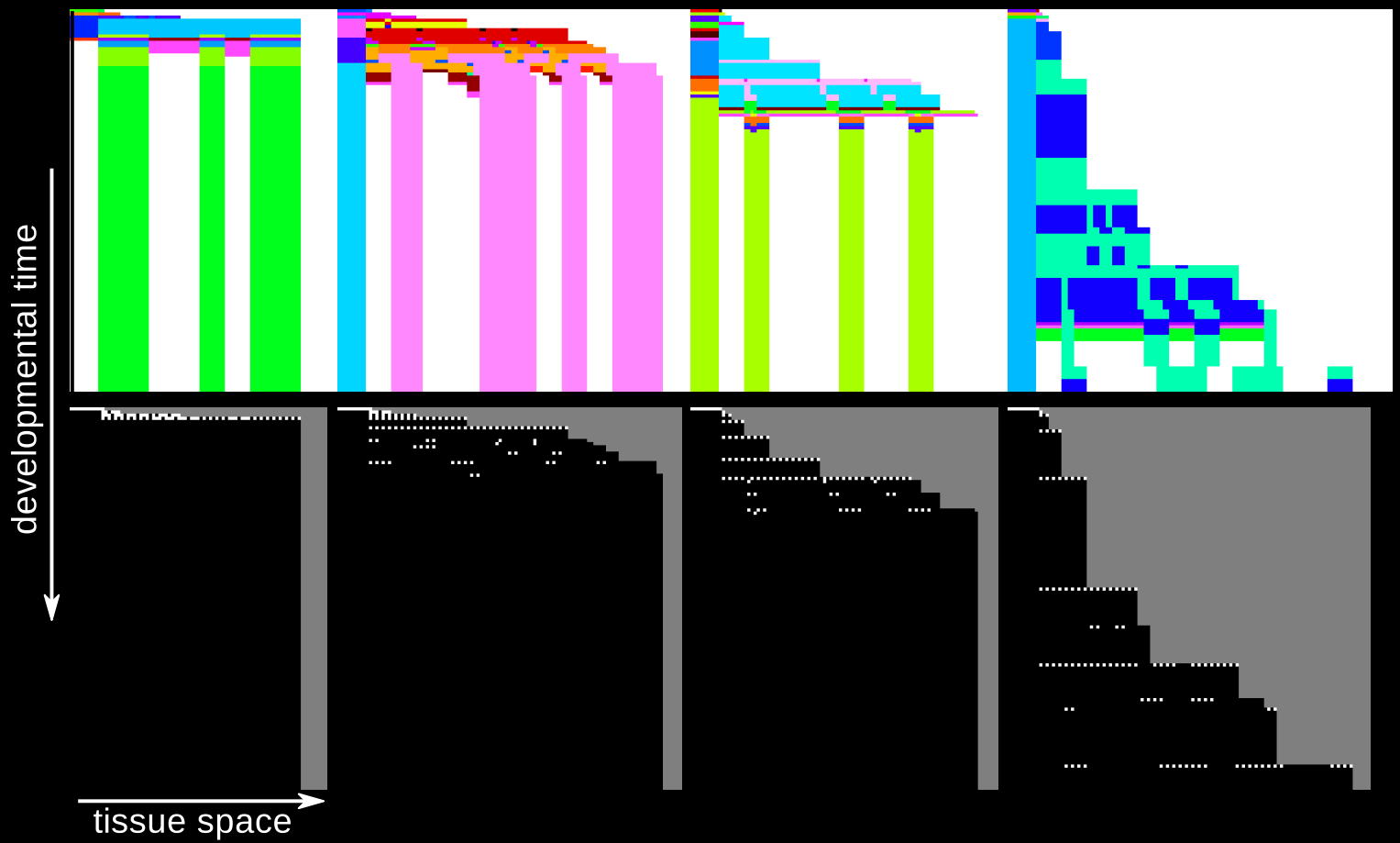
Two main outcomes



Can evolution “invent” a morphogen gradient?

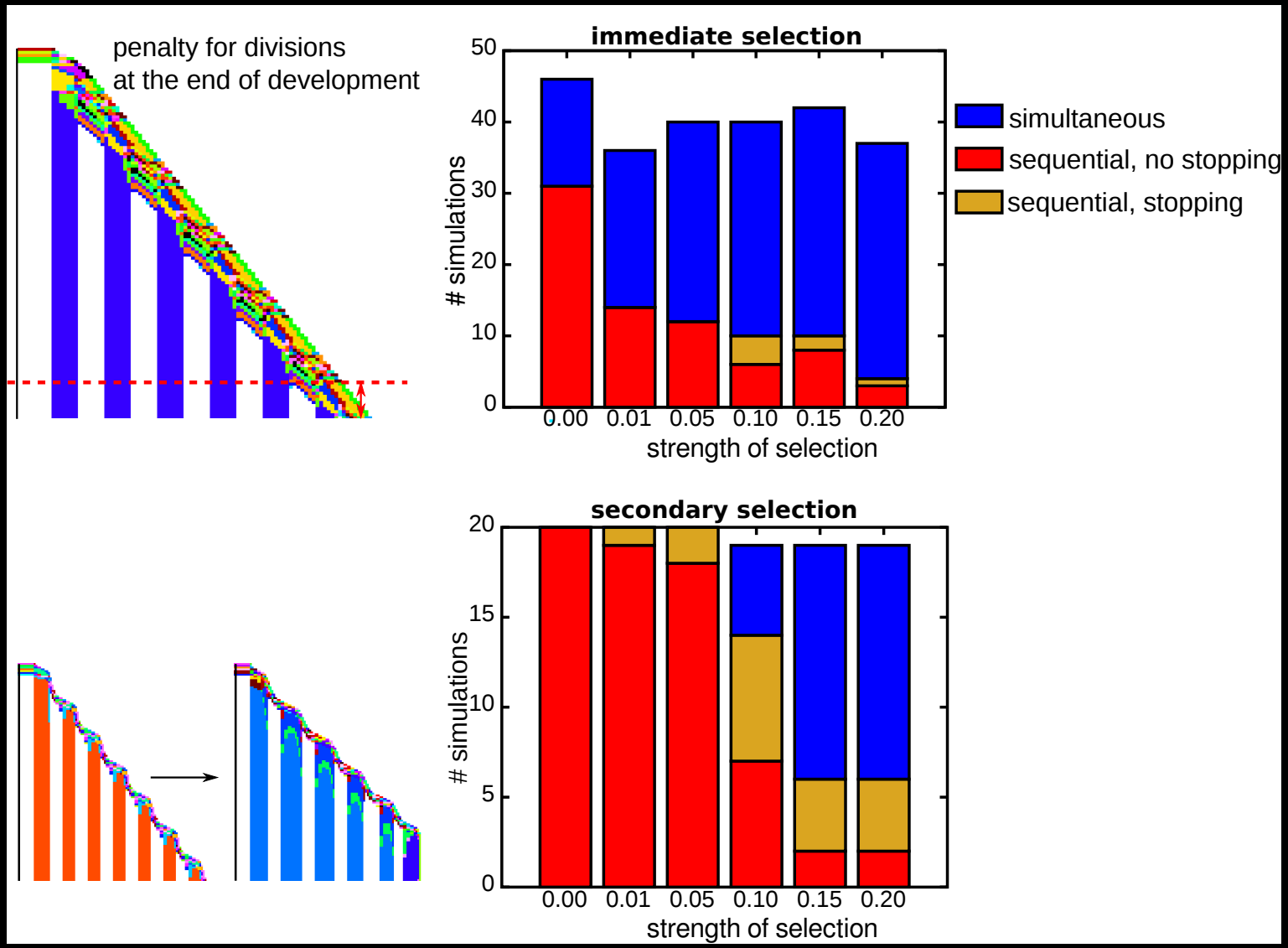


Prior presence of a morphogen gradient is essential



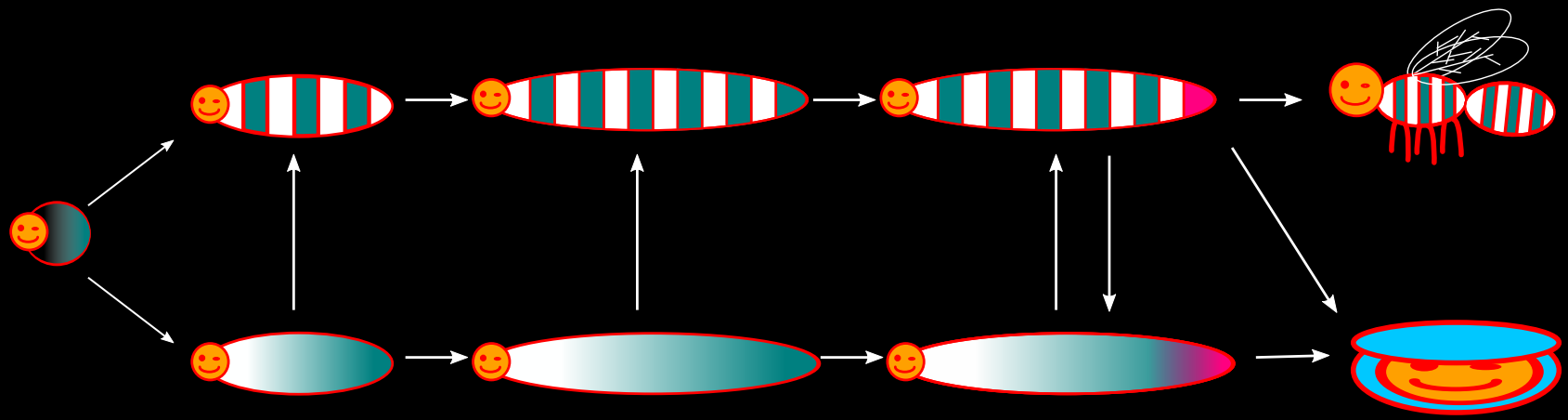
Mechanism uses division noise to steer different fates - very nonrobust.

Selection for stopping growth should come later

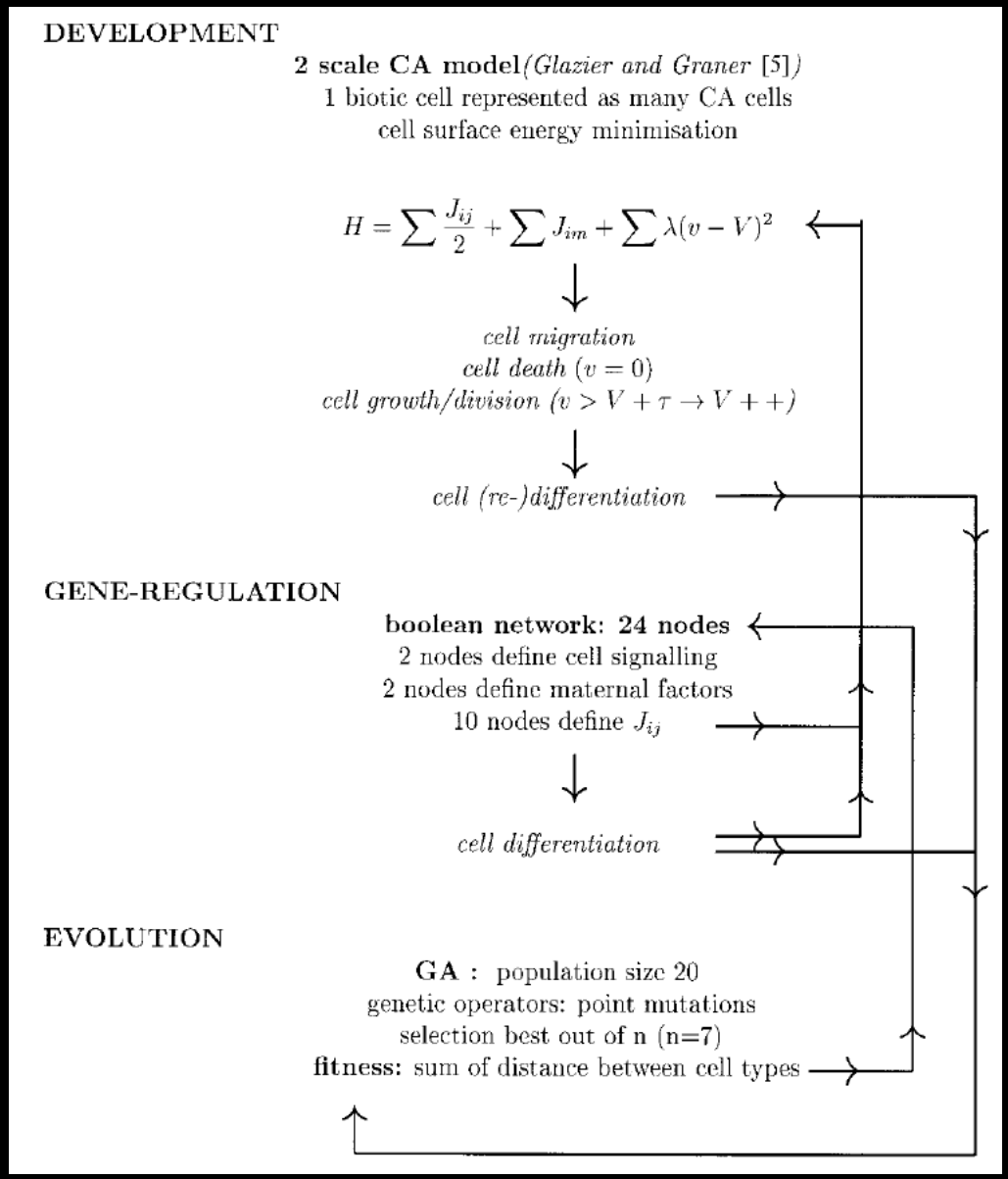


Conclusions

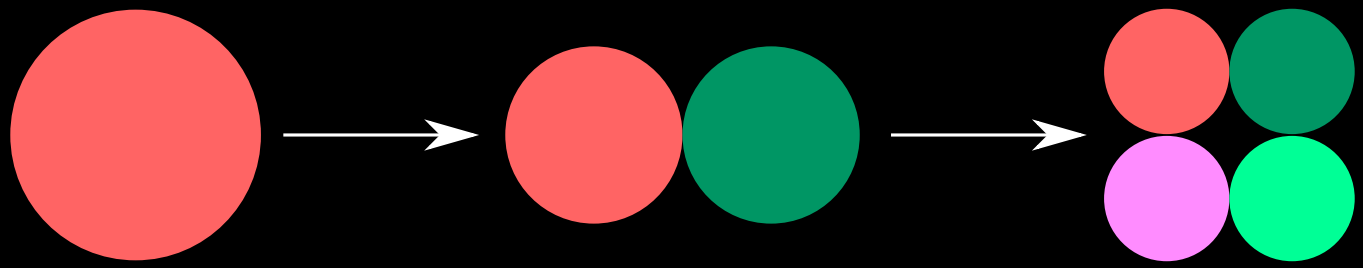
Posterior morphogen: posterior growth & sequential segmentation
Determinate growth only after evolution of A-P growth



Studying the evolution of side effects



First few cleavages are programmed



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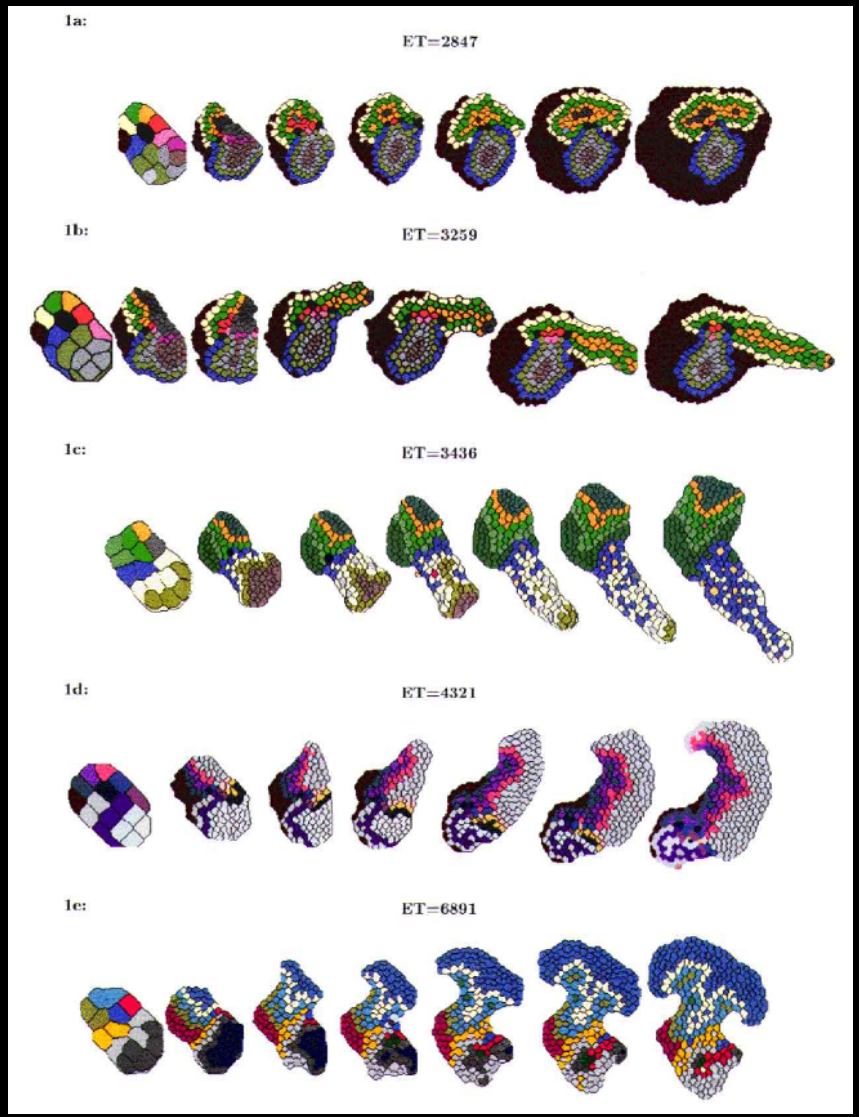

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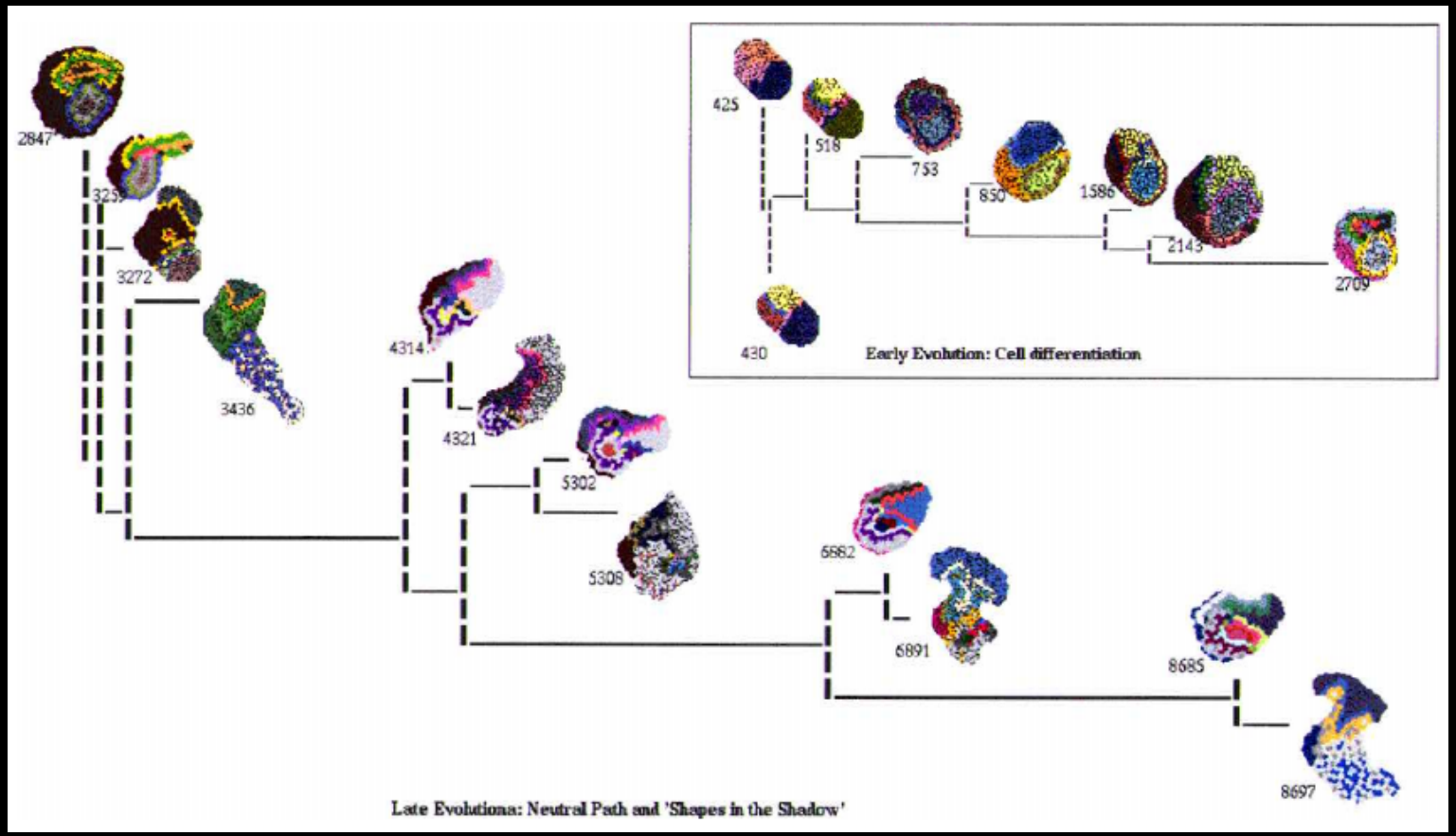
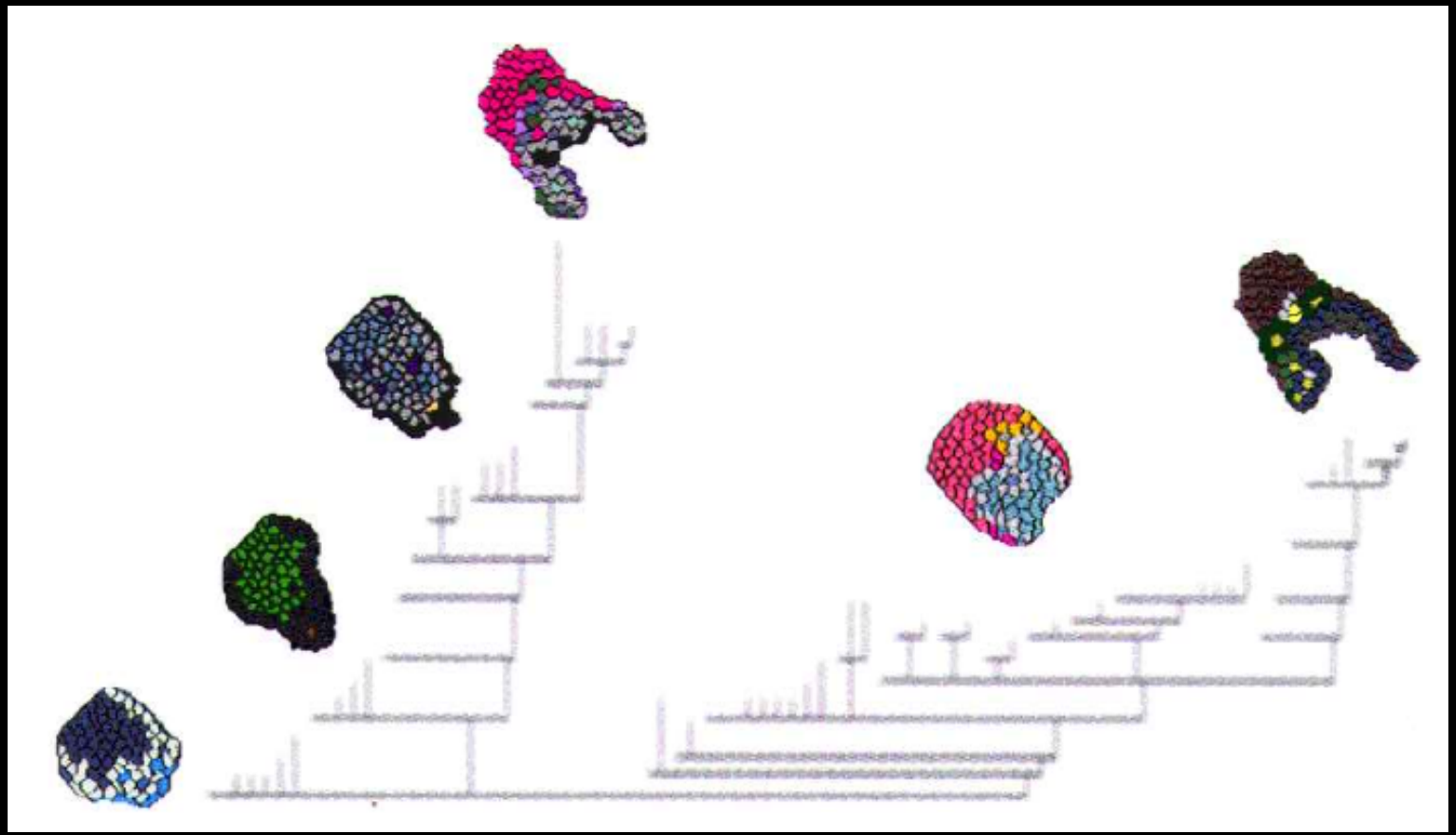


Studying the evolution of side effects



Models at different levels